A G E N D A
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
Salt Lake City, UT
Saturday, April 23, 2022, 12:15 pm - 2:00 pm

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Statistician:	**Stella Chen, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0703; E-mail: yuchen@mcw.edu**

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1. **Introduction**
   a. Minutes and Overview Plan from February 2021 meeting (Attachment 1)

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

3. **Presentations, published or submitted papers**

   a. **LY18-03** Herrera AF, Ahn KW, Litovich C, Chen Y, Assal A, Bashir Q, Bayer R-L, Coleman M, DeFilipp Z, Farhadfar N, Greenwood M, Hahn T, Horwitz M, Jacobson C, Jaglowski S, Lachance S, Langston A, Mattar B, Maziarz RT, McGuirk J, Mian MAH, Nathan S, Phillips A, Rakszawski K, Sengeloev H, Shenoy S, Stuart R, Sauter CS, Kharfan-Dabaja MA, Hamadani M. Autologous and allogeneic hematopoietic cell transplantation for diffuse large B-cell lymphoma-type Richter syndrome. ***Blood Advances. 2021 Sep 28; 5(18):3528-3539. doi:10.1182/bloodadvances.2021004865. Epub 2021 Sep 8. PMC8945575.***

   b. **LY19-02** Scordo M, Wang TP, Ahn KW, Chen Y, Ahmed S, Awan FT, Beitinjaneh A, Chen A, Chow VA, Dholaria B, Epperla N, Farooq U, Ghosh N, Grover N, Hamad N, Hildebrandt GC, Holmberg L, Hong S, Inwards DJ, Jimenez-Jimenez A, Karmali R, Kenkre VP, Khimani F, Klyuchnikov E, Krem MM, Munshi PN, Nieto Y, Prestidge T, Ramakrishnan Geethakumari P, Rezvani AR, Riedell PA, Seo S, Shah NN, Solh M, Yared JA, Kharfan-Dabaja MA, Herrera A, Hamadani M, Sauter CS. Outcomes associated with thiotepa-based conditioning in patients with primary central nervous system lymphoma after autologous hematopoietic cell transplant. ***JAMA Oncology. 2021 Jul 1; 7(7):993-1003. doi:10.1001/jamaoncol.2021.1074. Epub 2021 May 6. PMC8283558***. ***Oral presentation, ASH 2020.***

c. **LY17-01b** Shah NN, Ahn KW, Litovich C, Sureda A, Kharfan-Dabaja MA, Awan FT, Ganguly S, Gergis U, Inwards D, Karmali R, Lazaryan A, Lekakis L, Munshi P, Nathan S, Saad AA, Solh M, Steinberg A, Vij R, Wood WA, Fenske TS, Smith S, Hamadani M. Correction: Allogeneic transplantation in elderly patients ?65 years with non-Hodgkin lymphoma: A time-trend analysis. ***Blood Cancer Journal. 2021 Apr 29; 11(4):82. doi:10.1038/s41408-021-00472-w. Epub 2021 Apr 29. PMC8085088.***

d. **LY18-02a** Riedell PA, Hamadani M, Ahn KW, Litovich C, Murthy GSG, Locke FL, Brunstein CG, Merryman RW, Stiff PJ, Pawarode A, Nishihori T, Kharfan-Dabaja MA, Herrera AF, Sauter CS, Smith SM. Outcomes and utilization trends of front-line autologous hematopoietic cell transplantation for mantle cell lymphoma. ***Transplantation and Cellular Therapy. 2021 Nov 1; 27(11):911.e1-911.e7. doi:10.1016/j.jtct.2021.08.014. Epub 2021 Aug 24. PMC8556305.***

e. **LY18-02b** Riedell PA, Hamadani M, Ahn KW, Litovich C, Brunstein CG, Cashen AF, Cohen JB, Epperla N, Hill BT, Im A, Inwards DJ, Lister J, McCarty JM, Ravi Kiran Pingali S, Shadman M, Shaughnessy P, Solh M, Stiff PJ, Vose JM, Kharfan-Dabaja MA, Herrera AF, Sauter CS, Smith SM. Effect of time to relapse on overall survival in patients with mantle cell lymphoma following autologous haematopoietic cell transplantation. ***British Journal of Haematology. 2021 Dec 1; 195(5):757-763. doi:10.1111/bjh.17865. Epub 2021 Sep 28. PMC8627449.***

f. **LY20-01** Shadman M, Pasquini M, Ahn KW, Chen Y, Turtle CJ, Hematti P, Cohen JB, Khimani F, Ganguly S, Merryman RW, Yared JA, Locke FL, Ahmed N, Munshi PN, Beitinjaneh A, Reagan P, Herrera AF, Sauter CS, Kharfan-Dabaja MA, Hamadani M. Autologous transplant vs chimeric antigen receptor T-cell therapy for relapsed DLBCL in partial remission. ***Blood. 2022 Mar 3; 139(9):1330-1339. doi:10.1182/blood.2021013289. Epub 2021 Sep 27. PMC8900276.***

g. **LY19-01a** Hamadani M, Ngoya M, Sureda A, Bashir Q, Litovich CA, Finel H, Chen Y, Boumendil A, Zain J, Castagna L, Cashen AF, Blaise D, Shadman M, Pastano R, Khimani F, Arat M, Dietrich S, Schmitz N, Glass B, Kharfan-Dabaja MA, Corradini P, Sauter CS, Montoto S, Kwon M, Herrera AF, Dreger P. Outcome of allogeneic transplantation for mature T-cell lymphomas: impact of donor source and disease characteristics. ***Blood Advances. 2022 Feb 8; 6(3):920-930. doi:10.1182/bloodadvances.2021005899. Epub 2021 Dec 3. PMC8945300.***

h. **LY18-01d** Mei M, Hamadani M, Ahn KW, Chen Y, Kharfan-Dabaja MA, Sauter C, Herrera AF. Autologous hematopoietic cell transplantation in diffuse large B-cell limphoma after 3 or more lines of prior therapy: evidence of durable benefit. ***Haematologica. doi:10.3324/haematol.2021.279999. Epub 2022 Feb 3.***

i. **LY19-01b** Savani M, Ahn KW, Chen Y, Ahmed S, Cashen AF, Shadman M, Modi D, Khimani F, Cutler CS, Zain J, Brammer JE, Rezvani AR, Fenske TS, Sauter CS, Kharfan-Dabaja MA, Herrera AF, Hamadani M. Impact of conditioning regimen intensity on the outcomes of peripheral T-cell lymphoma, anaplastic large cell lymphoma and angioimmunoblastic T-cell lymphoma patients undergoing allogeneic transplant. ***British Journal of Haematology. doi:10.1111/bjh.18052. Epub 2022 Feb 2.***

j. **LY18-01e** Outcomes of autologous hematopoietic cell transplantation in elderly patients with diffuse large b cell lymphoma. (Pashna N Munshi) ***Submitted***

4. Studies in progress (Attachment 3)

a. **LY20-02** Outcomes of Allogeneic HCT in patients with Hodgkin Lymphoma in the era of Checkpoint Inhibitors: A joint CIBMTR and EBMT analysis. (Miguel-Angel Perales/Ana Maria Sureda) **Analysis**

b. **LY19-01c** Outcomes of Allogeneic Hematopoietic Cell Transplantation (alloHCT) in Anaplastic Large Cell Lymphoma (ALCL). (Mehdi Hamadani) **Manuscript preparation**

5. Future/proposed studies

a. **PROP 2109-07** Outcomes with autologous hematopoietic stem cell transplant in peripheral T-cell lymphoma (Aasems Jacob; Chaitanya Iragavarapu) (Attachment 4)
b. **PROP 2109-08** Bendamustine, etoposide, cytarabine, melphalan (BeEAM) vs. carmustine, etoposide, cytarabine, melphalan (BEAM) in relapsed B-cell lymphoma (Matthew Mei; Alex Herrera) (Attachment 5)
c. **PROP 2110-11** Chimeric Antigen Receptor T-cell Therapy versus Autologous Hemopoietic Cell Transplantation for Relapsed Myc-Rearranged DLBCL in Partial or Complete Remission (Joanna Zurko; Mehdi Hamadani) (Attachment 6)
d. **PROP 2110-131** Autologous Hematopoietic Stem Cell Transplantation for Intravascular Large B-cell Lymphoma (IVLBCL): a CIBMTR registry analysis (Praveen Ramakrishnan Geethakumari; Farrukh T. Awan) (Attachment 7)
e. **PROP 2110-190** Impact of pre-leukapheresis bendamustine-containing therapies on outcomes of CD19 CAR T-cell therapy for large B-cell lymphoma (Jordan Gauthier) (Attachment 8)
f. **PROP 2110-223** Risk of therapy-related myeloid neoplasm (t-MN) following autologous hematopoietic cell transplantation (auto-HCT) for relapsed and refractory diffuse large B-cell lymphoma (DLBCL): A comparison of platinum-containing salvage regimens (Mariam Nawas; Michael Scordo) (Attachment 9)
g. **PROP 2110-16/ 2110-83/2110-117/2110-57** Impact of Prior Therapies on Outcomes in Relapsed/Refractory Mantle Cell Lymphoma Patients treated with Brexucabtagene autoleucel. (Mazyar Shadman; Mehdi Hamadani; Nausheen Ahmed; Swetha Kambhampati; Alex Herrera; Natalie Grover) (Attachment 10)
h. **PROP 2110-98/ 2110-181/2110-22/2110-85/2110-116** CART Outcomes in rare subtypes of aggressive B-cell lym (Priyanka Pophali; Shwetha Kambhampati; Joshua Fein; Narendranath Epperla; Mazyar Shadman; Jordan Gauthier; Kalyan Nadiminti; Roni Shouval; Mehdi Hamadani; Alex Herrera) (Attachment 11)
i. **PROP 2109-26/2110-94/2110-275** Impact of CD19 directed CAR T-cell therapy on outcomes for primary and secondary central nervous system B-cell lymphomas (Narendranath Epperla; Santiago Mercadal; Hamza Hashmi; Catherine Joy Lee; Mehdi Hamadani; Sairah Ahmed) (Attachment 12)
j. **PROP 2110-82/2110-90** Outcome of patients with large cell lymphoma receiving ASCT vs. CAR-T therapy while in complete remission. (Mehdi Hamadani; Mazyar Shadman; Antonio Jimenez; Trent Wang) (Attachment 13)

Proposed studies; not accepted for consideration at this time

a. **PROP 2109-10** Characteristics and Outcomes of Adolescents and Young Adults with Relapsed/Refractory Non-Hodgkin Lymphoma Undergoing First Autologous Hematopoietic Stem Cell Transplant.
b. **PROP 2109-21** Outcomes of Autologous vs Allogeneic Stem Transplant after first line or second line therapy for patients with Double Hit and Triple Hit DLBCL.
c. **PROP 2110-15** Impact of early versus late relapse pre Chimeric Antigen Receptor (CAR) T-Cell therapy on clinical outcomes of CAR-T cell therapy for Diffuse Large B-Cell Lymphoma (DLBCL)
d. **PROP 2110-17** Effect of Time to Relapse on Overall Survival in Diffuse large B cell lymphoma (DLBCL) patients following CD19-Chimeric antigen receptor T cell (CART) therapy.

e. **PROP 2110-127** Outcomes of Salvage Autologous Transplant in Double Hit DLBCL.
f. **PROP 2110-133** Outcomes of relapsed/refractory post-transplant lymphoproliferative disorders-diffuse large B cell lymphoma (PTLD-DLBCL) treated with hematopoietic stem cell transplant (HSCT) or chimeric antigen T cell (CART) therapy.
g. **PROP 2110-134** Search of optimal conditioning regimen for autologous stem cell transplant (ASCT) for treatment of relapsed and refractory lymphoma – A comparison of BEAM vs. BUCYVP16 using CIBMTR database.
h. **PROP 2110-136** Outcomes of relapsed/refractory post-transplant lymphoproliferative disorders-diffuse large B cell lymphoma (PTLD-DLBCL) treated with hematopoietic stem cell transplant (HSCT) or chimeric antigen T cell (CART) therapy.
i. **PROP 2110-144** Outcomes of Autologous Stem Cell Transplantation for Early Versus Late Relapsing Nodular Lymphocyte-Predominant Hodgkin Lymphoma.
j. **PROP 2110-152** Outcomes of HIV+ Lymphoma treated with Chimeric Antigen Receptor T-Cell Therapy.
k. **PROP 2110-156** Evaluating outcomes of Hematopoietic Cell Transplantation in Hepatosplenic T Cell Lymphoma.
l. **PROP 2110-159** Trend in survival in Lymphoma (NHL/HL) Patients post-autologous SCT.
m. **PROP 2110-161** Efficacy and Safety of CAR T-cells in patients with Relapsed/Refractory Post-Transplant Lymphoproliferative Disease.
n. **PROP 2110-166** Outcome of allogeneic hematopoietic stem cell transplant for refractory cutaneous T-cell lymphoma.
o. **PROP 2110-171** Outcomes of CAR T-cell therapy for Diffuse Large B cell Lymphoma patients with HIV or viral hepatitis.
p. **PROP 2110-172** Hematopoietic Stem Cell Transplantation for Mature T- and NK-cell Malignancies in Children, Adolescents, and Young Adults.
q. **PROP 2110-187** Autologous stem cell transplantation for diffuse large B cell lymphoma: impact of CD19 CAR T-cell therapy approvals on patient characteristics and outcomes.
r. **PROP 2110-197** Real world practice pattern and clinical outcomes of subsequent therapy after CAR-T treatment in patients with lymphoma.
s. **PROP 2110-209** Autologous Hematopoietic Stem Cell Transplantation for Intravascular Large B-Cell Lymphoma (IVLBCL): A CIBMTR Registry Analysis.
t. **PROP 2110-219** Outcomes of Large B-cell lymphoma Progressing following CAR T-cell therapy.
u. **PROP 2110-225** Clinical outcomes of chimeric antigen receptor T cell therapy after allogeneic stem cell transplant in patients with relapsed/refractory aggressive B-cell lymphoma.
v. **PROP 2110-232** Clinical outcomes of allogeneic and autologous stem cell transplant after anti-CD19 chimeric antigen receptor T cell therapy in patients with relapsed/refractory aggressive B-cell lymphoma.
w. **PROP 2110-264** Clinical Impact of first-line therapy after CAR T cell failure.
x. **PROP 2110-269** Does access to CAR improves outcomes in DLBCL? The Phase 3 trial that will not be done.
y. **PROP 2110-270** Impact of Tumor Biology on Outcomes in Chimeric Antigen Receptor T-cell Therapies and Autologous Stem Cell Transplant in Diffuse Large B-cell Lymphoma.
z. **PROP 2110-277** Analysis of the outcomes of autologous stem cell transplant in peripheral T-cell lymphomas treated with brentuximab vedotin.
aa. **PROP 2110-286** Pre CAR-T Splenic and Extra nodal Disease to predict Relapse pattern post-CAR-T Therapy for Relapsed/Refractory Lymphoma.
bb. **PROP 2110-290** CAR-T versus allogeneic transplant in Mantle Cell Lymphoma: A Real world CIBMTR analysis.

cc. **PROP 2110-291** Comparison between outcomes of CAR-T cell therapy versus allo-HCT in R/R Mantle cell lymphoma.
dd. **PROP 2110-296** Efficacy and Safety of Allogeneic transplant after CAR T-cell therapy in patients with Relapsed/Refractory Diffuse Large B-cell Lymphoma.
ee. **PROP 2110-36** Outcomes of autologous and allogeneic hematopoietic cell transplantation for secondary central nervous system lymphoma.
ff. **PROP 2110-46** Outcomes of alloHCT for patients with lymphoid B cell malignancies who received treatment with bispecific antibodies.
gg. **PROP 2110-47** Autologous versus Allogeneic Stem Cell Transplantation for B cell lymphomas patients who failed anti-CD19 CART as first or second-line of therapy.
hh. **PROP 2110-56** Impact of Bridging Therapy on Outcomes of Diffuse Large B-cell Lymphoma Patients Undergoing Chimeric Antigen Receptor T-cell Therapy.
ii. **PROP 2110-73** Outcomes of Allogeneic Hematopoietic Stem Cell Transplantation in Relapsed/Refractory Aggressive B-Cell Lymphoma with Central Nervous System Involvement: a CIBMTR Analysis.
jj. **PROP 2110-96** Effect of time to relapse on survival in classical Hodgkin lymphoma patients undergoing autologous hematopoietic cell transplantation.
kk. **PROP 2110-302** Toxicities and outcomes after Chimeric Antigen Receptor (CAR) T-Cell therapy in Mantle cell Lymphoma (MCL).
ll. **PROP 2110-316** Allo-HCT versus CAR T therapy in relapsed mantle cell lymphoma.
mm. **PROP 2110-327** Outcomes of autologous HCT for diffuse large B-cell lymphoma by cell of origin and disease status.

7. **Other Business**

MINUTES
CIBMTR WORKING COMMITTEE SESSION
Thursday, February 11, 2021, 1:00 - 4:00 pm
Co-Chair: Bronwen Shaw, MD, PhD; CIBMTR Statistical Center, Milwaukee, WI; E-mail: beshaw@mcw.edu
Co-Chair: John Wingard, MD; University of Florida, Gainesville, FL; E-mail: wingajr@ufl.edu

INTRODUCTION:

Dr. Wingard opened the virtual meeting at 1:00 pm by welcoming the working committee members and the presenters. He discussed the proposal selection and voting process. Though the pandemic amended the process for proposal selection, 368 working committee proposals were submitted and evaluated altogether by CIBMTR Working Committee Chairs and Scientific Directors. About 61% were screened out, 30% had less-relative scientific merit, and 3% were combined with overlapping proposals with relevant nature. 21 proposals (about 6%), were considered for advancing of further pro-development. The proposals were pre-recorded 5-minutes presentations of the 15 semi-finalists, which were presented by the principal investigators. Each presentation was followed by a 5-minute question and answer session, in which audience was invited to submit questions via live chat. For those not able to attend the live session, a link was posted with the session recording and voting was closed on Monday, February 15, 2021. Audience was also instructed on where to locate the scoring and voting links for the presentations. It was mentioned that over 1,000 Working Committee members voted on the first screening of these proposals. Dr. Shaw led the second part of the meeting starting with presentation #9.

GENERAL REMINDERS:

The following reminders were mentioned and posted via the chat option:

a. Thank you for participating in the CIBMTR Working Committee Session! Please cast your score here: https://mcwisc.co1.qualtrics.com/jfe/form/SV_7QwO1ZvzfPZV1NY to vote on the proposals that were presented during the session.
b. Several presenters provided their email addresses for any future communication.

PRESENTATIONS:

1. **Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis.** This proposal was presented by Dr. Ana Alarcon Tomas. The primary objective of this proposal is to describe the incidence rate, risk factors, characteristics, and outcomes of subsequent neoplasms in patients receiving post-transplant cyclophosphamide (PTCy) and compare it with calcineurin inhibitors-based graft-versus-host disease prophylaxis and the general population. The CIBMTR identified 64,935 patients ≥18 years of age who underwent a first allogeneic for a malignant disease between 2008-2017. 5,771 (9%) of these patients developed a subsequent neoplasm. Currently, there are no published studies on the incidence of subsequent neoplasms in patients who received post-transplant cyclophosphamide. The following questions were answered during the Q&A:
    a. How are we going to prove that these secondary neoplasms are related to post-transplant cyclophosphamide or cyclophosphamide in conditioning and not due to "by chance" itself- as in general population? This is a case-controlled study. For example, for each patient received with a post-transplant cyclophosphamide will be matched with at least three patients who didn't receive post-transplant cyclophosphamide. Characteristics including primary disease, HLA complexity, survival, follow up time etc. would be used for matching and reviewing survival will also allow us to see that this is because of PTCy and not by coincidence.

b. What is the median follow up time from transplant and subsequent malignancy in post-transplant cyclophosphamide group? I assume it is much shorter than other cohort? Information is not available for each median follow up time cohort. What is available is the median follow up for all patients and some numbers related to the type of diseases for each group. Dr. Rachel Phelan included in the chat that the median follow-up for the PT-Cy group is 38.2 months, and for the proposed control population is 60.3 months.
c. How is this in comparison with matched unrelated donor and cord transplants? Cord transplants will be excluded from the analysis because we don't think we can match those patients.
d. Do we have adequate follow up to answer this important question? We have follow-up for mantle hematological diseases but less time for solid tumors. However, when we saw the numbers that we have (around 5,000 - 5,700) subsequent neoplasms, the majority of cases occurred after the 1st - 5th year of post- transplant and have a 5-year median follow up. We think we have enough numbers to address this question now and we should not wait because it hasn't been published before. This is a noble study and if we wait for a longer median follow up, we might lose that opportunity to have it published first.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix A.

2. **Outcomes of chimeric antigen receptor-T cell therapy for patients with antecedent chronic lymphocytic leukemia (Richter's Syndrome)**. This proposal was presented by Dr. Farrukh Awan. The objective of this proposal is to assess outcomes in adult patients with chronic lymphocytic leukemia undergoing transformation to diffuse large B-cell lymphoma (Richter's Syndrome) and undergoing CAR-T therapy. The CIBMTR identified 36 patients underwent CAR-T for Richter's Syndrome from 2015-2019. The following questions were answered during the Q&A:
   a. I know that in the Ohio State paper have many patients that used concurrent Bruton Tyrosine Kinase (BTK) inhibitors. Will you be able to collect data on concurrent BTK inhibitors for these patients? Yes, this information is available through the CIBMTR dataset.
   b. Are you looking at diffuse large B-cell lymphoma derived Richter's Syndrome or chronic lymphocytic leukemia derived Richter's Syndrome? Yes, but it is difficult to determine a clonality between related and unrelated Richter's syndrome. Any studies that show similarities versus dissimilarities in the clone would be very helpful but unfortunately, previous studies have shown that this has been consistently difficult.
   c. You mentioned the opportunity of comparing to other treatment groups. Can you talk about that a little more? We can compare to patients with de novo diffuse large B-cell lymphoma. There are multiple approved and ongoing studies within CIBMTR of diffuse large B-cell lymphoma patients, who do undergo CAR-T therapy and look at toxicity outcomes and infectious outcomes, for example. There are efforts in place to look at outcomes of transplantation for patients with Richter's Syndrome, which can improve the impact of this project and be a competitor to those other ongoing studies.
   d. How many pts do we have? 36 patients
   e. How do you plan to deal with the very low patient numbers (n=36) to make meaningful conclusion? I agree that it is a small number, but it is substantial. Despite the small numbers, if the right competitors are used, such as those mentioned previously, this study can still provide an impactful dataset.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix B.

3. **Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies**. This proposal was presented by Dr. Andrea Bauchat. The objectives of this proposal is to determine the impact of development of grade I-II acute graft versus host disease on relapse and leukemia-free survival, to assess the impact of development of grade III-IV acute graft versus host disease on relapse and leukemia-free survival, and to determine whether the impact of graft versus host disease on

relapse and leukemia-free survival is influenced by disease risk prior to HCT. The CIBMTR identified 1,345 children <18 years who received first HCT for acute lymphoblastic leukemia and acute myeloid leukemia receiving first allogeneic transplantation between 2008 - 2017. The following questions were answered during the Q&A:

a. What is the sample size of each sub-group: disease-risk index (DRI)-low, -intermediate, -high? Exact sample size not available but the high-risk group was less in comparison to others.
b. How will you factor in occurrence of chronic graft versus host disease in your analysis? Our main focus is on acute graft versus host disease because it will have more impact on our clinical practice. However, we will collect the data for the interactions of chronic graft versus host disease alone, and if the patient had a history of acute.
c. What is the biological basis for focusing this study on a pediatric population? The interest from our perspective is looking at the pediatric population compared to the adults. The literature on pediatric is severely lacking in comparison to adults and we need to expand on that for the patient population that we care for.
d. Are you going to separate acute myeloid leukemia and acute lymphoblastic leukemia numbers at DRI level? Yes, they are already divided from DRI protocol. Our acute lymphoblastic leukemia patients are about 1,300 and the acute myeloid leukemia are about 1,200.
e. Is the analysis going to be time dependent or landmark? Landmark
f. Do you have the date of this max acute graft versus host disease grade to take into account the time to event aspect of the effect? No
g. Do you have a plan to include/account for the various GVHD prophylaxis regimen "strengths?" We are taking into consideration of what GVHD prophylaxis regimen the patient uses. This data, which is already categorized, will show us the differences between trends.
h. What is the clinical benefit besides prognostic? This will help define a better foundation of which patients will benefit more from a little bit of graft versus host disease. If we can come up with a patient category that we see is beneficial to have exposure to a little bit of graft versus host disease, it can go forward with clinical trials and GVHD prophylaxis adjustment or manipulation to improve their Leukemia-free survival.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix C.

4. **Effect of HLA evolutionary divergence on survival and relapse following allogeneic hematopoietic cell transplant**. This proposal was presented by Dr. Christine Camacho-Bydume. The primary objective of this proposal is to determine if HLA evolutionary divergence (HED) of HLA class I alleles of HLA-A, -B, -C and HLA class II alleles of HLA-DR is associated with overall survival and relapse. The objective is to also evaluate association of HED with acute and chronic GVHD and treatment-related mortality (TRM). The CIBMTR identified pediatric and adult patients with acute myeloid leukemia, myelodysplastic syndromes, acute lymphoblastic leukemia, chronic myeloid leukemia, or lymphoma (non-Hodgkin or Hodgkin's lymphoma), who have received initial allogeneic 8/8 HLA-matched (HLA-A, -B, -C, -DR) transplant between 2008 - 2018. The following questions were answered during the Q&A:

   a. Could HLA diversity simply be a surrogate for race? How would you account for race in the study? Great question given there are particular HLA alleles that are more common in certain ethnic groups. We do think that evaluation of HED lows and highs within these different ethnicities can help to tease this out more, with potential to adjust for race more in this analysis. We think some of these differences in peptide binding grooves can help us to understand better the different peptides and how antigens are presented to T-cells.
   b. Extrapolating HLA data from solid tumors and checkpoint inhibitors and their antigen presentation is slightly challenging in context of allo donor T-cell interaction with antigen presented for bone marrow origin cancers. Yes, have to consider there could be some differences. Was a small previous study that

looked at this question, saw some signals there, larger population and different types of cancers, may be able to explore that more.

c. Leukemia (both lymphoblastic and myeloid) have low mutational burden as compared to melanoma and lung. Will the HED algorithm still work? Yes, we do expect to see differences in mutational burdens, and we do plan to look at the cohort at large to look at the disease subgroups to see more or less of this phenomenon in these groups. Do you have preliminary data in leukemias? There was a small study in Germany that looked at AML, to my knowledge only one that looked at leukemias. Mutational burden did see some differences, so we do expect it and also, besides the overall cohort, also plan to look at disease subgroups.
d. Given HED implications for infection surveillance, are you going to look at infectious sequelae differences? No, at the moment we have initially requested information in terms of tumor control, relapse, overall survival, graft versus host disease, and TRM. Not sure of availability of the other information but would be interesting to look at if available.
e. Would you please discuss the confounding effects of HLA mismatching for HLA-DRB3, 4, 5, DQ, and DP? Not known off the top of my head the percentages of mismatching differences in this cohort. For DR at least they will be matched, 8/8 matched, in terms of DP, don't have that info but if available it is something that can be looked at.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix D.

5. **Impact of IDH1 and IDH2 mutations on outcomes of acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation**. This proposal was presented by Dr. Evan C. Chen. The primary objective of this proposal is to identify differences in survival outcomes between mutIDH1/2 and wtIDH1/2 acute myeloid leukemia patients and to assess the prognostic significance of disease features in mutIDH1/2 and wtIDH1/2 acute myeloid leukemia patients. The CIBMTR identified patients ≥ 18 years old with a diagnosis of normal karyotype acute myeloid leukemia, receiving first allogeneic HCT during CR1 in 2013 - 2019. The following questions were answered during the Q&A:
   a. Is there any concern that patients with IDH1/2 mutated acute myeloid leukemia would have received more intensive conditioning / therapy than IDH1/2 wild-type? Yes, and it's important to look at how conditioning intensity can be an important covariant, which is a variable captured in CIBMTR.
   b. Will you have registry information on the type and duration of use of IDH inhibitors before/after HCT? It's currently not available with CIBMTR.
   c. IDH mutations are usually seen in older subjects. How will you a priori adjust for this known association? Age will certainly be a covariant in our multi-variant analysis.
   d. How reliable are the wild-type patients as some may just not be tested for IDH mutations? It is double checked. There is a datapoint in the forms that indicate whether or not testing has been done, versus if testing was done and IDH was found to be absent.
   e. Do you have information what the numbers will be like when you divide your patient groups with concomitant mutations such FLT3 or p53 that may have an impact on outcomes? Yes, the numbers are about 20-40 for co-mutated for ITD and NPM1 patients. p53 not provided.
   f. Is there data in CIBMTR forms that collect use of IDH inhibitors pre transplant? Will you be able to study their impact on the transplant? I'm not aware of this data point being available in the forms but it is something that we should follow up on.
   g. How do you analyze its (or ITS?) with multiple mutations? With regards to double-mutated patients, IDH1, and IDH2 patients, which are generally rarely reported, we would look at the CIBMTR forms to ensure accurate data entry. In regard to analyzing IDH with other co-mutations, we would include co-mutations as a co-variant in a multi-variant analysis, should the sample size permit.

h. What about other mutations in Wild type IDH? We focus on NPM1 and FLT3-ITD because they are prevalent in the cytogenetic risk population. We will look at the other mutations to see if they have any relevance at all.
i. Do the data forms reliably collect information on use of IDH inhibitors pretransplant? Data point is not available.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix E.

6. **Characteristics and outcomes of adolescent and young adults with multiple myeloma treated with autologous hematopoietic cell transplant**. This proposal was presented by Dr. Christin B. DeStefano. The primary objective of this proposal is to describe patient and disease related characteristics of adolescent and young adults (AYAs) with multiple myeloma treated with early high dose melphalan and AutoHCT and to characterize response to AutoHCT, survival outcomes, SPMs, and infections of AYA multiple myeloma patients and AutoHCT. The CIBMTR identified 1,142 AYA multiple myeloma patients who underwent autologous hematopoietic cell transplant) between 2008 -2018. The following questions were answered during the Q&A:
   a. What will differentiate this study from MM18-03 "To compare the outcomes in young patients with multiple myeloma at diagnosis undergoing upfront autologous hematopoietic stem cell transplant with older patients in the US: progression-free and overall survival"? There appears to be substantial population overlap. The Scientific Director clarified via the chat function that MM18-03 included the years 2013-2017 and excluded patients less than 40 years from the outcome analysis owing to small numbers.
   b. How do you plan to control for differences between your AYA group and older control group which would be attributable to age? In total, there are about 1,700 TED and CRF cases. We can adjust the critical variables of these cases, such as stage, treatment rendered, and cytogenetics, for example, to control for differences.
   c. Will results be stratified according to different induction regimens? Yes, we will adjust those critical variables amongst the CRF cases where this information is available.
   d. A cohort going back to 1995 seems too outdated. What was the N for a more recent group (since 2010)? There were 1,142 AYA cases between 2008-2018.
   e. This is a long cohort 1995-2019 with lots of changes in induction treatment, novel agents and time to bone marrow transplant. How will this be controlled for? We are going to study induction regimens, post-transplant treatment, use of tandem transplants in our analysis.
   f. Will you be also studying the effect of post-transplant maintenance therapy? Also, any effect of extramedullary plasmacytomas in this AYA group? We will for cases where this information is available. Extramedullary plasmacytomas are a good focus, as AYA patients may have a more aggressive presentation of myeloma.
   g. Are plasma cell leukemias included in this analysis? No

   Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix F.

7. **Impact of measurable residual disease status on outcomes of AML in patients 18-65 years old in CR1 undergoing Allo-HCT**. This proposal was presented by Dr. Firas El Chaer. The objectives of this proposal is to determine if acute myeloid leukemia measurable residual disease (MRD) analysis as currently performed has prognostic value when measured prior to AlloHCT, to explore factors that may modify the risk associated with detectable acute myeloid leukemia MRD pre-AlloHCT, and identification, using MRD combined with other clinical factors, of patients most at risk of post-AlloHCT relapse. The CIBMTR identified 753 MRD positive and 1986 MRD negative adult patients receiving first AlloHCT for de-novo AML in CR1 in 2007-2018. The following questions were answered during the Q&A:

a. What kind of MRD data is collected? Depending on the individual participating centers, the methodology uses molecular or immunotherapy? MRD
b. What is the rate of missing MRD status and are those patients different from those with MRD data available? The answer is not included in this study.
c. Are you going to also study the effect of post-transplant maintenance in AML FLT3, IHD mutations on relapse and overall survival? One of the aims of this study is to have future studies look at post-transplant maintenance from this study.
d. What do you mean by most "recent" pre-conditioning MRD assessment? Would testing need to be completed within a specific time frame before conditioning? All patients who will be receiving a stem cell transplant are required to get a bone marrow biopsy and peripheral blood aspiration before transplantation. Within a month before the transplant, we would look at data point.
e. What is your working definition of MRD? A combination of molecular testing as well as immunotherapy by NFC.
f. Are all mutations equivalent when thinking about MRD? Absolutely not.
g. How sure are you that the MRD patients are really MRD negative? We can never be absolutely sure.
h. How are you going to account for the different sensitivity of methods used to determine MRD? Are ELN risk available at CIBMTR, since when? The way that CIBMTR reports the acute myeloid leukemia data is by reporting their cytogenetics and mutation analysis so we can calculate the data for this population. The point of this study is to look at the commercial availability of these tests and we can rely on it or if we should standardize one testing at all centers.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix G.

8. **Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft versus host disease.** This proposal was presented by Dr. Nosha Farhadfar. The objectives of this proposal are to determine whether clinical manifestations and severity of chronic GVHD differ based on racial/ethnic and socioeconomical status (SES) differences, to determine whether treatment patterns of chronic GVHD differ based on racial/ethnic and SES differences, and to evaluate whether chronic GVHD treatment outcomes differ based on racial/ethnic and SES differences. The CIBMTR identified 17,665 patients, age 18 years or older, who have received first allogeneic transplant for hematologic malignancy (acute myeloid leukemia, acute lymphoblastic leukemia, myelodysplastic syndrome) between 2008 - 2019. The following questions were answered during the Q&A:
   a. I like the idea for looking at outcomes based on race/ethnicity/SES but not sure if incidence should be a primary outcome because it will be dependent on donor type which is very different amongst the groups. The primary outcome of this study is to look at the outcome of patients who develop chronic graft versus host disease. We need to look at the whole cohort, report the incidence, and then focus on chronic graft versus host disease cohort as the primary endpoint of this study.
   b. How will you correct for the impact of race on HLA mismatch between recipients and donors due to the lower chance of identifying a fully matched donor in non-Hispanic white patients? For the same reason, should cord blood recipients be excluded? We are going to include both the donor type, graft source and degree of HLA matching as covariables in a multi-variable analysis. Cord blood recipients should not be excluded, as there was near 14% of Non-Hispanic black, 14% Hispanic, and 15% Asian who received cord transplant. Approximately 7-8% of cord transplants were received by Non-Hispanic whites. We do have the number to look into cords but if a statistician reviews and determines we don't have the power, then we can eliminate the cords.
   c. Is it possible to access constitutional DNA to look at ancestry information markers in this population? This information is not available for the population. The analysis will focus on self-reported race/ethnicity.
   d. All patients in your cohort from 2008 were not reported with NIH consensus criteria for chronic GVHD. Since you have large numbers, should you limit this to more recent time period? We do have all of the

information on graft versus host disease and whether it was limited or extensive. There is information on whether graft versus host disease is progressive, de-novo or interrupted. We have organ involvement and maximum grade of chronic graft versus host disease. NIH scoring is available for at least the past 4 years and maybe we can look at that group separately. Within the past 4 years, the population limited to NIH grading only in about 1,500 non-Hispanic white, 270 non-Hispanic black, and 200 Hispanic, who have developed chronic graft versus host disease.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix H.

9. **Time from diagnosis to transplant as an important contributor for post allogeneic stem cell transplant infections, immune reconstitution and its associated mortality/morbidity**. This proposal was presented by Dr. Lohith Gowda. The objectives of this proposal are to identify density and types of early and late infections (bacterial, viral and fungal) in patients that went to transplant a) <6 months b) between 6- 12 months and c) > 12 months from diagnosis; to identify T cell lymphocyte absolute numbers at days 100 and 180 and CD4/CD8 ratio for the timeline cohorts examining individual donor types; to evaluate the impact of bacterial, viral or fungal infections by day 100 and day 180 on 1-year post-transplant outcomes (relapse, non-relapse mortality, disease free survival, acute and chronic graft versus host disease); and to evaluate quantitative immunoglobulin levels at D+ 100 and + 180 if available. The CIBMTR identified 6,877 ≥ 18 years old patients who underwent first allogeneic transplants for AML in CR1, ALL in CR1 or MDS in the United States from 2012 to 2019. The following questions were answered during the Q&A:
    a. How many patients in the registry have the immune parameters you wish to assess? >2100
    b. How will you account for the type of treatment used prior to transplant? For example, treatments such as hypomethylating agents may require months of treatment before transplant versus induction chemo that works more quickly. We do have some variables that are available, such as types of therapy, and we can analyze levels of intensity of therapy (low to high) and post-transplantation outcomes. The exact number of how many patients who have had different intensities of therapies is not available.

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix I.

10. **Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with secondary central nervous system involvement**. This proposal was presented by Dr. Hamza Hashmi. The primary objective of this proposal. The CIBMTR identified 55 adult patients (age ≥ 18) who received CD19 CAR T-cell therapy for B-cell NHL with secondary central nervous system (CNS) involvement. The following questions were answered during the Q&A:
    a. How will you differentiate between immune effector cell-associated neurotoxicity syndrome (ICANS) and CNS relapse? ICANS will be documented as a neurotoxicity and CNS relapse will be when the form is filled out.
    b. Is this active CNS disease or previously treated CNS disease? The data received from CIBMTR looks at CNS disease at the time of diagnosis and the CNS disease that is present at the time of cellular therapy.
    c. Do you have any registry information on concomitant CNS therapy (chemo/radiation) pre, peri and post transplantation? Answer was not available at this time.
    d. How many patients are in your study? How will you define whether the patients have cleared their CNS involvement? There are currently 60 patients in the history of this data. Of the 60, 40 had this disease at the time of diagnosis and 20 had this disease at the time of cellular therapy. Whether the patients have cleared their CNS involvement, this information is not available at the time.
    e. Since this is your primary endpoint, how will you account for the differences of frequency of CRS and ICANS across different products (e.g. high in Yescarta, lower in Kymriah, low in Breyanzi)? If you look at the toxicity profile of CD19 therapy, they seem to be relatively similar.

f. Could you please include other agents such as anakinra, siltuximab, and other agents? Dasatinib for this populations for ICANS? Also, was CNS disease under control at CAR-T therapy? As for Anakinra, siltuximab, and other agents, I'm not sure if CIBMTR is capturing this data. As for dasatinib, I'm not sure if this information is available as well. Per Dr. Pasquini of CIBMTR in the live chat, he commented "we capture treatment of ICANS, like siltuximab, dasatinib has been reported as other treatment."
g. Will you have detail on the nature and extender features of secondary CNS involvement to associate with the toxicity and outcome? I only have the essential data with me but am hopeful that this comprehensive research will have further detail.
h. Will all the patients included have active CNS disease at the time of CAR-T or, are treated CNS disease are also included? They are both included, and we are able to tell who has had active disease with a prior history at the time they got the CAR-T therapy.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix J.

11. **Haploidentical donor versus matched donor allogeneic hematopoietic cell transplantation in patients with myelofibrosis**. This proposal was presented by Dr. Tania Jain. The primary objective of this proposal is to explore the impact of donor type on overall survival of patients undergoing HCT for myelofibrosis. The CIBMTR identified 1,640 patients ≥18 years old diagnosed with primary, post-ET or post-PV myelofibrosis and undergoing first HCT between 2013 and 2019. The following questions were answered during the Q&A:
    a. Are you also going to compare the effect of pretransplant Ruxo in haplo vs MUD/MRD? Also, are you going to look for graft failures as well in these patient populations? Yes, this will be included. We also do look at graft failures in these populations.
    b. Is there a difference in time from diagnosis to HCT across the groups? The median time from diagnosis to transplant for haploidentical patients was 38 months, while for HLA- identical sibling and URD 8/8 was 21 and 24 months, respectively.
    c. Are you including all conditioning regimens types: MAC, RIC and NMA? Yes, and they will be looked at for comparison in the univariable and may be taken to the multivariable analysis as well.
    d. For the graft failure or rejection analysis are you going to include spleen size? Ideally it should be included but the spleen size measurement has many variables and it may not be a clean assessment. We don't collect precise spleen size in our forms, but it can be analyzed as spleen size as splenomegaly, no splenomegaly or splenectomy.
    e. Can you comment on the bone marrow vs peripheral blood in the three groups? Peripheral blood is more common in the donor source (about 80%).

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix K.

12. **Assessing utilization and clinical outcome differences by sex and race in CAR-T for relapsed/refractory NHL**. This proposal was presented by Dr. Arushi Khurana. The objective of this proposal is to enhance our understanding of sex- and race-based differences in utilization of CAR-T vs AutoHCT and outcomes after CAR-T. The CIBMTR identified 1,133 patients to compare sex and race/ethnicity rates for first cellular infusion (AutoHCT vs. CAR-T) for relapsed/refractory non-hodgkins lymphoma patients from 2017 – 2019 (aim 1a). The CIBMTR identified 619 non-hodgkins lymphoma patients who relapse after first AutoHCT to describe subsequent treatment patterns (e.g. CAR-T, second AutoHCT, AlloHCT, other treatment, no treatment) by sex and race/ethnicity (aim 1b). The CIBMTR identified 1,253 patients to identify sex-and race-based differences in response to CD19 CAR-T in aggressive lymphomas (aim 2). The following questions were answered during the Q&A:
    a. Is there gender and race-based difference in SEER data with or without treatment for diffuse large B-cell lymphoma even before CAR T? Yes, that data does exist.

b. Can this be stratified by center/geography (private/public, large urban/rural)? Yes, it will be shown based on zip code (of patient and of recorded center), which will allow us to differentiate from urban/rural as well.
c. We saw almost no neurotoxicity in women so would you be plotting CRS and ICANS based on gender and race? Yes, and we believe CIBMTR is the best resource for this because of the larger numbers
d. How do you differentiate between larger trial centers vs less resourced centers? The information is reported based on the center type. Basing on academic or zip code, or city versus rural center, that will also be a way to differentiate the centers.
e. Would disease response status prior to cellular therapy be taken into account for analysis? Yes, that is one of the co-variants that will be included.
f. How reliable is the data you will get to study "access", as there are many factors, depending on patient specific factors (education, resource, finances, mobility, support, performance, etc.), center specific (criteria), and also access depends on the hematologist/oncologist who sees these patients in the community? Access to a center is not one of the main issues in this study. It is more about why some of these minorities receiving other treatments when they should be receiving cellular therapy at the time of indication.
g. Is there any way to take into account insurance issues? We do look at the insurance statuses as one of the co-variants.
h. Would it be possible to look at differences in access based on commercial CAR T vs. clinical trials? The majority of the patients from the forms received are from commercial CAR T.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix L.

13. **Optimal GVHD prevention strategy in older, robust patients with acute leukemias and myeloid malignancies undergoing myeloablative, matched donor hematopoietic cell transplantation**. This proposal was presented by Dr. Richard J. Lin. The primary objective of this proposal is to compare CRFS among patients ≥ 60 years old undergoing myeloablative conditioned, allogeneic hematopoietic cell transplantation with following graft versus host disease prophylaxis in 2 matched-pair analysis and to compare other transplant outcomes in the above 2 matched-pair analysis. The CIBMTR identified 1,301 patients at ≥ 60 years old at the time of first allo-HCT between 2010 and 2019, with any myeloablative conditioning defined by CIBMTR, 8/8 matched related or unrelated donor only, graft versus host disease prophylaxis (ex-vivo TCD/CD34+ selection versus PTCy-based versus Tac/MTX). The following questions were answered during the Q&A:
    a. What do you mean by "robust?" Is it based on KPS, HCT-CI, or just the fact that someone got MA. regimen? We use the definition of a patient getting a myelo-conditioning as a way of saying that they are robust by their transplant centers.
    b. Are patients with In-vivo T cell depletion (Campath or ATG) excluded from this analysis? T cell depletion and CD34 selection does include ATG and does not include Campath.
    c. Why do you pool post-CY and ex vivoCD34+ selection? Can we still consider ex vivoCD34 selection to be a promising transplant modality in 2021? We wanted to compare a 2-match pair analysis and not a direct comparison between CD34 selection and post-CY. We do know which will be better for an older patient.
    d. Why exclude TBI? For older patients, we don't consider TBI to be a conditioning regimen.
    e. How many patients with Tac/methotrexate prophylaxis had ATG? Answer was not available at the time of Q&A.
    f. Do we know GFR (creatinine) coming into allo in these groups? In this study, we didn't include the GFR (creatinine) as a variable but we have some evidence in older patients that does play a major role. I can discuss with our statistician on whether we can include this as a variable.

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix M.

14. **Outcomes of elderly patients receiving CD-19 directed CAR-T therapy for B-cell lymphomas**. This proposal was presented by Dr. Sayeef Mirza. The primary objectives of this proposal to evaluate cumulative incidence grades, duration and median time to onset of CRS and CRES/ICANS in patients > 65 years of age receiving CD-19 directed CAR-T therapy, describe post CAR-T clinical outcomes and resource utilization in elderly, and identify disease biology, comorbidities and other clinical predictive markers of toxicity, response, and survival in elderly patients. The CIBMTR identified 1,036 patients (<65y,n=612; 65-74y, n=348; >75y, n=76) with the diagnosis of any B-cell lymphoid malignancy (indolent or aggressive lymphoma) receiving CAR-T cell product (CD19 target). The following questions were answered during the Q&A:
    a. Would you please also look at Incidence of pancytopenia, hypogammaglobulinemia and HLH in elderly versus younger in 3 cohorts <60, 60-75 ,>75? I think it's very important to look at this as the data becomes available to us. We are primarily looking at different age groups. We have 81 patients over the age of 75 and five patients over the age of 85. Overall, there are 435 (40 %) of the group are over 65 years old.
    b. How does this defer from the data presented by Dr. Pasquini last year in older patients? This data will be more helpful in including both CAR-T products.
    c. In case of CAR T was used for post-alloHCT relapse, would the donor age of the CART source be analyzed? This is something that we should include in our analysis.
    d. Are data on baseline geriatric scores or HCT-CI available for all? The answer was not available at the time of the Q&A.
    e. Do we have registry information on whether CAR-T production succeeded or not, when attempted? The answer was not available at the time of the Q&A but the moderator did state that on behalf of CIBMTR, this information is not captured.

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix N.

15. **Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation**. This proposal was presented by Dr. Joseph Pidala. The primary objective of this proposal is to validate prediction models for immune suppression discontinuation (ISD) and ISD failure developed in prior DISCIS-defined population, explore ISD and ISD failure in a new population inclusive of full range of diversity in current HCT practices, construct and validate dynamic prediction models of ISD and ISD failure in the expanded population. The CIBMTR identified 20,031 patients with a hematologic malignancy who received an allogeneic HCT from matched sibling donor, matched or mismatched unrelated donor, umbilical cord blood or haploidentical donor between 2009-2018. The following questions were answered during the Q&A:
    a. Can you explain how the ISD data information was made feasible? We used CIBMTR follow up data in the previous analysis that led to the development of the prediction model for ISD that we intend to validate in this study.
    b. Can you provide more granularity on how the time of discontinuation of immune suppression will be defined? In the CIBMTR data, there is a hard stop date for a complete discontinuation of immune suppression. That granular data is available, and it was the data we used for the prior project. We used that hard stop of all systemic immune suppression because that's an unambiguous measure of success.
    c. Many with PTCY may be discontinuing by days 100 or 60- likely based on center practice rather than patient response, how will this be addressed? Our prior project was successfully addressed this issue, specifically within that study population. The first step in this project is to validate those findings. We will definitely be studying how immune suppression was performed and what are the subsequent outcomes.
    d. Do you plan to use age as one of the variables regarding likelihood to discontinue IST, or will you have a separate pediatric specific model? Yes, we will consider age as a variable and evaluate the need for a pediatric specific model.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix O.

CLOSING:

Dr. Shaw, on behalf of herself and co-chair, Dr. John Wingard, did thank presenters, conference organizers, and the CIBMTR staff for having coordinated this virtual session. She did mention that this session was recorded and encouraged attendees to take survey, as access would be available until Monday, February 15, 2021.

APPENDICES:

A. Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis.

1. How will authorship work for these studies? The same as usual, there are fewer studies being accepted but the process otherwise is the same
2. What if a higher risk of cancer is related to the almost uniform use of 2GyTBI in these patients rather than PTCY?
3. What is the breakdown of haploidentical versus matched sib/MUD in the post-transplant cyclophosphamide group?
4. How can we r/o genetic predisposition on samples and variables of TBI based conditioning therapies?
5. What is your sample size and follow-up period?
6. How long post BMT you will follow up? From where will you receive the SN data?
7. Will you be adjusting for chronic GVHD when looking at your outcome of SN?
8. Is this study statistically powered to detect a difference between PTCY and above a certain threshold? What is the threshold?
9. Will analysis be conducted separately for TBI/non-TBI and MAC/RIC conditioning? Are you evaluating all malignancies?
10. Since the total CY exposure is likely not that different in PTCY vs. BU/CY or CY/TBI, is your hypothesis that the timing of exposure to CY may lead to a difference in risk? And if so, why?
11. Information on skin cancers - ssc, bcc available?
12. Matching for HLA matching could be a limitation because the PTCY patients are more likely to receive haploidentical grafts.

B. Outcomes of chimeric antigen receptor-T cell (CAR-T) therapy for patients with antecedent chronic lymphocytic leukemia (Richter's Syndrome).

1. If patients had failed an auto or allo, how do you plan to compare to the results of auto? Isn't it a different group?
2. Can you please provide your thoughts if the small n will be able to generate meaningful results at this time?
3. Would you include both transformed lymphoma from other low-grade lymphoma and Richter's transformation?
4. Are there concerns about underreporting Richter's?
5. Since the numbers are small, can we go back to centers to establish clonality?

C. Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies. *No additional questions*

D. Effect of HLA evolutionary divergence on survival and relapse following allogeneic hematopoietic cell transplant.

1. Does the HED algorithm take into account variations outside the peptide binding groove?

2. What is the size of the cohort you are looking at?

E. Impact of IDH1 and IDH2 mutations on outcomes of acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation. *No additional questions*

F. Characteristics and outcomes of adolescent and young adults with multiple myeloma treated with autologous hematopoietic cell transplant.

1. How do you plan to control for differences between your AYA group and older control group?

G. Impact of MRD status on outcomes of AML in patients 18-65 years old in CR1 undergoing Allo-HCT.

1. How are you going to account for the different sensitivity of methods used to determine MRD? Are ELN risk available at CIBMTR, since when?
2. Hi Firas, How are defining the MRD?
3. The methods for MRD assessment may be quite heterogeneous, including the threshold of detection. How will you deal with the high likelihood of false MRD negative assessments from using inadequately sensitive quantification?
4. MRD test is different from different centers. How can you control for this?
5. How do you account for different MRD- cut-offs?
6. To clarify, if AML-MRD is to become a "precision medicine tool", does that mean is will be used to guide treatment decisions in addition to being prognostic?
7. How will control for the various methods for detecting MRD as different techniques have different sensitivities/accuracy?
8. if both multiparameter flow and NGS are available and are discordant on the same patient, how will that be analyzed?
9. is the MRD before alloSCT is the one to be analyzed?
10. Will this require more data from centers to answer some of the questions above?

H. Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft versus host disease.

1. Is age significantly different in your Hispanic cohort? How do you adjust for it?
2. Was the MMUD recipient cohort limited to single antigen mismatch? Or all mismatches (understanding most MMUD will likely be single antigen MM)?
3. Do you have information on health insurance? Why not to study this question in a more homogeneous patient population to avoid the complexity and interactions in different factors?
4. Are there any other sociodemographic variables available that could be used to adjust for socioeconomic status, or is median income in the patient's ZIP code the only one?
5. Baker et al 2009 demonstrated no impact of household income on GVHD (acute or chronic) and only minimal impact of race on Grade III-IV aGVHD (none of cGVHD). Why do you think this null relationship should be pursued again?
6. Is there a plan to study as per continent distribution?
7. Is there a better index to gauge SES or poverty level?
8. Are Native American/Hawaiian/Pacific islanders being grouped elsewhere?

I. Time from diagnosis to transplant as an important contributor for post allogeneic stem cell transplant infections, immune reconstitution and its associated mortality/morbidity.

1. Do you plan to address the confounding influence of different factors leading to delay in transplant timing?
2. How are you going to account for number of cycles of chemotherapy versus no

chemotherapy as a confounder in the time delay?

J. Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with secondary central nervous system involvement.

1. Is site-specific response (CNS vs. other lesions) and pattern of relapse/progression (CNS vs. systemic) available?
2. Why not to consider a comparative group?
3. Will you stratify patients according if they received IT chemo vs radiation therapy?

K. Haploidentical donor versus matched donor allogeneic hematopoietic cell transplantation in patients with myelofibrosis.

1. Availability of somatic mutations?
2. Is pretransplant Splenectomy data available? Are you going to factor this in the outcomes?
3. At least look at splenectomies?
4. What risk stratification is being used? DIPSS or DIPSS+?

L. Assessing utilization and clinical outcome differences by sex and race in CAR-T for relapsed/refractory NHL. *No additional questions*

M. Optimal GVHD prevention strategy in older, robust patients with acute leukemias and myeloid malignancies undergoing myeloablative, matched donor hematopoietic cell transplantation. *No additional questions*

N. Outcomes of elderly patients receiving CD-19 directed CAR-T therapy for B-cell lymphomas. *No additional questions*

O. Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation.

1. How is immune suppression stop defined in the CIBMTR database?
2. How long after HCT do you expect data regarding ongoing IST usage to be reliable since many patients leave the transplant center and are managed elsewhere long-term?
3. How long will you deal with restart IST?

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2021

	HLA-Identical Sibling		Alternative Donor		Autologous	
	TED only	Research	TED only	Research	TED only	Research
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Anaplastic large cell	313	55	407	148	1884	173
PIF	41 (13)	9 (16)	44 (11)	24 (16)	182 (10)	14 (8)
CR1	41 (13)	10 (18)	58 (14)	24 (16)	754 (40)	74 (43)
Rel 1	32 (10)	8 (15)	26 (6)	10 (7)	178 (9)	20 (12)
CR2	88 (28)	17 (31)	117 (29)	43 (29)	453 (24)	37 (21)
Other/Unknown	111 (35)	11 (20)	162 (40)	47 (32)	317 (17)	28 (16)
Burkitt/small noncleaved	169	57	104	97	578	133
PIF	19 (11)	8 (14)	8 (8)	19 (20)	58 (10)	25 (19)
CR1	35 (21)	14 (25)	19 (18)	17 (18)	200 (35)	51 (38)
Rel 1	24 (14)	7 (12)	9 (9)	15 (15)	52 (9)	13 (10)
CR2	42 (25)	21 (37)	36 (35)	34 (35)	144 (25)	34 (26)
Other/Unknown	49 (29)	7 (12)	32 (31)	12 (12)	124 (21)	10 (8)
Diffuse large cell/Immunoblastic	1855	312	2071	670	22038	2318
PIF	331 (18)	79 (25)	339 (16)	193 (29)	2691 (12)	311 (13)
CR1	184 (10)	50 (16)	229 (11)	91 (14)	3941 (18)	453 (20)
Rel 1	290 (16)	41 (13)	213 (10)	74 (11)	3766 (17)	417 (18)
CR2	250 (13)	29 (9)	345 (17)	94 (14)	6281 (29)	673 (29)
Other/Unknown	800 (43)	113 (36)	954 (46)	218 (33)	5359 (24)	464 (20)
Follicular	1505	506	1378	645	5129	840
PIF	171 (11)	67 (13)	137 (10)	108 (17)	508 (10)	66 (8)
CR1	108 (7)	37 (7)	91 (7)	41 (6)	587 (11)	108 (13)
Rel 1	208 (14)	101 (20)	157 (11)	96 (15)	892 (17)	158 (19)
CR2	186 (12)	75 (15)	183 (13)	79 (12)	1257 (25)	200 (24)
Other/Unknown	832 (55)	226 (45)	810 (59)	321 (50)	1885 (37)	308 (37)
Lymphoblastic	172	49	133	98	281	31
PIF	18 (10)	7 (14)	8 (6)	12 (12)	14 (5)	2 (6)
CR1	50 (29)	11 (22)	21 (16)	18 (18)	124 (44)	17 (55)
Rel 1	28 (16)	8 (16)	10 (8)	16 (16)	24 (9)	0 (0)
CR2	32 (19)	12 (24)	36 (27)	33 (34)	35 (12)	5 (16)
Other/Unknown	44 (26)	11 (22)	58 (44)	19 (19)	84 (30)	7 (23)
Mantle	939	202	1184	399	8606	855
PIF	124 (13)	38 (19)	113 (10)	64 (16)	735 (9)	77 (9)
CR1	183 (19)	39 (19)	178 (15)	75 (19)	5815 (68)	583 (68)

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2021

	HLA-Identical Sibling		Alternative Donor		Autologous	
	TED only	Research	TED only	Research	TED only	Research
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Rel 1	145 (15)	35 (17)	183 (15)	66 (17)	254 (3)	26 (3)
CR2	184 (20)	30 (15)	354 (30)	83 (21)	456 (5)	56 (7)
Other/Unknown	303 (32)	60 (30)	356 (30)	111 (28)	1346 (16)	113 (13)
Marginal	91	27	100	38	378	41
PIF	11 (12)	8 (30)	14 (14)	9 (24)	42 (11)	9 (22)
CR1	9 (10)	3 (11)	16 (16)	5 (13)	65 (17)	4 (10)
Rel 1	10 (11)	1 (4)	12 (12)	6 (16)	49 (13)	3 (7)
CR2	12 (13)	3 (11)	8 (8)	4 (11)	75 (20)	10 (24)
Other/Unknown	49 (54)	12 (44)	50 (50)	14 (37)	147 (39)	15 (37)
NK T cell	257	51	320	111	774	72
PIF	40 (16)	7 (14)	62 (19)	21 (19)	98 (13)	14 (19)
CR1	63 (25)	13 (25)	88 (28)	41 (37)	329 (43)	31 (43)
Rel 1	26 (10)	6 (12)	21 (7)	8 (7)	53 (7)	4 (6)
CR2	47 (18)	4 (8)	66 (21)	25 (23)	126 (16)	12 (17)
Other/Unknown	81 (32)	21 (41)	83 (26)	16 (14)	168 (22)	11 (15)
T cell	945	197	1299	446	3623	376
PIF	227 (24)	62 (31)	306 (24)	168 (38)	411 (11)	47 (13)
CR1	177 (19)	43 (22)	244 (19)	91 (20)	1997 (55)	194 (52)
Rel 1	109 (12)	17 (9)	128 (10)	44 (10)	265 (7)	38 (10)
CR2	134 (14)	26 (13)	235 (18)	44 (10)	370 (10)	47 (13)
Other/Unknown	298 (32)	49 (25)	386 (30)	99 (22)	580 (16)	50 (13)
NHL Not specified	180	24	123	99	888	26
PIF	15 (8)	4 (17)	8 (7)	30 (30)	94 (11)	7 (27)
CR1	13 (7)	0 (0)	5 (4)	13 (13)	112 (13)	6 (23)
Rel 1	28 (16)	2 (8)	12 (10)	13 (13)	64 (7)	5 (19)
CR2	15 (8)	2 (8)	23 (19)	14 (14)	114 (13)	2 (8)
Other/Unknown	109 (61)	16 (67)	75 (61)	29 (29)	504 (57)	6 (23)
Other	659	175	827	299	7028	704
PIF	135 (20)	48 (27)	195 (24)	82 (27)	1213 (17)	129 (18)
CR1	126 (19)	28 (16)	162 (20)	77 (26)	2258 (32)	225 (32)
Rel 1	64 (10)	18 (10)	72 (9)	29 (10)	821 (12)	75 (11)
CR2	87 (13)	10 (6)	142 (17)	35 (12)	1746 (25)	156 (22)
Other/Unknown	247 (37)	71 (41)	256 (31)	76 (25)	990 (14)	119 (17)

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2021

	HLA-Identical Sibling		Alternative Donor		Autologous	
	TED only	Research	TED only	Research	TED only	Research
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Hodgkin	1440	222	2110	492	18885	1748
PIF	214 (15)	39 (18)	266 (13)	96 (20)	2699 (14)	285 (16)
CR1	75 (5)	13 (6)	128 (6)	55 (11)	2243 (12)	225 (13)
Rel 1	169 (12)	46 (21)	233 (11)	68 (14)	3529 (19)	315 (18)
CR2	160 (11)	26 (12)	279 (13)	61 (12)	5586 (30)	546 (31)
Other/Unknown	822 (57)	98 (44)	1204 (57)	212 (43)	4828 (26)	377 (22)
Graft type	8525	1877	10065	3542	70092	7317
BM	859 (10)	174 (9)	1757 (17)	793 (22)	695 (1)	52 (1)
PBSC	7603 (89)	1698 (90)	7605 (76)	2251 (64)	68354 (98)	7210 (99)
Other/Unknown	63 (1)	5 (0)	703 (7)	498 (14)	1043 (1)	55 (1)

Unrelated Donor HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired samples, recipient only samples and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	4949	1414	870
Source of data			
CRF	2390 (48)	567 (40)	372 (43)
TED	2559 (52)	847 (60)	498 (57)
Number of centers	198	140	192
Disease at transplant			
NHL	4032 (81)	1194 (84)	710 (82)
Hodgkins Lymphoma	917 (19)	220 (16)	160 (18)
NHL Disease status at transplant			
CR1	556 (14)	205 (17)	90 (13)
CR2	741 (18)	223 (19)	117 (17)
CR3+	345 (9)	102 (9)	66 (9)
PR	439 (11)	110 (9)	76 (11)
Advanced	1866 (47)	531 (45)	346 (49)
Missing	65 (2)	15 (1)	12 (2)
Recipient age at transplant			
0-9 years	54 (1)	9 (1)	12 (1)
10-19 years	227 (5)	44 (3)	35 (4)
20-29 years	606 (12)	154 (11)	102 (12)
30-39 years	706 (14)	195 (14)	122 (14)
40-49 years	936 (19)	253 (18)	173 (20)
50-59 years	1349 (27)	380 (27)	223 (26)
60-69 years	992 (20)	334 (24)	191 (22)
70+ years	79 (2)	45 (3)	12 (1)
Median (Range)	50 (2-79)	52 (3-77)	50 (2-77)
Recipient race/ethnicity			
Caucasian, non-Hispanic	4268 (86)	1173 (83)	656 (75)
African-American, non-Hispanic	220 (4)	64 (5)	37 (4)
Asian, non-Hispanic	88 (2)	32 (2)	26 (3)
Pacific islander, non-Hispanic	4 (<1)	2 (<1)	0
Native American, non-Hispanic	4 (<1)	8 (1)	1 (<1)
Hispanic	259 (5)	85 (6)	44 (5)
Missing	106 (2)	50 (4)	106 (12)
Recipient sex			
Male	3111 (63)	934 (66)	577 (66)
Female	1838 (37)	480 (34)	293 (34)
Karnofsky score			
10-80	1688 (34)	521 (37)	293 (34)
90-100	3018 (61)	820 (58)	534 (61)
Missing	243 (5)	73 (5)	43 (5)
HLA-A B DRB1 groups - low resolution			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
<=3/6	4 (<1)	3 (<1)	0
4/6	10 (<1)	8 (1)	5 (1)
5/6	598 (12)	144 (11)	97 (12)
6/6	4246 (87)	1140 (88)	729 (88)
Unknown	91 (N/A)	119 (N/A)	39 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	46 (1)	8 (1)	3 (<1)
6/8	122 (3)	16 (2)	12 (2)
7/8	931 (20)	173 (16)	140 (22)
8/8	3568 (76)	868 (82)	478 (76)
Unknown	282 (N/A)	349 (N/A)	237 (N/A)
HLA-DPB1 Match			
Double allele mismatch	782 (28)	80 (20)	60 (25)
Single allele mismatch	1557 (57)	203 (50)	137 (57)
Full allele matched	412 (15)	119 (30)	42 (18)
Unknown	2198 (N/A)	1012 (N/A)	631 (N/A)
High resolution release score			
No	2345 (47)	1410 (>99)	858 (99)
Yes	2604 (53)	4 (<1)	12 (1)
KIR typing available			
No	4173 (84)	1412 (>99)	870 (100)
Yes	776 (16)	2 (<1)	0
Graft type			
Marrow	1033 (21)	260 (18)	179 (21)
PBSC	3914 (79)	1142 (81)	690 (79)
PBSC+UCB	2 (<1)	12 (1)	0
Others	0	0	1 (<1)
Number of cord units			
Unknown	4949 (N/A)	1414 (N/A)	870 (N/A)
Conditioning regimen			
Myeloablative	1966 (40)	475 (34)	276 (32)
RIC/Nonmyeloablative	2943 (59)	929 (66)	584 (67)
TBD	40 (1)	10 (1)	10 (1)
Donor age at donation			
To Be Determined/NA	32 (1)	206 (15)	20 (2)
0-9 years	1 (<1)	3 (<1)	0
10-19 years	122 (2)	39 (3)	24 (3)
20-29 years	2221 (45)	598 (42)	364 (42)
30-39 years	1418 (29)	325 (23)	252 (29)
40-49 years	900 (18)	186 (13)	154 (18)
50+ years	255 (5)	57 (4)	56 (6)
Median (Range)	31 (7-69)	29 (7-68)	31 (18-61)
Donor/Recipient CMV serostatus			
+/+	1130 (23)	332 (23)	184 (21)
+/-	589 (12)	204 (14)	133 (15)
-/+	1465 (30)	367 (26)	245 (28)
-/-	1704 (34)	449 (32)	287 (33)
CB - recipient +	1 (<1)	2 (<1)	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CB - recipient -	0	2 (<1)	0
Missing	60 (1)	58 (4)	21 (2)
GvHD Prophylaxis			
No GvHD Prophylaxis	16 (<1)	5 (<1)	1 (<1)
TDEPLETION alone	3 (<1)	2 (<1)	1 (<1)
TDEPLETION +- other	52 (1)	8 (1)	11 (1)
CD34 select alone	0	1 (<1)	1 (<1)
CD34 select +- other	73 (1)	36 (3)	12 (1)
Cyclophosphamide alone	25 (1)	32 (2)	12 (1)
Cyclophosphamide +- others	179 (4)	113 (8)	49 (6)
FK506 + MMF +- others	817 (17)	186 (13)	145 (17)
FK506 + MTX +- others(not MMF)	2146 (43)	596 (42)	276 (32)
FK506 +- others(not MMF,MTX)	296 (6)	113 (8)	58 (7)
FK506 alone	160 (3)	46 (3)	21 (2)
CSA + MMF +- others(not FK506)	526 (11)	104 (7)	93 (11)
CSA + MTX +- others(not MMF,FK506)	406 (8)	91 (6)	107 (12)
CSA +- others(not FK506,MMF,MTX)	77 (2)	19 (1)	18 (2)
CSA alone	48 (1)	7 (<1)	28 (3)
Other GVHD Prophylaxis	73 (1)	18 (1)	14 (2)
Missing	52 (1)	37 (3)	23 (3)
Donor/Recipient sex match			
Male-Male	2252 (46)	637 (45)	387 (44)
Male-Female	1154 (23)	286 (20)	157 (18)
Female-Male	841 (17)	264 (19)	178 (20)
Female-Female	672 (14)	174 (12)	131 (15)
CB - recipient M	0	8 (1)	0
CB - recipient F	2 (<1)	4 (<1)	0
Missing	28 (1)	41 (3)	17 (2)
Year of transplant			
1986-1990	3 (<1)	1 (<1)	1 (<1)
1991-1995	52 (1)	12 (1)	8 (1)
1996-2000	258 (5)	62 (4)	44 (5)
2001-2005	808 (16)	152 (11)	177 (20)
2006-2010	1416 (29)	254 (18)	193 (22)
2011-2015	1601 (32)	419 (30)	236 (27)
2016-2020	761 (15)	469 (33)	187 (21)
2021	50 (1)	45 (3)	24 (3)
Follow-up among survivors, Months			
N Eval	1909	648	361
Median (Range)	73 (2-315)	48 (0-291)	49 (3-236)

Unrelated Cord Blood Transplant Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired, recipient only and cord blood only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006-recipient only), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	491	116	127
Source of data			
CRF	373 (76)	87 (75)	76 (60)
TED	118 (24)	29 (25)	51 (40)
Number of centers	89	39	55
Disease at transplant			
NHL	394 (80)	89 (77)	100 (79)
Hodgkins Lymphoma	97 (20)	27 (23)	27 (21)
NHL Disease status at transplant			
CR1	60 (15)	6 (7)	18 (18)
CR2	74 (19)	20 (22)	31 (31)
CR3+	44 (11)	10 (11)	9 (9)
PR	67 (17)	12 (13)	11 (11)
Advanced	146 (37)	40 (45)	28 (28)
Missing	0	1 (1)	2 (2)
Recipient age at transplant			
0-9 years	23 (5)	5 (4)	3 (2)
10-19 years	35 (7)	5 (4)	10 (8)
20-29 years	61 (12)	14 (12)	16 (13)
30-39 years	89 (18)	18 (16)	27 (21)
40-49 years	88 (18)	31 (27)	21 (17)
50-59 years	117 (24)	19 (16)	31 (24)
60-69 years	73 (15)	23 (20)	18 (14)
70+ years	5 (1)	1 (1)	1 (1)
Median (Range)	45 (1-73)	45 (5-73)	44 (7-71)
Recipient race/ethnicity			
Caucasian, non-Hispanic	276 (56)	75 (65)	68 (54)
African-American, non-Hispanic	96 (20)	23 (20)	18 (14)
Asian, non-Hispanic	34 (7)	6 (5)	8 (6)
Pacific islander, non-Hispanic	1 (<1)	0	1 (1)
Native American, non-Hispanic	6 (1)	0	0
Hispanic	64 (13)	10 (9)	16 (13)
Missing	14 (3)	2 (2)	16 (13)
Recipient sex			
Male	288 (59)	69 (59)	66 (52)
Female	203 (41)	47 (41)	61 (48)
Karnofsky score			
10-80	145 (30)	33 (28)	26 (20)
90-100	325 (66)	75 (65)	97 (76)
Missing	21 (4)	8 (7)	4 (3)
HLA-A B DRB1 groups - low resolution			
<=3/6	18 (4)	4 (4)	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
4/6	243 (51)	48 (48)	63 (56)
5/6	180 (38)	38 (38)	41 (36)
6/6	31 (7)	10 (10)	9 (8)
Unknown	19 (N/A)	16 (N/A)	14 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	257 (64)	48 (69)	64 (70)
6/8	97 (24)	15 (21)	17 (18)
7/8	35 (9)	6 (9)	8 (9)
8/8	15 (4)	1 (1)	3 (3)
Unknown	87 (N/A)	46 (N/A)	35 (N/A)
HLA-DPB1 Match			
Double allele mismatch	45 (35)	4 (40)	9 (47)
Single allele mismatch	70 (55)	6 (60)	8 (42)
Full allele matched	12 (9)	0	2 (11)
Unknown	364 (N/A)	106 (N/A)	108 (N/A)
High resolution release score			
No	407 (83)	113 (97)	126 (99)
Yes	84 (17)	3 (3)	1 (1)
KIR typing available			
No	414 (84)	116 (100)	126 (99)
Yes	77 (16)	0	1 (1)
Graft type			
UCB	447 (91)	104 (90)	123 (97)
PBSC+UCB	42 (9)	12 (10)	2 (2)
Others	2 (<1)	0	2 (2)
Number of cord units			
1	387 (79)	0	85 (67)
2	103 (21)	0	42 (33)
3	1 (<1)	0	0
Unknown	0 (N/A)	116 (N/A)	0 (N/A)
Conditioning regimen			
Myeloablative	202 (41)	49 (42)	40 (31)
RIC/Nonmyeloablative	289 (59)	66 (57)	86 (68)
TBD	0	1 (1)	1 (1)
Donor age at donation			
To Be Determined/NA	13 (3)	11 (9)	10 (8)
0-9 years	432 (88)	90 (78)	110 (87)
10-19 years	13 (3)	6 (5)	5 (4)
20-29 years	10 (2)	2 (2)	0
30-39 years	7 (1)	2 (2)	1 (1)
40-49 years	7 (1)	2 (2)	1 (1)
50+ years	9 (2)	3 (3)	0
Median (Range)	3 (0-68)	5 (0-68)	3 (0-43)
Donor/Recipient CMV serostatus			
+/+	114 (23)	20 (17)	26 (20)
+/-	60 (12)	11 (9)	16 (13)
-/+	81 (16)	23 (20)	18 (14)
-/-	53 (11)	14 (12)	17 (13)
CB - recipient +	114 (23)	26 (22)	34 (27)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CB - recipient -	63 (13)	16 (14)	12 (9)
CB - recipient CMV unknown	6 (1)	6 (5)	4 (3)
GvHD Prophylaxis			
No GvHD Prophylaxis	2 (<1)	0	0
TDEPLETION +- other	4 (1)	1 (1)	1 (1)
CD34 select +- other	32 (7)	9 (8)	2 (2)
Cyclophosphamide +- others	1 (<1)	1 (1)	5 (4)
FK506 + MMF +- others	169 (34)	29 (25)	31 (24)
FK506 + MTX +- others(not MMF)	13 (3)	5 (4)	2 (2)
FK506 +- others(not MMF,MTX)	32 (7)	7 (6)	7 (6)
FK506 alone	26 (5)	10 (9)	3 (2)
CSA + MMF +- others(not FK506)	174 (35)	47 (41)	63 (50)
CSA + MTX +- others(not MMF,FK506)	4 (1)	2 (2)	1 (1)
CSA +- others(not FK506,MMF,MTX)	12 (2)	2 (2)	4 (3)
CSA alone	1 (<1)	0	2 (2)
Other GVHD Prophylaxis	16 (3)	2 (2)	3 (2)
Missing	5 (1)	1 (1)	3 (2)
Donor/Recipient sex match			
CB - recipient M	288 (59)	69 (59)	66 (52)
CB - recipient F	203 (41)	47 (41)	61 (48)
Year of transplant			
1996-2000	1 (<1)	0	0
2001-2005	7 (1)	9 (8)	1 (1)
2006-2010	155 (32)	33 (28)	44 (35)
2011-2015	252 (51)	52 (45)	52 (41)
2016-2020	74 (15)	22 (19)	30 (24)
2021	2 (<1)	0	0
Follow-up among survivors, Months			
N Eval	218	42	46
Median (Range)	72 (3-166)	66 (12-194)	60 (2-144)

Related Donor HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired, recipient only and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	1044	178	78
Source of data			
CRF	343 (33)	48 (27)	24 (31)
TED	701 (67)	130 (73)	54 (69)
Number of centers	65	34	18
Disease at transplant			
NHL	856 (82)	141 (79)	61 (78)
Hodgkins Lymphoma	188 (18)	37 (21)	17 (22)
NHL Disease status at transplant			
CR1	154 (18)	32 (23)	11 (18)
CR2	162 (19)	31 (22)	8 (13)
CR3+	93 (11)	15 (11)	2 (3)
PR	67 (8)	13 (9)	5 (8)
Advanced	371 (44)	49 (35)	34 (56)
Missing	5 (1)	0	1 (2)
Recipient age at transplant			
0-9 years	10 (1)	2 (1)	0
10-19 years	50 (5)	11 (6)	1 (1)
20-29 years	108 (10)	25 (14)	6 (8)
30-39 years	116 (11)	25 (14)	11 (14)
40-49 years	172 (16)	25 (14)	19 (24)
50-59 years	307 (29)	51 (29)	25 (32)
60-69 years	262 (25)	36 (20)	15 (19)
70+ years	19 (2)	3 (2)	1 (1)
Median (Range)	52 (3-76)	50 (2-73)	51 (20-72)
Recipient race/ethnicity			
Caucasian, non-Hispanic	691 (66)	97 (54)	54 (69)
African-American, non-Hispanic	115 (11)	26 (15)	7 (9)
Asian, non-Hispanic	46 (4)	14 (8)	2 (3)
Pacific islander, non-Hispanic	3 (<1)	1 (1)	0
Native American, non-Hispanic	4 (<1)	0	0
Hispanic	143 (14)	21 (12)	10 (13)
Missing	42 (4)	19 (11)	5 (6)
Recipient sex			
Male	663 (64)	116 (65)	49 (63)
Female	381 (36)	62 (35)	29 (37)
Karnofsky score			
10-80	349 (33)	58 (33)	23 (29)
90-100	651 (62)	111 (62)	51 (65)
Missing	44 (4)	9 (5)	4 (5)
Graft type			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Marrow	139 (13)	29 (16)	15 (19)
PBSC	905 (87)	148 (83)	63 (81)
BM+PBSC	0	1 (1)	0
Conditioning regimen			
Myeloablative	375 (36)	57 (32)	22 (28)
RIC/Nonmyeloablative	666 (64)	119 (67)	55 (71)
TBD	3 (<1)	2 (1)	1 (1)
Donor age at donation			
To Be Determined/NA	5 (<1)	1 (1)	0
0-9 years	17 (2)	1 (1)	0
10-19 years	66 (6)	11 (6)	2 (3)
20-29 years	126 (12)	33 (19)	10 (13)
30-39 years	157 (15)	28 (16)	17 (22)
40-49 years	197 (19)	33 (19)	15 (19)
50+ years	476 (46)	71 (40)	34 (44)
Median (Range)	48 (0-81)	45 (0-71)	47 (15-74)
Donor/Recipient CMV serostatus			
+/+	420 (40)	83 (47)	26 (33)
+/-	137 (13)	16 (9)	9 (12)
-/+	192 (18)	32 (18)	19 (24)
-/-	276 (26)	43 (24)	19 (24)
Missing	19 (2)	4 (2)	5 (6)
GvHD Prophylaxis			
No GvHD Prophylaxis	6 (1)	1 (1)	0
TDEPLETION +- other	9 (1)	2 (1)	1 (1)
CD34 select +- other	20 (2)	10 (6)	1 (1)
Cyclophosphamide alone	11 (1)	6 (3)	1 (1)
Cyclophosphamide +- others	265 (25)	49 (28)	22 (28)
FK506 + MMF +- others	100 (10)	11 (6)	4 (5)
FK506 + MTX +- others(not MMF)	426 (41)	46 (26)	30 (38)
FK506 +- others(not MMF,MTX)	98 (9)	36 (20)	13 (17)
FK506 alone	9 (1)	0	0
CSA + MMF +- others(not FK506)	9 (1)	4 (2)	0
CSA + MTX +- others(not MMF,FK506)	21 (2)	0	0
CSA +- others(not FK506,MMF,MTX)	14 (1)	4 (2)	1 (1)
CSA alone	2 (<1)	0	0
Other GVHD Prophylaxis	23 (2)	1 (1)	2 (3)
Missing	31 (3)	8 (4)	3 (4)
Donor/Recipient sex match			
Male-Male	396 (38)	63 (35)	33 (42)
Male-Female	192 (18)	25 (14)	14 (18)
Female-Male	266 (25)	52 (29)	16 (21)
Female-Female	189 (18)	37 (21)	15 (19)
Missing	1 (<1)	1 (1)	0
Year of transplant			
2006-2010	120 (11)	15 (8)	8 (10)
2011-2015	481 (46)	63 (35)	32 (41)
2016-2020	423 (41)	83 (47)	37 (47)
2021	20 (2)	17 (10)	1 (1)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Follow-up among survivors, Months			
N Eval	630	106	50
Median (Range)	50 (3-148)	37 (3-123)	60 (6-143)

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Lymphoma Working Committee Members

FROM: Mehdi Hamadani, MD; Scientific Director for the Lymphoma Working Committee

RE: Studies in Progress Summary

LY20-02 Outcomes of Allogeneic HCT in patients with Hodgkin Lymphoma in the era of Checkpoint Inhibitors: A joint CIBMTR and EBMT analysis. (Miguel-Angel Perales/Ana Maria Sureda).

This study will combine data from the CIBMTR and EBMT to assess outcomes in adult patients with Hodgkin lymphoma undergoing either myeloablative or reduced intensity allo-HCT with or without prior exposure to checkpoint inhibitors. This study is currently in Analysis. The goal of this study is to submit by December 2022.

LY19-01c Outcomes of Allogeneic Hematopoietic Cell Transplantation (alloHCT) in Anaplastic Large Cell Lymphoma (ALCL). (Internal)

This study evaluates outcomes of patients undergoing Allogeneic Hematopoietic Cell Transplantation for Anaplastic Large Cell Lymphoma. This study is currently in manuscript preparation. The goal of this study is to submit by June 2022.

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Outcomes with autologous hematopoietic stem cell transplant in peripheral T-cell lymphoma

Q2. Key Words

autologous transplant, stem cell transplant, peripheral T-cell lymphoma, non-hodgkin lymphoma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Aasems Jacob
Email address:	aasems.jacob@pikevillehospital.org
Institution name:	Pikeville Medical Center
Academic rank:	Hematologist

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Chaitanya Iragavarapu
Email address:	Chaitanya.iragavarapu@uky.edu
Institution name:	University of Kentucky
Academic rank:	Assistant Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

Aasems Jacob

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

- Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

None

Q13. PROPOSED WORKING COMMITTEE:

- Lymphoma

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

What are the outcomes with autologous hematopoietic stem cell transplant in peripheral T-cell lymphoma?

Q16. RESEARCH HYPOTHESIS:

Outcome from autologous hematopoietic transplant in mature T-cell non-Hodgkin lymphoma have improved since previously published results from 1996-2006 period and factors affecting outcome is still not understood.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

1. Determining the outcomes with autologous hematopoietic transplant (ASCT) in mature T-cell non-Hodgkin lymphoma between 2010-2021 including non-relapse mortality, relapse rates, progression free survival and overall survival.
2. Determine the factors determining outcome like age, comorbidities, different induction regimens, first CR vs. second or subsequent CR, type of peripheral T-cell lymphoma.

The study involves retrospective analysis of CIBMTR data between 2010 and 2021 among patients who meet the inclusion criteria. Outcome in each histologic type of peripheral T-cell lymphoma to be assessed individually. Probabilities of PFS and OS to be calculated using Kaplan-Meier product limit estimates. Probability of NRM, relapse/progression calculated using cumulative incidence curves. Associations between factors of interest to be assessed by multivariate Cox proportional hazards regression. Patients without disease relapse or progression to be censored at last follow-up. Factors of interest include age (65 and above/below 65, 70 and above/below 70), Race, ECOG/KPS, CI, conditioning regimen, year of transplant (2010-2015, 2015-2021), IPI score, PIT score, CNS involvement, CR1 vs. CR2 vs. subsequent CR . If sufficient number of patients not available in rarer subgroups to calculate effect of individual factors, they will be grouped together. Based on assumption PTCL-NOS, AITL, ALCL should be powered enough for determining effect.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Although autologous transplant is increasingly used in peripheral T cell lymphoma, the data available on outcome is outdated. Several questions in the field including selection of patients for autologous transplant, outcomes in different groups (age, comorbidity, IPI/PIT risk groups, types of lymphoma), ASCT at first vs. second/subsequent CR etc are unknown. Hematologists and patients currently make decision on a treatment with significant morbidity and healthcare expenditure involved without clear information. The study could change practice based on the difference in outcome in the above subgroups in deciding on appropriateness of ASCT. This study could also produce more thought-provoking questions prompting clinical trials in a disease with limited literature and prospective studies.

Q19. 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.

Peripheral T-cell lymphomas are a heterogenous group of lymphoid neoplasms of mature T cells and NK cells and constitute less than 15% of all Non-Hodgkin Lymphoma (NHL) in adults. It includes peripheral T cell lymphoma, unspecified (PTCL NOS), angioimmunoblastic T cell lymphoma (AITL), anaplastic large cell lymphoma, extranodal NK/T cell nasal type lymphoma, subcutaneous panniculitis-like T cell lymphoma, hepatosplenic T cell lymphoma and enteropathy associated T cell lymphoma. The poor outcomes in certain peripheral T-cell lymphoma after conventional chemotherapy generated interest in consolidation therapy.

From our extensive review of literature, the latest data available on outcomes with autologous stem cell transplant in T-cell non-Hodgkin lymphoma is from 2014 Swedish Lymphoma registry analysis by Ellin et al.(1) Latest available data from the US is a study published in 2013 by Smith et al which was an evaluation of CIBMTR with outcome data on 241 patients between 1996 to 2006.(2) This study had very limited number of patients with rarer conditions like angioimmunoblastic T-cell lymphoma, hepatosplenic T-cell lymphoma, and enteropathy associated T-cell lymphoma. Currently, it is not possible for a hematologist to discuss with the patient the true outcomes of any of these conditions with ASCT as medical care and supportive treatments have significantly improved reducing treatment related morbidity and mortality. Studies among myeloma patients have shown improvement in transplant related mortality over the years. (3) Our assumption is that outcomes with ASCT has significantly improved since the last available data published in 2013 and updated outcome data is required for patients and physicians to make an informed decision. For clinical purposes, we requested CIBMTR data on AITL and had outcome data on 1099 patients who underwent ASCT between 2008-2019 from 174 centers. Smith et al had 15 patients with AITL in their analysis. We believe that we could derive meaningful outcome data with the better sample size and more detailed information on factors affecting the outcome. Detailed evaluation of conditioning regimens and outcome change over the years also need to be assessed to guide hematologists in appropriate management of a group of patients who are not well represented in clinical trials.

1. Ellin F, Landstrom J, Jerkeman M, Relander T. Real-world data on prognostic factors and treatment in peripheral T-cell lymphomas: a study from the Swedish Lymphoma Registry. Blood. 2014;124(10):1570-7.
2. Smith SM, Burns LJ, van Besien K, Lerademacher J, He W, Fenske TS, et al. Hematopoietic cell transplantation for systemic mature T-cell non-Hodgkin lymphoma. J Clin Oncol. 2013;31(25):3100-9.
3. Nishimura KK, Barlogie B, van Rhee F, Zangari M, Walker BA, Rosenthal A, et al. Long-term outcomes after autologous stem cell transplantation for multiple myeloma. Blood Adv. 2020;4(2):422-31.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

1. Age: ≥18 years
2. Disease: Peripheral mature T cell lymphoma including
a. Peripheral T cell lymphoma, NOS (PTCL-NOS)
b. Angioimmunoblastic T cell lymphoma (AITL)
c. Anaplastic large cell lymphoma (ALCL), ALK positive
d. Anaplastic large cell lymphoma (ALCL), ALK negative
e. Enteropathy- associated T cell lymphoma
f. Extranodal NK/T cell nasal type lymphoma
g. Hepatosplenic T cell lymphoma
3. Disease stage: Any stage
4. Year of transplant: 2010-2021
5. Graft and donor types: First autologous hematopoietic stem cell transplant with any type of grafts
6. Prior treatments: any
7. Specific transplant regimens: none

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Outcomes of adult patients undergoing autologous stem cell transplant for peripheral T-cell lymphoma is unknown.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

1. Age: ≥18 years
2. Disease: Peripheral mature T cell lymphoma including
a. Peripheral T cell lymphoma, NOS (PTCL-NOS)
b. Angioimmunoblastic T cell lymphoma (AITL)
c. Anaplastic large cell lymphoma (ALCL), ALK positive
d. Anaplastic large cell lymphoma (ALCL), ALK negative
e. Enteropathy- associated T cell lymphoma
f. Extranodal NK/T cell nasal type lymphoma
g. Hepatosplenic T cell lymphoma
3. Disease stage: Any stage
4. Year of transplant: 2010-2021
5. Graft and donor types: First autologous hematopoietic stem cell transplant with any type of grafts
6. Prior treatments: any
7. Specific transplant regimens: none

Data Requirements

1. Data from forms required:
a. Form 2018 R6.0: Hodgkin and Non-Hodgkin Lymphoma Pre-Infusion Data
b. Form 2018 R5.0: Hodgkin and Non-Hodgkin Lymphoma Pre-Infusion Data
c. Form 2118 R4.0: Hodgkin and Non-Hodgkin Lymphoma Post-HCT Data
d. Form 2118 R3.0: Hodgkin and Non-Hodgkin Lymphoma Post-HCT Data
e. Form 095-LYM
f. Form 095-LYMFU
g. Form 002- DCI-LYM
2. No supplemental data required.
3. List of variables for each subtype of peripheral mature T cell lymphoma
a. Demographics: Age at transplant, Gender, Race/ethnicity
b. Clinical: Karnofsky/ECOG score at transplantation, Comorbidity Index
c. At Diagnosis: Histology, stage, IHC CD30+, number of extranodal sites involved, LDH
d. At transplant: Stage, platelet count, LDH, number of extranodal sites involved, Bone marrow involvement, CNS/CSF involvement, best response to treatment prior to transplant
e. Number of lines of therapy prior to transplant
f. Time from diagnosis to transplant
g. Transplant procedure: Year of transplant, conditioning regimen used, graft source
h. Follow up period
i. Status: Alive/Dead
j. Cause of death
4. Desired outcome variables
a. Non-relapse mortality (death as a result of any cause in the first 28 days of transplant or death without evidence of lymphoma relapse/progression, relapse to be considered a competing risk.) at 6 month and 1-year and 3-year.
b. Relapse/progression (progression/recurrence of lymphoma after complete remission, NRM considered competing event) at 6-months, 1-year, 3-year and 5-year.
c. Treatment failure (time of relapse, progression or death as a result of any cause)
d. Progression-free survival (PFS), a patient was considered a treatment failure at the time of progression/relapse or death from any cause. (Patients alive without evidence of disease relapse or progression to be censored at the last follow-up)
e. Overall survival

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

No PRO data required

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

No biologic samples required

Q25. 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, i.e., neither database contains all the data required to answer the study question.

CIBMTR Research Database will be the only data source use. No data linkage with external records required.

Q26. REFERENCES:

1. Ellin F, Landstrom J, Jerkeman M, Relander T. Real-world data on prognostic factors and treatment in peripheral T-cell lymphomas: a study from the Swedish Lymphoma Registry. Blood. 2014;124(10):1570-7.
2. Smith SM, Burns LJ, van Besien K, Lerademacher J, He W, Fenske TS, et al. Hematopoietic cell transplantation for systemic mature T-cell non-Hodgkin lymphoma. J Clin Oncol. 2013;31(25):3100-9.
3. Nishimura KK, Barlogie B, van Rhee F, Zangari M, Walker BA, Rosenthal A, et al. Long-term outcomes after autologous stem cell transplantation for multiple myeloma. Blood Adv. 2020;4(2):422-31.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1. Baseline characteristics for adult patients with T cell lymphoma received autoHCT during 2010-2021

Characteristic	N (%)
No. of patients	3461
No. of centers	237
Track - no. (%)	
TED	3125 (90.3)
CRF	336 (9.7)
Age at HCT - median (min-max)	57.7 (18.1-83.1)
Age at HCT - no. (%)	
18-29	204 (5.9)
30-39	290 (8.4)
40-49	523 (15.1)
50-59	960 (27.7)
60-69	1148 (33.2)
>=70	336 (9.7)
Recipient sex - no. (%)	
Male	2115 (61.1)
Female	1346 (38.9)
KPS - no. (%)	
90-100	2193 (63.4)
< 90	1183 (34.2)
Not reported	85 (2.5)
HCT-CI - no. (%)	
0	1100 (31.8)
1	469 (13.6)
2	503 (14.5)
3+	1266 (36.5)
Not reported	123 (3.6)
Race - no. (%)	
White	2472 (71.4)
Black or African American	366 (10.6)
Asian	195 (5.6)
Native Hawaiian or other Pacific Islander	7 (0.2)
Native American	15 (0.4)
Unknown	7 (0.2)
Not reported	399 (11.5)
Lymphoma histology - no. (%)	
PTCL	1269 (36.2)
AITL	1110 (31.8)
ALCL	1082 (23)

Characteristic	**N (%)**
Disease status prior to HCT (NHL/HD) - no. (%)	
CR	2565 (74.1)
PR	747 (21.6)
Chemoresistant	103 (3.0)
Untreated	4 (0.1)
Unknown	42 (1.2)
Graft type - no. (%)	
Bone marrow	14 (0.4)
Peripheral blood	3442 (99.5)
Not reported	5 (0.1)
Time from diagnosis to HCT - no. (%)	
< 12 months	2558 (74.0)
>= 12 months	895 (25.8)
Missing	8 (0.2)
Year of HCT - no. (%)	
2010	283 (8.2)
2011	252 (7.3)
2012	299 (8.6)
2013	309 (8.9)
2014	318 (9.2)
2015	352 (10.2)
2016	352 (10.2)
2017	348 (10.1)
2018	360 (10.4)
2019	353 (10.2)
2020	224 (6.5)
2021	11 (0.3)
Follow-up - median (range)	75.3 (1.6-267.6)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Bendamustine, etoposide, cytarabine, melphalan (BeEAM) vs. carmustine, etoposide, cytarabine, melphalan (BEAM) in relapsed B-cell lymphoma

Q2. Key Words

Bendamustine, autologous stem cell transplantation, lymphoma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Matthew Mei, MD
Email address:	mamei@coh.org
Institution name:	City of Hope
Academic rank:	Associate Clinical Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Alex Herrera, MD
Email address:	aherrera@coh.org
Institution name:	City of Hope
Academic rank:	Assistant Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Lymphoma

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Alex Herrera

Q15. RESEARCH QUESTION:

Does substituting bendamustine for carmustine in the most commonly used autologous transplant regimen BEAM (carmustine, etoposide, cytarabine, melphalan) result in improved outcomes in patients with lymphoma?

Q16. RESEARCH HYPOTHESIS:

Patients with relapsed B-cell lymphoma who undergo autologous stem cell transplant (ASCT) with bendamustine, etoposide, cytarabine, and melphalan (BeEAM) conditioning have superior progression-free survival (PFS) compared to patients who undergo ASCT with carmustine, etoposide, cytarabine, and melphalan (BEAM)

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

To compare the outcomes of patients with lymphoma who undergo ASCT with BeEAM vs. BEAM. For the purposes of the statistical analysis, the patients will be stratified by histology (Hodgkin lymphoma and non-Hodgkin lymphoma)
Primary Objective: Progression-free survival (PFS)
Secondary Objectives:
- Time to neutrophil and platelet engraftment
- Overall survival (OS)
- Cumulative incidence of non-relapse mortality (NRM)
- Cumulative incidence of disease relapse or progression
- Causes of death

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

This study could help establish BeEAM as a standard ASCT regimen for patients with lymphoma. This is a newer regimen with significant supporting data for safety and efficacy, but direct comparison with BEAM is still lacking. It could also support a randomized prospective trial of BeEAM vs. BEAM

Q19. 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.

ASCT is a commonly used treatment modality for lymphoma across a number of disease histologies. For instance, patients with relapsed and refractory Hodgkin lymphoma patients who undergo ASCT while in CR have an over 50% chance of cure. One of the most commonly used regimens at present is BEAM which is used across multiple histologies and at least in Hodgkin lymphoma appears to be superior to other commonly used regimens. Although overall quite safe, relapse remains a significant issue after BEAM-conditioned ASCT. To improve on the outcomes with BEAM-conditioned ASCT, substitution of bendamustine for carmustine (BeEAM) has been done. BeEAM was shown to be safe and effective with a 72% PFS in a group of patients with high-risk relapse with 0% 100-day TRM. Since then, it has been evaluated in multiple histologies. The Lymphoma Study Association (LYSA) studied BeEAM in chemosensitive relapsed follicular lymphoma (FL) with a 2-year PFS and OS of 70% and 90%, respectively. The Grupo Español de Linfomas y Trasplante Autólogo de Médula Ósea (GELTAMO) published results of BeEAM-conditioned ASCT in multiple histologies including follicular lymphoma, aggressive lymphoma (grade 3B FL, DLBCL, PTCL) in a single-arm phase 2 trial with a 3-year PFS/OS of 58%/75% respectively. Finally, the LYSA also retrospectively compared MCL patients who received BeEAM vs. BEAM conditioning for ASCT and found superior 3-year PFS with BeEAM vs. BEAM (84% vs 63%, p = 0.03).
Although 100-day mortality is low and comparable to results with BEAM, one unique toxicity with BeEAM is acute kidney injury which occurred in 46% of patients in the LYSA trial which is significantly more than what is seen in BEAM, and overall adverse events appear to be increased compared to BEAM in cross-trial comparisons. However, given promising efficacy results in smaller studies of BeEAM and increasing use of this regimen over the preceding decade, a retrospective analysis would help inform the choice of regimen.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion Criteria:
- Adult patients (≥ 18 years old) with B-cell lymphoma
- Patients must have undergone ASCT between 2012 – 2019.
- At least 2 prior lines of therapy prior to ASCT
- Conditioning regimen was either BeEAM or BEAM

Exclusion criteria:
- T-cell lymphoma
- ASCT in CR1
- Bone marrow graft

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Very few pediatric patients would have had this regimen (BeEAM).

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient characteristics (age, gender, KPS), disease-specific characteristics (disease histology, # of prior-line of therapy, disease status at ASCT). Outcome measures will include PFS, OS, NRM, relapse, and toxicities.

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/A

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

N/A

Q25. 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, i.e., neither database contains all the data required to answer the study question.

N/A

Q26. REFERENCES:

Chen Y-B, Lane AA, Logan BR, Zhu X, Akpek G, Aljurf MD, et al. Impact of Conditioning Regimen on Outcomes for Patients with Lymphoma Undergoing High-Dose Therapy with Autologous Hematopoietic Cell Transplantation. Biology of Blood and Marrow Transplantation. 2015;21(6):1046-53.

2. Visani G, Malerba L, Stefani PM, Capria S, Galieni P, Gaudio F, et al. BeEAM (bendamustine, etoposide, cytarabine, melphalan) before autologous stem cell transplantation is safe and effective for resistant/relapsed lymphoma patients. Blood. 2011;118(12):3419-25.

3. Visani G, Stefani PM, Capria S, Malerba L, Galieni P, Gaudio F, et al. Bendamustine, etoposide, cytarabine, melphalan, and autologous stem cell rescue produce a 72% 3-year PFS in resistant lymphoma. Blood. 2014;124(19):3029-31.

4. Ghesquières H, Dalban C, Nicolas-Virelizier E, Jardin F, Le Bras F, Le Gouill S, et al. BeEAM (bendamustine, etoposide, cytarabine, melphalan) prior to autologous stem cell transplant for chemosensitive relapses in patients with follicular lymphoma: a prospective multicentre phase II study in Lymphoma Study Association centres(†). British journal of haematology. 2021;192(3):e94-e8.

5. Redondo AM, Valcárcel D, González-Rodríguez AP, Suárez-Lledó M, Bello JL, Canales M, et al. Bendamustine as part of conditioning of autologous stem cell transplantation in patients with aggressive lymphoma: a phase 2 study from the GELTAMO group. British journal of haematology. 2019;184(5):797-807.

6. Hueso T, Gastinne T, Garciaz S, Tchernonog E, Delette C, Casasnovas R-O, et al. Bendamustine-EAM versus BEAM regimen in patients with mantle cell lymphoma undergoing autologous stem cell transplantation in the frontline setting: a multicenter retrospective study from Lymphoma Study Association (LYSA) centers. Bone Marrow Transplantation. 2020;55(6):1076-84.

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1. Baseline characteristics for adult patients who underwent ASCT for B cell lymphoma between 2017 – 2021.

Characteristic	BEAM	BEeam
No. of patients	3208	69
No. of centers	180	16
Track - no. (%)		
TED	2056 (68.7)	30 (90.9)
CRF	938 (31.3)	3 (9.1)
Age at infusion, yrs - median (min-max)	56.1 (18.0-83.7)	57.8 (19.1-73.9)
Age - no. (%)		
18-30	490 (15.3)	10 (14.5)
30-39	393 (12.3)	4 (5.8)
40-49	367 (11.4)	11 (15.9)
50-59	683 (21.3)	15 (21.7)
60-69	869 (27.1)	22 (31.9)
>70	406 (12.7)	7 (10.1)
Sex - no. (%)		
Male	1918 (59.8)	41 (59.4)
Female	1290 (40.2)	28 (40.6)
KPS - no. (%)		
90-100	1996 (62.2)	37 (53.6)
< 90	1118 (34.9)	29 (42.0)
Not reported	94 (2.9)	3 (4.3)
HCT-CI - no. (%)		
0	856 (26.7)	16 (23.2)
1	454 (14.2)	14 (20.3)
2	541 (16.9)	5 (7.2)
3+	1318 (41.1)	34 (49.3)
Not reported	39 (1.2)	0 (0)
Race - no. (%)		
White	2413 (75.2)	52 (75.4)
Black or African American	270 (8.4)	9 (13.0)
Asian	113 (3.5)	0 (0.0)
Native Hawaiian or other Pacific Islander	6 (0.2)	0 (0.0)
American Indian or Alaska Native	21 (0.7)	3 (4.3)
More than one race	8 (0.2)	0 (0.0)
Not reported	377 (11.8)	5 (7.2)
Disease type- no. (%)		
DLBCL	1573 (49.0)	35 (50.7)
Mantle Cell Lymphoma	89 (2.8)	3 (4.3)
Follicular Lymphoma	269 (8.4)	6 (8.7)
Hodgkin Lymphoma	1277 (39.8)	25 (36.2)
Disease status- no. (%)		

Characteristic	BEAM	BEeam
CR2+	1831 (57.1)	26 (37.7)
PR	1177 (36.7)	39 (56.5)
Resistant	180 (5.6)	2 (2.9)
Untreated	4 (0.1)	0 (0.0)
Unknown	16 (0.5)	2 (2.9)
Time from diagnosis to HCT- no. (%)		
0-6 months	143 (4.5)	4 (5.8)
6-12 months	479 (14.9)	11 (15.9)
>=12 months	2585 (80.6)	54 (78.3)
Not reported	1 (0.0)	0 (0.0)
HCT year - no. (%)		
2017	202 (6.3)	1 (1.4)
2018	1089 (33.9)	8 (11.6)
2019	1157 (36.1)	24 (34.8)
2020	726 (22.6)	36 (52.2)
2021	34 (1.1)	0 (0.0)
Follow-up - median (range)	14.4 (0.6-50.4)	12.2 (3.7-26.3)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Chimeric Antigen Receptor T-cell Therapy versus Autologous Hemopoietic Cell Transplantation for Relapsed Myc-Rearranged DLBCL in Partial or Complete Remission

Q2. Key Words

high-grade B-cell lymphoma, double-hit lymphoma, myc-rearrangement, CAR T-cell therapy, autologous transplant, diffuse large B-cell lymphoma, relapsed/refractory

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Joanna Zurko MD
Email address:	jzurko@mcw.edu
Institution name:	Medical College of Wisconsin
Academic rank:	Hematology & Oncology fellow, third year

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Mehdi Hamadani
Email address:	mhamadani@mcw.edu
Institution name:	Medical College of Wisconsin
Academic rank:	Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

Joanna Zurko MD

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Lymphoma

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Mehdi Hamadani MD

Q15. RESEARCH QUESTION:

In patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) with myc-rearrangement or high-grade b-cell lymphoma with myc and bcl2 and/or bcl6 rearrangements (double hit lymphoma [DHL]/triple hit lymphoma [THL]) who achieve a complete response (CR) or partial response (PR) with salvage therapy, does anti-CD19 chimeric antigen receptor T-cell therapy lead to similar or improved outcomes compared to autologous hematopoietic cell transplantation (autoHCT)?

Q16. RESEARCH HYPOTHESIS:

In patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) with myc-rearrangement or high-grade b-cell lymphoma with myc and bcl2 and/or bcl6 rearrangements (double hit lymphoma [DHL]/triple hit lymphoma [THL]) who achieve a complete response (CR) or partial response (PR) with salvage therapy, anti-CD19 chimeric antigen receptor T-cell therapy may lead to equivalent or improved outcomes compared to autologous hematopoietic cell transplantation (autoHCT).

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.) *Suggested word limit of 200 words:*

To compare outcomes of patients with DLBCL with myc-rearrangement or high-grade b-cell lymphoma with myc and bcl2 and/or bcl6 rearrangements who receive either commercial CAR T-cell therapy or autoHCT after achieving a CR or PR after salvage chemotherapy for R/R disease.

• Primary outcome will be to evaluate progression-free survival (PFS), overall survival (OS), non-relapse mortality (NRM), and relapse rates.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Whether there is any benefit to CAR T-cell therapy over autoHCT in patients who achieve a CR or PR with salvage chemotherapy for R/R myc-positive DLBCL is unclear. There is evidence that patients with double hit lymphoma (DHL) or triple hit lymphoma (THL) have worse PFS and OS than other subgroups overall and with autoHCT. This analysis would help inform treatment decisions for physicians and guide further research when treating this high-risk population.

Q19. 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.

There was a recent analysis of autoHCT versus CAR T-cell therapy in DLBCL patients who achieve a PR as best response to salvage therapy, with superior overall survival and a lower rate of relapse/progression demonstrated with consolidation with autoHCT [1]. Nonetheless, there was no analysis how the subgroup of patients with myc-rearranged DLBCL (single hit lymphoma) or DHL/THL and fared with autoHCT versus CAR T-cell therapy in this analysis. This an important subgroup to analyze given that outcomes of patients with DHL compared to non-DHL are worse after autoHCT with a 4-year PFS of 28% vs 57% and a 4-year OS of 25% vs 61% [2]. Despite the aggressive nature of DHL/THL, these patients have high ORRs with CAR T-cell therapy [3] with a 90% ORR in the seven patients with high grade B-cell lymphoma/DHL treated on ZUMA-1, although longer term survival data in these patients is lacking. ZUMA-7, TRANSFORM, and BELINDA are all phase 3 trials comparing CAR T-cell therapy (axicabtagene ciloleucel, lisocabtagene maraleucel and tisagenlecleucel respectively) with salvage chemotherapy and autoHCT in patients with R/R DLBCL in the second line setting. Nonetheless, these data are still immature and even if these studies ultimately do show a benefit to second line CAR T-cell therapy, they do not answer the question of what to do if patients achieve a CR or PR with salvage chemoimmunotherapy. The available data suggests that patients with single hit and DHL/THL have worse outcomes with autoHCT but maintain high responses to CAR T-cell therapy; therefore, determining if CAR-T in the second line in patients who achieve a CR or PR with salvage leads to better outcomes is important to determine.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Patient eligibility population:
Inclusion criteria:
• Received autoHCT from 2013 to 2020 or anti-CD19 CAR T-cell therapy from 2017 to 2020
• Adults 18 years of age at the time of transplant or CAR T-cell therapy
• Diagnosis of R/R DLBCL with myc rearrangement or high-grade b-cell lymphoma with myc and bcl2 and/or bcl6 rearrangements
• Achieve a CR or PR with salvage therapy
Exclusion criteria:
• Prior autoHCT
• Prior CAR T-cell therapy
• Prior allogeneic hematopoietic cell transplantation

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

There is not an approval for CAR-T in this setting

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Data requirements:
• Data will be captured through CIBMTR collection forms
Demographic/patient level variables to be analyzed:
Main effect:
Compare survival outcomes of patients with R/R DLBCL with myc rearrangement with achieve a CR or PR with salvage therapy and undergo CAR T-therapy versus autoHCT.
Patient-related:
• Age at CAR-T or autoHCT (<60 or ≥60)
• Gender: male or female
Disease-related:
• R-IPI
• Single hit (myc-arrangement alone) or double/triple hit (myc and bcl2 and/or bcl6 rearrangements)
• Disease stage at diagnosis: I/II vs III/IV
• Extranodal disease (at diagnosis)
• Lines of therapy prior to autoHCT or CAR-T
• Refractory to first line treatment
• Interval between diagnosis and autoHCT or CAR-T (≥12 months or <12 months)
• Time to relapse (≥12 months or <12 months) [in those without primary refractory disease]
• CNS disease at diagnosis or at relapse
• Response to salvage (CR or PR)
Transplant-related
• Conditioning regimen or lymphodepletion regimen
• Karnofsky performance status at autoHCT or CAR-T: < 90% vs. ≥ 90%

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

n/a

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

n/a

Q25. 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, i.e., neither database contains all the data required to answer the study question.

n/a

Q26. REFERENCES:

1. Shadman, M., et al., Autologous Transplant versus Chimeric Antigen Receptor T-cell Therapy for Relapsed DLBCL in Partial Remission. Blood, 2021.
2. Herrera, A.F., et al., Relapsed or Refractory Double-Expressor and Double-Hit Lymphomas Have Inferior Progression-Free Survival After Autologous Stem-Cell Transplantation. J Clin Oncol, 2017. 35(1): p. 24-31.
3. Jacobson, C.A., et al., Axicabtagene Ciloleucel in the Non-Trial Setting: Outcomes and Correlates of Response, Resistance, and Toxicity. J Clin Oncol, 2020. 38(27): p. 3095-3106.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1. Baseline characteristics for R/R DLBCL with myc rearrangement or high-grade b-cell lymphoma with myc and bcl2 and/or bcl6 rearrangements received autoHCT from 2015 to 2021 or CAR T-cell therapy from 2017 to 2021

Characteristic	CAR-T	autoHCT
No. of patients	123	272
No. of centers	52	90
Age at infusion, yrs - median (min-max)	62.9 (24.9-90.8)	62.1 (28.1-79.6)
Age - no. (%)		
18-29	1 (0.8)	2 (0.7)
30-39	9 (7.3)	9 (3.3)
40-49	12 (9.8)	31 (11.4)
50-59	21 (17.1)	69 (25.4)
60-69	49 (39.8)	117 (43.0)
>=70	31 (25.2)	44 (16.2)
Recipient Sex - no. (%)		
Male	68 (55.3)	172 (63.2)
Female	55 (44.7)	100 (36.8)
KPS - no. (%)		
90-100	56 (45.5)	142 (52.2)
< 90	55 (44.7)	118 (43.4)
Not reported	12 (9.8)	12 (4.4)
HCT-CI - no. (%)		
0	35 (28.5)	73 (26.8)
1	26 (21.1)	46 (16.9)
2	22 (17.9)	33 (12.1)
3+	32 (26.0)	117 (43.0)
Not reported	8 (6.5)	3 (0.0)
Recipient race - no. (%)		
White	94 (76.4)	202 (74.3)
African-American	5 (4.1)	13 (4.8)
Asian	6 (4.9)	9 (3.3)
Pacific Islander	1 (0.8)	0 (0.0)
Native American	0 (0.0)	1 (0.4)
More than one race	1 (0.8)	0 (0.0)
Unknown	9 (7.3)	0 (0.0)
Not reported	7 (5.7)	47 (17.3)
Disease status prior to CT - no. (%)		
CR	21 (17.1)	203 (74.6)
PR	102 (82.9)	69 (25.4)
Number of lines of prior therapy - no. (%)		
1	4 (3.3)	85 (31.3)
2+	114 (92.7)	163 (59.9)

Table 1. Baseline characteristics for R/R DLBCL with myc rearrangement or high-grade b-cell lymphoma with myc and bcl2 and/or bcl6 rearrangements received autoHCT from 2015 to 2021 or CAR T-cell therapy from 2017 to 2021

Characteristic	CAR-T	autoHCT
Missing	5 (4.0)	24 (8.8)
Time from diagnosis to CT - no. (%)		
<12 month	73 (59.3)	186 (68.4)
>=12 month	50 (40.7)	86 (31.6)
Year of CT - no. (%)		
2015	0 (0.0)	10 (3.7)
2016	0 (0.0)	6 (2.2)
2017	0 (0.0)	12 (4.4)
2018	13 (10.6)	88 (32.4)
2019	38 (30.9)	98 (36.0)
2020	44 (35.8)	55 (20.2)
2021	28 (22.8)	3 (1.1)
Follow-up - median (range)	13.2 (1.0-36.5)	14.8 (1.2-74.6)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Autologous Hematopoietic Stem Cell Transplantation for Intravascular Large B-cell Lymphoma (IVLBCL): a CIBMTR registry analysis

Q2. Key Words

intravascular large B-cell lymphoma (IVLBCL); autologous stem cell transplantation; overall survival; progression-free survival

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Praveen Ramakrishnan Geethakumari, MD, MS
Email address:	praveen.ramakrishnan@utsouthwestern.edu
Institution name:	UT Southwestern Medical Center
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Farrukh T. Awan, MD, MS
Email address:	Farrukh.awan@utsouthwestern.edu
Institution name:	UT Southwestern Medical Center
Academic rank:	Associate Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

Praveen Ramakrishnan Geethakumari, MD

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

Determinants of outcomes after CAR T cells for Lymphoma (study number: CT20-03) - Co-investigator

Q13. PROPOSED WORKING COMMITTEE:

- Lymphoma

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Mehdi Hamadani, MD

Q15. RESEARCH QUESTION:

Does autologous stem cell transplantation improve survival outcomes in patients with intravascular large B-cell lymphoma?

Q16. RESEARCH HYPOTHESIS:

Consolidative high dose chemotherapy and autologous stem cell transplantation (SCT) for patients with intravascular large B-cell lymphoma (IVLBCL) improves overall (OS) and progression-free (PFS) survival, compared to chemo-immunotherapy alone.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary Objectives:
To analyze the survival outcomes of patients with intravascular large B-cell lymphoma treated with autologous hematopoietic stem cell transplantation (autoSCT).
Secondary Objectives:
To study the impact of the timing of autoSCT in managing IVLBCL (CR1 vs PR vs ≥CR2)
The following outcomes will be evaluated:
Primary Outcomes
Overall survival: Time to death. Death from any cause will be considered an event. Surviving patients will be censored at the time of last follow up.
Secondary Outcomes
Progression-free survival: Survival following autoSCT without relapse or progression. Relapse or progression of disease are considered events.
Non-relapse mortality: Cumulative incidence of NRM. NRM is defined as death without preceding disease relapse/progression. Relapse and progression are competing events.
Relapse/progression: Progressive disease or recurrence(s) of disease would be counted as events. Treatment related death, defined as death without relapse or progression, is the competing event. Those who survive without recurrence or progression would be censored at the time of last contact.
Causes of death: Transplant-related, infection, relapsed disease, second malignancy or other.

Q18. 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 optimal treatment strategy for patients with intravascular large B-cell lymphoma (IVLBCL) is not established and prognosis for this aggressive disease remains guarded. Current day practice is largely guided by small retrospective studies and phase 2 trial data. Only limited data exist exploring the role of HSCT in this rare, aggressive disease entity. A comprehensive CIBMTR registry analysis of the outcomes of patients with IVLBCL undergoing consolidative autologous stem cell transplantation has not been performed. The EBMT experience was published in 2017 exploring autoHSCT in IVLBCL and showed promising 2-year survival outcomes compared to historical chemotherapy-alone cohorts.[1] A larger current-day CIBMTR registry analysis would enable analysis of practice patterns and the clinical experience to date. The findings of this analysis could impact practice guidelines for managing IVLBCL and aid in design of future clinical trials.

Q19. 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.

Intravascular large B-cell lymphoma (IVLBCL) is a rare, aggressive extra-nodal large B-cell lymphoma characterized by the predominant growth of large neoplastic B-cells within the lumina of different-sized blood vessels. [2] Due to the rarity of the disease, most published data is based on case reports and series, with only a few retrospective global and registry analyses performed to date. This disease has been nicknamed the "oncologist's great mimicker" and a "chameleon with multiple faces and masks" due to the inherent difficulty in diagnosing the disease, aggressive multi-system involvement and thus up to 40% cases being diagnosed at autopsy. Based on clinical presentation, 3 different variants have been described: (1) classical variant with predominant cutaneous and nervous system involvement seen mostly in Western countries, (2) hemophagocytosis syndrome (HLH)-associated variant seen mainly in Asia, and the rarer (3) cutaneous variant comprising 25% of all IVLBCL and having a more favorable outcome.[2,3] The molecular biology of the disease is being unearthed and targeted IHC and NGS approaches have shown most cases to be of non-geminal center phenotype (75-80%), and harbor high CD5 positivity (22-38%), higher frequencies of MyD88 L265P (44%) and CD79b Y196 (26%) mutations, and immune evasion markers with high PD-L1/PD-L2 over expression.[4-6]
There are no established standards-of-care for the management of IVLBCL due to the lack of randomized prospective trials and survival outcomes remain unsatisfactory. Rituximab-based chemo-immunotherapy regimens have shown to have improved outcomes over traditional chemotherapy alone. With induction R-CHOP therapy, 2-year PFS and OS of 56% and 66% have been reported from Japan [7] and a 3-year OS of up to 81% from the West.[8,9] A SEER database analysis of IVLBCL in the US showed 3 – and 5-year OS of 51.8% and 46.3%. respectively.[10] In a recent phase 2, multicenter, single-arm PRIMEUR-IVL trial, conducted in Japan, the addition of CNS prophylaxis with intrathecal and intravenous high-dose methotrexate showed a 2-year PFS of 76% and a CNS-relapse rate of 3%.[11]
The favorable experience with high-dose chemotherapy and autologous hematopoietic stem cell transplantation (autoSCT) has been reported in IVBCL both in CR1 and at relapse, mostly though in small case series. In the rituximab-era, long term remissions post autoSCT have been reported from Asia.[12,13] The EBMT experience of autoSCT in IVLBCL from 2002-2013 was published in 2017.[1] The final cohort had 11 patients with a median age of 55 years (range: 34-65). All patients had stage IV disease with CNS involvement reported in five. Seven patients received autoSCT in CR1 and 3 at relapse, with the median time from diagnosis to autoSCT of 6 months (range: 4-31). The most common conditioning regimen employed was BEAM (5/11 patients). Eight patients were alive and free of progression at a median follow up of 51 months. Two patients who relapsed had undergone autoSCT after >1 prior therapy. Two-year PFS and OS were 81% and 91% respectively. Thus, in this registry analysis, autoSCT was safe and effective and associated with a favorable outcome compared to R-CHOP chemotherapy alone. A recent retrospective study from Korea also supported these findings with the efficacy of autoSCT dampened in relapsed disease, compared to upfront consolidation.[14]
The optimal conditioning regimen, timing, and outcomes of stem cell transplantation in the management of IVLBCL is unclear. Most published evidence is from phase II studies that show efficacy of consolidative HSCT and have not shown superiority of one preparatory regimen over other. Thus, although up to one-half of all patients with IVLBCL could be eligible for HSCT as the median age at diagnosis is 70 years, several eligible patients may not be receiving autologous HSCT in CR1 due to this lack of consensus in practice guidelines. Allogeneic stem cell transplantation has shown efficacy only in a select group of patients with relapsed/refractory IVLBCL.[15]
We therefore propose a retrospective evaluation of the outcomes of patients undergoing autoSCT for IVLBCL utilizing the CIBMTR registry.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion Criteria
• Adults ≥ 18 years of age at the time of stem cell transplantation
• Diagnosis of intravascular large B-cell lymphoma (IVLBCL)
• Autologous stem cell transplantation during the years January 2000- December 2020
Exclusion Criteria
• Diagnosis of intravascular T-cell or NK-cell lymphoma

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

IVLBCL is a disease of older adults with a median age at diagnosis of 70-years.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient-related:
• Age at transplant/cellular therapy, Continuous & by age group: decades
• Patient sex: male vs. female
• Karnofsky performance status: ≥ 90 vs. < 90 vs. missing
• HCT comorbidity index: 0 vs 1-2 vs ≥ 3 vs. missing
• Race: Caucasian vs. others vs. missing
Disease-related:
• Remission status at HSCT: CR1 vs ≥CR2 vs PR vs. refractory vs. untreated/unknown
• IVBCL variant: classical vs HLH-associated vs cutaneous
• Type of CNS involvement: parenchymal vs leptomeningeal vs both
• Number of prior regimens of therapy: ≤1 vs ≥2
• History of prior radiation use: no vs yes
• Time from diagnosis to HCT: ≥12 months vs.<12 months
Transplant/cellular therapy-related:
• Graft source: peripheral blood vs. bone marrow
• Conditioning regimen for autoSCT: BEAM vs BCNU-thiotepa vs TBC vs other
• Thiotepa used in conditioning: yes vs. no vs. missing
• Year of transplant: Continuous

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/A

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

No biologic samples required.

Q25. 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, i.e., neither database contains all the data required to answer the study question.

N/A

Q26. REFERENCES:

1 Meissner, J. et al. Autologous hematopoietic stem cell transplantation for intravascular large B-cell lymphoma: the European Society for Blood and Marrow Transplantation experience. Bone Marrow Transplant 52, 650-652, doi:10.1038/bmt.2016.339 (2017).
2 Ponzoni, M., Campo, E. & Nakamura, S. Intravascular large B-cell lymphoma: a chameleon with multiple faces and many masks. Blood 132, 1561-1567, doi:10.1182/blood-2017-04-737445 (2018).
3 Ferreri, A. J. et al. Variations in clinical presentation, frequency of hemophagocytosis and clinical behavior of intravascular lymphoma diagnosed in different geographical regions. Haematologica 92, 486-492, doi:10.3324/haematol.10829 (2007).
4 Schrader, A. M. R. et al. High prevalence of MYD88 and CD79B mutations in intravascular large B-cell lymphoma. Blood 131, 2086-2089, doi:10.1182/blood-2017-12-822817 (2018).
5 Shimada, K. et al. Frequent genetic alterations in immune checkpoint-related genes in intravascular large B-cell lymphoma. Blood 137, 1491-1502, doi:10.1182/blood.2020007245 (2021).
6 Suzuki, Y. et al. PD-L1 (SP142) expression in neoplastic cells predicts a poor prognosis for patients with intravascular large B-cell lymphoma treated with rituximab-based multi-agent chemotherapy. Cancer Med 9, 4768-4776, doi:10.1002/cam4.3104 (2020).
7 Murase, T. et al. An Asian variant of intravascular large B-cell lymphoma: clinical, pathological and cytogenetic approaches to diffuse large B-cell lymphoma associated with haemophagocytic syndrome. Br J Haematol 111, 826-834 (2000).
8 Ferreri, A. J. et al. The addition of rituximab to anthracycline-based chemotherapy significantly improves outcome in 'Western' patients with intravascular large B-cell lymphoma. Br J Haematol 143, 253-257, doi:10.1111/j.1365-2141.2008.07338.x (2008).
9 Ferreri, A. J. et al. Can rituximab change the usually dismal prognosis of patients with intravascular large B-cell lymphoma? J Clin Oncol 26, 5134-5136; author reply 5136-5137, doi:10.1200/JCO.2008.19.1841 (2008).
10 Rajyaguru, D. J., Bhaskar, C., Borgert, A. J., Smith, A. & Parsons, B. Intravascular large B-cell lymphoma in the United States (US): a population-based study using Surveillance, Epidemiology, and End Results program and National Cancer Database. Leuk Lymphoma 58, 1-9, doi:10.1080/10428194.2017.1287363 (2017).
11 Shimada, K. et al. Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone combined with high-dose methotrexate plus intrathecal chemotherapy for newly diagnosed intravascular large B-cell lymphoma (PRIMEUR-IVL): a multicentre, single-arm, phase 2 trial. Lancet Oncol 21, 593-602, doi:10.1016/S1470-2045(20)30059-0 (2020).
12 Kato, K. et al. Long-term remission after high-dose chemotherapy followed by auto-SCT as consolidation for intravascular large B-cell lymphoma. Bone Marrow Transplant 49, 1543-1544, doi:10.1038/bmt.2014.189 (2014).
13 Sawamoto, A. et al. Long-term remission after autologous peripheral blood stem cell transplantation for relapsed intravascular lymphoma. Bone Marrow Transplant 37, 233-234, doi:10.1038/sj.bmt.1705220 (2006).
14 Yoon, S. E., Kim, W. S. & Kim, S. J. Asian variant of intravascular large B-cell lymphoma: a comparison of clinical features based on involvement of the central nervous system. Korean J Intern Med 35, 946-956, doi:10.3904/kjim.2018.396 (2020).
15 Miura, Y. et al. Successful myeloablative unrelated bone marrow transplantation for relapsed intravascular large B cell lymphoma after autologous peripheral blood stem cell transplantation. Ann Hematol, doi:10.1007/s00277-020-04315-9 (2020).

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1. Baseline characteristics for adult patients with intravascular large B-cell lymphoma received autoHCT during 2000-2020

Characteristic	N (%)
No. of patients	38
No. of centers	27
Track - no. (%)	
TED	29 (76.3)
CRF	9 (23.7)
Age at HCT - median (min-max)	61.6 (28.7-75.5)
Age at HCT - no. (%)	
18-29	1 (2.6)
40-49	2 (5.3)
50-59	13 (34.2)
60-69	16 (42.1)
>=70	6 (15.8)
Recipient sex - no. (%)	
Male	19 (50.0)
Female	19 (50.0)
KPS - no. (%)	
90-100	18 (47.4)
< 90	19 (50.0)
Not reported	1 (2.6)
HCT-CI - no. (%)	
0	16 (42.1)
1	5 (13.2)
2	7 (18.4)
3+	10 (26.4)
Race - no. (%)	
White	22 (57.9)
Black or African American	1 (2.6)
Asian	9 (23.7)
Not reported	6 (15.8)
Disease status prior to HCT (NHL/HD) - no. (%)	
CR	29 (76.3)
PR	9 (23.7)
Graft type - no. (%)	
Peripheral blood	38 (100)
Time from diagnosis to HCT - no. (%)	
0-12 months	24 (63.2)
>12 months	14 (36.8)
Conditioning regimen - no. (%)	

Characteristic	**N (%)**
Bu/Cy	6 (15.8)
Bu/Mel	2 (5.3)
Flu/Bu	1 (2.6)
CBV	5 (13.2)
BEAM	19 (50.0)
Mel/other(s)	3 (7.9)
Other(s)	2 (5.3)
Year of HCT - no. (%)	
2012	1 (2.6)
2013	2 (5.3)
2014	6 (15.8)
2015	6 (15.8)
2016	6 (15.8)
2017	7 (18.4)
2018	4 (10.5)
2019	4 (10.5)
2020	2 (5.3)
Follow-up - median (range)	48.1 (3.5-73.7)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Impact of pre-leukapheresis bendamustine-containing therapies on outcomes of CD19 CAR T-cell therapy for large B-cell lymphoma

Q2. Key Words

CAR T cell therapy; DLBCL; bendamustine; bridging therapy

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Jordan Gauthier, MD, MSc
Email address:	jgauthier@fredhutch.org
Institution name:	Fred Hutch
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	N/A
Email address:	N/A
Institution name:	N/A
Academic rank:	N/A

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

N/A

Q8. Do you identify as an underrepresented/minority?

N/A

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Cellular Immunotherapy for Cancer

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

To investigate the impact of pre-leukapheresis therapies – specifically bendamustine-containing regimens – on outcomes of CD19 CAR T-cell therapy for relapsed or refractory (R/R) large B-cell lymphoma (LBCL).

Q16. RESEARCH HYPOTHESIS:

We would like to test the hypothesis that bendamustine-containing regimens administered prior to leukapheresis are associated with worse outcomes after CD19 CAR T-cell therapy for R/R LBCL compared to alternative regimens.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

- Primary endpoint: complete response rate (at time of best response)
- Secondary endpoints:
- Overall response rate (at time of best response)
- Duration of response after CD19 CAR T-cell therapy
- Progression-free and overall survival after CD19 CAR T-cell therapy
- CRS incidence and severity
- ICANS incidence and severity

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Confirmation that Bendamustine-based regimens should be avoided prior to leukapheresis will significantly impact current practice, guiding the choice of bridging therapies for CAR T cell patients, and potentially improving outcomes of CD19 CAR T-cell therapy for R/R LBCL.

Q19. 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.

• Bendamustine-based regimens are very common salvage therapies for patients with relapsed or refractory large B cell lymphoma (e.g., polatuzumab-bendamustine-rituximab [Sehn et al, J Clin Oncol, 2020], bendamustine-etoposide-carboplatin [Budde et al, Br J Haematol 2018).
• Bendamustine is known to induce prolonged CD4+ lymphopenia (Ohmachi et al, J Clin Oncol 2013; Martinez-Calle et al, Br J Haematol, 2019; Gaiolla et al Hematol Oncol 2021) and to profoundly alter T cell function (Duell et al J Immunother 2019; Stokes et al, Cancers 2021). Recognizing its lymphotoxic ability, bendamustine has been used successfully as lymphodepleting chemotherapy prior to CAR-T administration (tisagenlecleucel; Schuster et al, NEJM, 2019).
• With these recognitions, the possibility exists that bendamustine administered prior to leukapheresis for CD19 CAR T-cell manufacturing could have a detrimental impact on the eventual anti-tumor effects of CAR T-cell therapy.
• There is to our knowledge no published data or ongoing analysis addressing this specific question.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

• Age > 18
• DLBCL, NOS DLBCL, high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements, transformed follicular lymphoma
• Treatment with an FDA-approved, commercially-available CD19 CAR T-cell product (ie, axicabtagene ciloleucel, tisagenlecleucel, lisocabtagene maraleucel).

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

FDA labels do not include pediatric NHL.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

List of variables for descriptive statistics and multivariable modeling:
• Key variables:
• Type of prior therapies (bendamustine-containing versus other) – Form 2018R6
• Number of cycles of bendamustine-containing regimen – Form 2018R6
• Time between last bendamustine-containing regimen and leukapheresis – Form 2018R6, 4003R4
• Time between last salvage chemotherapy regimen and leukapheresis – Form 2018R6, 4003R4
• Prior auto HCT- yes or no
• ALC prior to lymphodepletion chemotherapy – Form 4000R8
• Commercial product out of specification – Form 4003R4
• Standard patient/disease characteristics:
• Age
• HCT-CI
• Karnofsky performance status
• Refractoriness to first line
• Number of prior therapies
• Interval between diagnosis and CAR T-cell therapy
• Response to last therapy
• Largest node prior to lymphodepletion chemotherapy
• LDH prior to lymphodepletion chemotherapy

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

Not applicable

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

Not applicable

Q25. 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, i.e., neither database contains all the data required to answer the study question.

Not applicable

Q26. REFERENCES:

Sehn et al, J Clin Oncol, 2020
Budde et al, Br J Haematol 2018
Ohmachi et al, J Clin Oncol 2013
Martinez-Calle et al, Br J Haematol, 2019
Gaiolla et al Hematol Oncol 2021
Duell et al J Immunother 2019
Stokes et al, Cancers 2021
Schuster et al, NEJM 2019

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- Yes, I have conflicts of interest pertinent to this proposal

Q27a. 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.

- Consulting: Eusapharma, JMP, Larvol, Multerra Bio
- Advisory board: Legend Biotech/Janssen
- Research Funding: Sobi, Juno Therapeutics

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1. Baseline characteristics for adult patients with large B-cell lymphoma received CD19 CAR T-cell therapy during 2017-2021

Characteristic	Without Bridging Therapy	With Bridging Therapy
No. of patients	2223	766
No. of centers	119	102
Age at infusion, yrs - median (min-max)	63.6 (19.6-89.0)	62.8 (19.0-90.8)
Age - no. (%)		
18-29	56 (2.5)	22 (2.9)
30-39	112 (5.0)	38 (5.0)
40-49	187 (8.4)	74 (9.7)
50-59	490 (22.0)	174 (22.7)
60-69	805 (36.2)	276 (36.0)
>=70	573 (25.8)	182 (23.8)
Recipient Sex - no. (%)		
Male	1366 (61.4)	485 (63.3)
Female	857 (38.6)	281 (36.7)
Performance score prior to CT - no. (%)		
90-100	930 (41.8)	272 (35.5)
< 90	1033 (46.5)	410 (53.5)
Not reported	260 (11.7)	84 (11.0)
HCT-CI - no. (%)		
0	647 (29.1)	212 (27.7)
1	450 (20.2)	136 (17.8)
2	314 (14.1)	105 (13.7)
3+	681 (30.6)	268 (35.0)
Not reported	131 (5.9)	45 (5.9)
Recipient race - no. (%)		
White	1736 (78.1)	603 (78.7)
African American	105 (4.7)	32 (4.2)
Asian	151 (6.8)	57 (7.4)
Pacific Islander	4 (0.2)	2 (0.3)
Native American	6 (0.3)	2 (0.3)
More than one race	11 (0.5)	4 (0.5)
Not reported	110 (9.5)	66 (8.6)
Disease status prior to CT - no. (%)		
CR	104 (4.7)	24 (3.1)
PR	447 (20.1)	161 (21.0)
Resistant	1431 (64.4)	524 (68.4)
Untreated	147 (6.6)	14 (1.8)
Unknown	94 (4.2)	43 (5.6)
Number of prior therapies - no. (%)		
1	145 (6.5)	25 (3.3)

Characteristic	Without Bridging Therapy	With Bridging Therapy
2	705 (31.7)	35 (4.6)
>=3	1358 (61.1)	706 (92.2)
Missing	15 (0.7)	0 (0)
Bendamustine-containing therapies - no. (%)	433 (19.5)	239 (10.8)
Time from diagnosis to CT - no. (%)		
<12 months	830 (37.3)	374 (48.8)
>=12 months	1392 (62.6)	392 (51.2)
Not reported	1 (0.0)	0 (0.0)
Year of CT - no. (%)		
2017	5 (0.2)	0 (0.0)
2018	373 (16.8)	96 (12.5)
2019	644 (29.0)	230 (30.0)
2020	735 (33.1)	256 (33.4)
2021	466 (21.0)	184 (24.0)
Follow-up - median (range)	12.6 (0.9-41.1)	12.5 (1.0-39.2)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Risk of therapy-related myeloid neoplasm (t-MN) following autologous hematopoietic cell transplantation (auto-HCT) for relapsed and refractory diffuse large B-cell lymphoma (DLBCL): A comparison of platinum-containing salvage regimens

Q2. Key Words

therapy-related myeloid neoplasm, clonal hematopoiesis, lymphoma, salvage

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Mariam Nawas MD
Email address:	nawasm@bsd.uchicago.edu
Institution name:	University of Chicago
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Michael Scordo MD
Email address:	scordom@mskcc.org
Institution name:	Memorial Sloan Kettering Cancer Center
Academic rank:	Assistant Attending

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

Mariam Nawas

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

n/a

Q13. PROPOSED WORKING COMMITTEE:

- Lymphoma

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Craig Sauter and Mehdi Hamadani

Q15. RESEARCH QUESTION:

Do rates of therapy-associated myeloid neoplasm (t-MN) after autologous hematopoietic cell transplantation (auto-HCT) differ among patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) based on the salvage regimen used?

Q16. RESEARCH HYPOTHESIS:

We hypothesize that t-MN rates after auto-HCT with BCNU, etoposide, Ara-C, and melphalan (BEAM) conditioning in patients with relapsed or refractory DLBCL are higher in patients who received ifosfamide/carboplatin/etoposide (ICE) salvage therapy compared to other platinum-containing salvage regimens.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Aim 1: Compare the incidences of t-MN after auto-HCT with BEAM conditioning in patients receiving platinum-based salvage regimens for relapsed or refractory DLBCL.
a. Specifically, the main comparison will be (rituximab) ICE vs. all other non-carboplatin containing platinum-based salvage regimens (e.g., DHAX, DHAP, ESHAP, GDP, Gem-Ox)
Aim 2: Compare the differences in non-relapse mortality (NRM) after auto-HCT with BEAM conditioning in patients with relapsed or refractory DLBCL based on salvage regimen received.
Aim 3: Compare causes of death after auto-HCT with BEAM conditioning in patients with relapsed or refractory DLBCL based on salvage regimen received.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

t-MN is a rare, but serious and potentially fatal complication of cytotoxic chemotherapy including auto-HCT. Patients with DLBCL who are refractory to or progress after first-line therapy often receive a platinum-based salvage regimen followed by auto-HCT for those eligible for transplantation. Clonal hematopoiesis (CH) has been found to be significantly associated with exposure to carboplatin, but not other platinum agents, and likely represents the precursor clone for t-MN1. If certain platinum-based salvage regimens are associated with significantly higher rates of t-MN compared to other regimens, this may have significant clinical implications on the treatment of relapsed/refractory disease and may be useful in counseling patients prior to auto-HCT.

Q19. 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.

Therapy-associated myeloid neoplasm (t-MN) is a rare but highly fatal complication of cytotoxic chemotherapy. About 30% of t-MN cases arise in patients with hematologic malignancies, most commonly lymphoma2. t-MN is most closely associated with certain alkylating agents (e.g., melphalan), topoisomerase II inhibitors (e.g., etoposide) and platinum agents3,4. Patients with DLBCL who relapse after initial anthracycline-containing regimens often receive platinum-based salvage regimens to achieve chemo-sensitive remission prior to consolidative auto-HCT. While these platinum-based regimens are felt to produce comparable results with regards to antitumor activity5,6, little data exists on the relative impact of these salvage regimens on t-MN risk.

Data are emerging on the relative association of various platinum agents with t-MN. Among patients with solid tumors, rates of t-MN are highest following exposure to carboplatin as compared to other platinum agents7. Along these lines, clonal hematopoiesis (CH) has been found to be significantly associated with exposure to carboplatin (OR=1.4, p=0.001) but not cisplatin (OR=1.1, p=0.10) or oxaliplatin (OR=0.98, p=0.88)1, highlighting that specific cancer therapies can uniquely shape clonal selection. Findings from this study of >9,000 cancer patients exposed to oncologic therapy suggest a direct link between CH and t-MN, whereby CH likely represents the precursor clone for t-MN.

In patients with lymphoma, CH at the time of auto-HCT - particularly when involving genes of the DNA repair pathway - has been associated with increased risk of t-MN and reduced overall survival post-transplant8–10. Interestingly, CH at time of receipt of chimeric antigen receptor T-cell (CAR-T) therapy is associated with increased complete response rate in patients with non-Hodgkin lymphoma under age 6011.

Importantly, CH is felt to predate cytotoxic treatment in patients with cancer. Patients with lymphoma who eventually develop t-MN frequently exhibit CH in the bone marrow prior to any receipt of cancer therapy, in contrast to patients with lymphoma who do not develop t-MN; subsequent chemotherapy can then facilitate clonal selection in the progression towards leukemic transformation12. Therefore, it is conceivable that in the future, presence of CH in patients with relapsed DLBCL could steer providers away from recommending auto-HCT and preferentially toward recommending CAR T therapy in those eligible for both treatment modalities.

More data is needed to define how different cytotoxic therapies influence the risk of t-MN development in patients following auto-HCT. The ICE salvage regimen for relapsed or refractory aggressive lymphoma uniquely combines carboplatin, etoposide and ifosfamide. We hypothesize that patients who receive ICE salvage therapy prior to auto-HCT may be at higher risk of t-MN compared to patients receive other platinum-based salvage regimens that do not contain (1) carboplatin and (2) the unique combination of a platinum agent with an alkylating agent and a topoisomerase II inhibitor (e.g., DHAP, ESHAP, DHAX, GDP, Gem/Ox, etc.).

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion: Adult patients with relapsed or refractory DLBCL first-line anthracycline-containing combination therapy, who received one line of any platinum-containing salvage therapy as second line therapy followed by auto-HCT with BEAM conditioning.

Exclusion:

- Patients who received a non-platinum containing salvage therapy prior to auto-HCT
- Patients transplanted for diagnoses other than DLBCL
- Patients who received conditioning with regimens other than BEAM
- Patients who did not receive an anthracycline-containing first-line therapy

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Median age for DLBCL diagnosis is ~70 years of age and therefore receipt of auto-HCT for this diagnosis is very uncommon in younger patients.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Data collected by CIBMTR before and after AHCT, including essential pre autoHCT data forms such as Forms 2000, 2006, 2018, 2100, 2118, 2400, 2402, specifically the variables and outcomes listed below.
Of note, the 2020 CIBMTR analysis LY18-01a comparing outcomes in patients receiving BEAM vs R-BEAM (Jadadeesh et al, Cancer 2020 May 15;126(10):2279-2287) contains all the elements needed for this proposed analysis, except for t-MN events which would need to be queried.
Patient- and disease-specific characteristics, including:
- Age at time of auto-HCT
- Sex
- Race
- Karnofsky performance status or ECOG performance status
- Hematopoietic cell transplantation-comorbidity index
- Disease risk
- Disease status prior to auto-HCT (CR, PR, etc.)
- Number of lines of therapy prior to auto-HCT
- Previous treatments, if available
o Specifically: salvage regimen used prior to auto-HCT
Transplantation-specific characteristics, including:
- Stem cell dose
- Year of auto-HCT
Outcome measures, including:
- Incidence of t-MN post auto-HCT
- Cumulative incidence of NRM at 1 and 2 years post-AHCT
- Cumulative incidence of relapse
- Cause of death
- PFS at 1 and 2 years post auto-HCT
- OS at 1 and 2 years post auto-HCT

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

n/a

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

n/a

Q25. 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, i.e., neither database contains all the data required to answer the study question.

n/a

Q26. REFERENCES:

1. Bolton KL, Ptashkin RN, Gao T, et al. Cancer therapy shapes the fitness landscape of clonal hematopoiesis. Nat Genet. 2020;52(11):1219-1226. doi:10.1038/s41588-020-00710-0
2. Kayser S, Döhner K, Krauter J, et al. The impact of therapy-related acute myeloid leukemia (AML) on outcome in 2853 adult patients with newly diagnosed AML. Blood. 2011;117(7):2137-2145. doi:10.1182/blood-2010-08-301713
3. Travis LB, Holowaty EJ, Bergfeldt K, et al. Risk of leukemia after platinum-based chemotherapy for ovarian cancer. N Engl J Med. 1999. doi:10.1056/NEJM199902043400504
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11. Miller PG, Sperling AS, Brea EJ, et al. Clonal hematopoiesis in patients receiving chimeric antigen receptor T-cell therapy. Blood Adv. 2021;5(15):2982-2986. doi:10.1182/bloodadvances.2021004554
12. Katagiri S, Makishima H, Azuma K, et al. Predisposed genomic instability in pre-treatment bone marrow evolves to therapy-related myeloid neoplasms in malignant lymphoma. Haematologica. 2020;105(7):e337-e339. doi:10.3324/haematol.2019.229856

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- Yes, I have conflicts of interest pertinent to this proposal

Q27a. 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.

M.T.N. has no disclosures to report.
M.S. reports research support/funding: Angiocrine Bioscience, Inc. Consultancy: Angiocrine Bioscience, Inc.; Omeros Corporation; McKinsey & Company. One-time ad-hoc advisory board: Kite – A Gilead Company; One-time speaking commitment: i3Health (CME).

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1. Baseline characteristics for adult patients with R/R DLBCL received autoHCT (CRF track)

Characteristic	N (%)
No. of patients	1262
No. of centers	126
Age at infusion, yrs - median (min-max)	59.0 (18.2-80.0)
Age - no. (%)	
18-30	60 (4.8)
30-39	81 (6.4)
40-49	178 (14.1)
50-59	349 (27.7)
60-69	451 (35.7)
>70	143 (11.3)
Sex - no. (%)	
Male	778 (61.6)
Female	484 (38.4)
KPS - no. (%)	
90-100	761 (60.3)
< 90	453 (35.9)
Not reported	48 (3.8)
HCT-CI - no. (%)	
0	235 (18.6)
1	105 (8.3)
2	135 (10.7)
3+	317 (25.1)
TBD, inconsistent main and sub-questions	6 (0.5)
N/A, before 2007	458 (36.3)
Missing	6 (0.5)
Race - no. (%)	
White	1021 (80.9)
Black or African American	122 (9.7)
Asian	62 (4.9)
Native Hawaiian or other Pacific Islander	4 (0.3)
American Indian or Alaska Native	11 (0.9)
Other	15 (1.2)
More than one race	4 (0.3)
Not reported	23 (1.8)
Disease status - no. (%)	
CR	637 (50.5)
PR	508 (40.3)
Resistant	85 (6.7)
Untreated	5 (0.4)
Missing	27 (2.1)
Graft type in merge - no. (%)	

Characteristic	**N (%)**
Bone marrow	27 (2.2)
Peripheral blood	1235 (97.9)
Number of prior line of therapy - no. (%)	
2	702 (55.6)
3+	560 (44.4)
Regimens of 2nd line - no. (%)	
ICE	527 (41.8)
Other non-carboplatin containing platinum-based	43 (3.4)
Other	614 (48.6)
Missing	78 (6.2)
Time from diagnosis to transplant (months) - no. (%)	
0-6 months	74 (5.9)
6-12 months	290 (23.0)
>=12 months	896 (71.0)
Not reported	2 (0.2)
HCT year - no. (%)	
1993	3 (0.2)
1994	2 (0.2)
1995	2 (0.2)
1996	3 (0.2)
1997	10 (0.8)
1998	25 (2.0)
1999	33 (2.6)
2000	34 (2.7)
2001	37 (2.9)
2002	38 (3.0)
2003	22 (1.7)
2004	31 (2.5)
2005	54 (4.3)
2006	87 (6.9)
2007	103 (8.2)
2008	200 (15.8)
2009	67 (5.3)
2010	12 (1.0)
2011	19 (1.5)
2012	19 (1.5)
2013	64 (5.1)
2014	67 (5.3)
2015	87 (6.9)
2016	73 (5.8)
2017	55 (4.4)
2018	58 (4.6)
2019	43 (3.4)

Characteristic	N (%)
2020	14 (1.1)
Follow-up - median (range)	75.3 (1.6-267.6)

Merged Proposal for MCL and CD19 CAR-T Therapy: Impact of Prior Therapies on Outcomes in Relapsed/Refractory Mantle Cell Lymphoma Patients treated with Brexucabtagene autoleucel

Research Question:

We hypothesize that CD-19 CAR-T efficacy is independent of the number and type of prior therapies, including BTK exposure.

Keywords:

Mantle Cell lymphoma

CAR-T

brexucabtagene autoleucel (Brexu-cel)

Principal Investigator Information:

Co-investigators: Nausheen Ahmed, MD; Mehdi Hamadani, MD; Natalie Grover, MD; Mazyar Shadman, MD, MPH; Swetha Kambhampati; Alex Herrera

Research Question:

Are clinical outcomes after CD 19 CAR-T for MCL impacted by number, type, or response to prior treatments, including exposure to BTKi?

Identify the impact of patient and disease related factors (MIPI score, TP53 mutation, blastoid variant, Ki67) on outcomes of response rates, PFS, OS

To compare early toxicity of CAR-T therapy for those who have more lines of therapy compared to less and those who have prior BTKi exposure vs no exposure.

Specific Objectives:

1. To compare ORR, CR, OS, PFS, and relapse rate in patients who received CAR-T therapy after prior BTK inhibitor vs. no prior.
2. To compare ORR, CR, OS, PFS and relapse rate in patients who received CAR-T therapy after 1 vs. 2 vs. 3-4 vs. >4 lines of prior therapy.
3. To compare ORR, CR, OS, PFS and relapse rate in patients who received CAR-T therapy after a prior autologous stem cell transplant (ASCT) vs. no prior transplant
4. To compare ORR, CR, ORR, CR, OS, PFS, and relapse rate in patients who received CAR-T therapy had had a relapse within 24 months of finishing induction (POD24) treatment vs. others.

Exploratory Objective:

1. Identify impact of patient and disease related factors (MIPI score, TP53 mutation, blastoid variant, Ki67) on outcomes of ORR, CR, OS, PFS, and relapse rate after treatment with brexucabtagene autoleucel (brexu-cel).

2. To compare toxicity (CRS and neurotoxicity) of patients who have had prior BTKi vs no BTKi, and more lines of therapy vs less.

3. To evaluate the effect of therapy prior to collection, including bendamustine, on response rates, PFS, and OS after treatment with brexu-cel

Scientific Impact:

CAR-T is approved for Mantle Cell lymphoma in second line or later[1]. While studies on the efficacy of the currently approved CD19-CART therapy, brexu-cel, included BTK exposed/ refractory patients, the FDA label does not require patients to have had prior BTK therapy. The EU EMA approval, however, requires BTK inhibitor exposure [2]. CIBMTR/ EBMT guidelines also recommend sequencing CD19-CART only after BTK failure. The FDA approval without mention of BTK exposure has led to heterogeneity in practices.

We look at several factors to help understand if earlier use with regards to BTK inhibitors, autologous transplant and lines of therapy result in significant improvement in survival. CIBMTR is a large database that captures demographics, and outcomes of patients undergoing immune effector cell therapy for relapsed refractory mantle cell lymphoma. We would also correlate with disease and patient characteristics to possibly identify differences with high-risk features. This would help guide clinicians on possible benefit of earlier use versus saving CAR-T cells for later lines of treatment. Since MCL remains incurable any data that guides treatment timing and sequencing will be extremely valuable.

Scientific Justification:

> Mantle cell lymphoma is a heterogeneous disease with high-risk features associated with poor prognosis include clinical factors like multiple comorbidities, performance status as well as disease characteristics like CNS involvement, high MIPI score of >6.2, Ki-67 over 30%, blastoid variant, transformed histology, TP53 aberrations (mutation, deletion, overexpression on IHC), complex karyotype and early progression after first-line therapy (POD24) [3] [4] [5, 6]. Moreover, OS shortens after every line of therapy [7]. In fit patients, autologous transplant is generally recommended at first remission, but its role in the relapsed setting is not established[8].

CD19-CART cell therapy has been a recent exciting advancement in the field of r/r MCL, particularly in the high-risk group including BTK resistant groups, where the prognosis is extremely poor. On July 24th, 2020, the FDA accelerated the approval of brexu-cel for r/r/ MCL based on the ZUMA-2 data. This approval was based on the Zuma 2 study which was an open-label multicenter, single-arm trial of 74 patients with relapsed or refractory mantle cell lymphoma who had previously received anthracycline or bendamustine-containing chemotherapy or antiCD20 antibody, and a BTKi. Of the 60 patients evaluable for efficacy based on a minimum duration of follow-up for response of 6 months, the objective response rate was 93%, with a complete remission rate of 67% [1]. The 12-month PFS was 61% and 57% of all patients in the primary efficacy analysis had ongoing responses at 12.3 months[1]. Early results from real world analyses even in patients who would not have met criteria for Zuma-2 have shown comparable results[9]. This pivotal trial notably only included patients who were refractory or intolerant to BTK inhibitor therapy. The FDA label did not restrict to BTK exposed patients. One unanswered question is

the role of prior BTK inhibitors as well as timing of and length of exposure to BTK inhibitor in responses to brexu-cel. There have been hypotheses that treatment with BTK inhibitor proximal to collection could enhance T cell phenotype as well as function of CAR-T cell product, with potentially improved benefits from ibrutinib due to its additional ITK inhibition. In a small study of CLL patients, prolonged treatment with ibrutinib prior to collection for CAR-T cell manufacturing led to improved expansion of CAR-T cells[10]. In addition, in mouse models, ibrutinib exposure led to improved CAR-T cell engraftment, anti-tumor activity, and survival[10]. Other unanswered questions include impact of other therapies proximal to time of collection on outcomes. For example, many patients with mantle cell lymphoma are exposed to bendamustine which can deplete T cells and negatively impact T cell function[11].

The other question is whether MCL patients with high-risk features, such as TP53 aberrations or blastoid variant, have similar efficacy compared to other patients. In the Zuma-2 trial, these high-risk patients had similar outcomes, but numbers were small[1]. There is an unmet need to understand the efficacy of CAR-T cell therapy in MCL to propose best sequencing strategies with current novel therapies.

Selection Criteria:

1. Inclusion - All adult (age 18 years of age at the time of CART) patients with r/r MCL who received CD19-CART from 2017 to 2021

2. Exclusion - Patients who have not provided consent for research - Patients from embargoed centers

Data Requirements:

Cell therapy forms 4000, 4003 and 4100 and Form 2018

Patient-related

- Patient Age at diagnosis
- Patient age at CART
- Patient sex (M/F)
- Patient ethnicity (Hispanic/Non-Hispanic/Other)
- Race: (White/Black/Other)

Disease/CART Related

- POD24 (yes, no)
- Lines of therapy ___
- BTK inhibitor (acalabrutinib, ibrutinib, zanubrutinib, clinical trial) use prior to CART (yes/no)
- Bendamustine prior to CART (yes/no)
- Autologous Transplant (yes/no)
- Allogeneic transplant (yes/no)

Baseline at diagnosis (for MIPI score)

WBC

LDH

Karnofsky score or ECOG score

Pre CAR-T

- Karnofsky performance at CAR T: 90% vs. ≥90%
- HCT CI score at CAR-T:
- Baseline (Pre-CART) LDH: (median, range)
- Extranodal involvement at CART
- Ki 67 (<30, > 30%, unknown)
- Gene rearrangement: p53 (yes/no)
- 17p del / 17p - (yes/no)

Post CAR-T

- Lymphodepletion: (FLUCY vs others)
- Bridging therapy: (yes vs. no)
- Bridging therapy used (BTK vs other)
- CART therapy: (investigational; brexu-cel)
- Year of CART

Outcomes post cell therapy infusion:

- Cytokine-release syndrome (CRS) (yes/no, grade)
- Neurotoxicity (NT) (yes/no, grade)
- Response at first assessment (1 month) (CR, PR, SD,PD)
- Relapse (yes/no)
- Date of relapse
- Died (yes/no)
- Date of death
- Date of last contact

References:

1. Wang, M., et al., *KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma.* N Engl J Med, 2020. **382**(14): p. 1331-1342.
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Baseline characteristics for adult patients who underwent CAT-T therapy for Mantle cell lymphoma between 2017 – 2021

Characteristic	N (%)
No. of patients	260
No. of centers	72
Age at CT Treatment - median (min-max)	66.5 (34.1-89.1)
Age - no. (%)	
30-40	4 (1.5)
40-50	7 (2.7)
50-60	49 (18.8)
60-70	115 (44.2)
>=70	85 (32.7)
Gender - no. (%)	
Male	205 (78.8)
Female	55 (21.2)
Performance score prior to CT - no. (%)	
90-100	96 (36.9)
< 90	148 (56.9)
Not reported	16 (6.2)
HCT-CI - no. (%)	
0	69 (26.5)
1	70 (26.9)
2	36 (13.8)
3+	68 (26.2)
Not reported	17 (6.5)
Recipient race - no. (%)	
White	221 (85.0)
African American	15 (5.8)
Asian	3 (1.2)
Native American	1 (0.4)
More than one race	2 (0.8)
Unknown	12 (4.6)
Not reported	6 (2.3)
Recipient ethnicity - no. (%)	
Hispanic or Latino	22 (8.5)
Non-Hispanic or non-Latino	226 (86.9)

Characteristic	N (%)
N/A - Not a resident of the U.S.	4 (1.5)
Unknown	8 (3.1)
Disease status prior to CT - no. (%)	
CR	13 (5.0)
PR	58 (22.3)
Resistant	162 (62.3)
Untreated	11 (4.2)
Unknown	16 (6.2)
Product - no. (%)	
Kymriah	2 (0.8)
Yescarta	10 (3.8)
Tecartus	248 (95.4)
Prior HCT - no. (%)	
No prior HCT	179 (68.9)
Allo	5 (1.9)
Auto	70 (26.9)
Allo and Auto	4 (1.5)
Not reported	2 (0.8)
Lines of therapy - no. (%)	
1	19 (7.2)
2	26 (10)
3+	176 (67.8)
Not reported	39 (15)
Bridging therapy - no. (%)	
No	171 (65.8)
Yes	38 (14.6)
Not reported	51 (19.6)
BTK inhibitor use prior to CART- no. (%)	
Yes	161 (61.9)
No	60 (24.1)
Not reported	39 (15)
Time from diagnosis to CT - no. (%)	
0-12 months	37 (14.2)
>=12 months	223 (85.8)
Year of CT - no. (%)	
2018	1 (0.4)
2019	1 (0.4)
2020	71 (27.3)
2021	187 (71.9)
Follow-up - median (range)	6.0 (2.2-13.0)

I. Study Title: CART Outcomes in rare subtypes of aggressive B-cell lymphoma

II. Key Words: CART, lymphoma

III. Principal Investigator Information

Co-investigators: Priyanka Pophali, MD, Shwetha Kambhampati, MD, Joshua Fein, MD, Narendranath Epperla, MD, Mazyar Shadman, MD, Jordan Gauthier, MD, Kalyan Nadiminti, MD, Roni Shouval, MD, Mehdi Hamadani, MD, Alex Herrera, MD

IV. Proposed Working Committee: Lymphoma

V. Research Question:

What are the outcomes of relapsed/refractory rare subtypes of aggressive B-cell lymphomas (THRLBCL, PMBCL, HGBCL, transformed iNHL, Richter transformation of CLL) treated with CART in the real-world setting?

VI. Research Hypothesis

Based on the published literature on disease biology and therapy outcomes in certain rare subtypes of aggressive B-cell lymphomas, we hypothesize that CART-related outcomes differ among the rare subtypes of aggressive B-cell lymphomas (THRLBCL, PMBCL, HGBCL, transformed iNHL, Richter transformation of CLL)

VII. Specific Objectives/Outcomes to be Investigated (200 words)

Primary Outcome:

- Overall survival: time to death. Death from any cause will be considered an event. Surviving patients will be censored at time of last follow-up.

Secondary outcomes:

- Progression-free survival: Survival following CART without relapse or progression. Relapse or progression of disease and death are considered events.
- Non-relapse mortality: Cumulative incidence of NRM. NRM is defined as death without preceding disease relapse/progression. Relapse and progression are competing events.
- Relapse/progression: Progressive disease or recurrences of disease would be counted as events. Treatment-related death, defined as death without relapse or progression, is the competing event. Those who survive without recurrence or progression would be censored at the time of last contact.
- Duration of response
- Response rates at D100, 6 months and 1-year post-CART
- Rates of CRS and ICANS
- Neutrophil and platelet recovery
- Cause of death: descriptive

Specific aim: To describe the outcomes (as defined above) for the rare subtypes of aggressive B cell lymphomas with CART therapy

VIII. Scientific Impact

CART is FDA approved for large B cell lymphoma after 2 lines of therapy. Rare subtypes of aggressive B cell lymphomas are often treated similar to DLBCL especially in the relapsed/refractory setting. Since the commercial approval of CART for DLBCL, many patients with these rarer histologies have undergone CART, but the outcomes for these specific subtypes is unknown. This study can help identify the histological subtypes that benefit from CART versus not thus allowing for better patient selection and improved care utilization. This project has the potential to impact patient care decisions for these difficult to treat aggressive B-cell lymphomas.

IX. Scientific Justification

Currently 3 different CART products (Axi-cel, Tisa-cel, Liso-cel) are approved for treatment of large-B cell lymphoma that is relapsed or refractory to at least 2 systemic therapies. The clinical trials that lead to the approval of these CART products predominantly included DLBCL histology and very few patients with the rare subtypes of aggressive B-cell lymphomas were included:

CART trial/Rare histology	**THRLBCL**	**PMBCL**	**HGBCL**	**Transformed iNHL**	**Richters transformation of CLL**
Axi-cel ZUMA-1[1]	0	8	19	16 (tFL)	0
Tisa-cel JULIET[2]	0	0	19	21 (tFL)	0
Liso-cel TRANSCEND NHL-001[3]	0	15	36	78 (60tFL, 18 other)	0

Therefore, data from subgroup analysis by histology is limited and hard to interpret. A CIBMTR info request showed that there are 38 cases with THRLBCL, 62 cases with PMBL and 283 cases with HBGCL in ***the CIBMTR CART registry which would be the largest available cohort of these rare aggressive B-cell lymphomas treated with CART***. Therefore, we are proposing an analysis to understand the outcomes of these rare lymphoma subtypes with CART through the CIBMTR.

T-cell Histiocyte rich B-cell lymphoma (THRLBCL): THRLBCL is rare (<10% of DLBCL) and was separated out from DLBCL in the WHO classification based on the morphological appearance and worse outcome with early relapses. A retrospective study in the rituximab era has reported survival rates comparable to DLBCL with intensive chemo-imunotherapy[4]. Based on limited available evidence regarding specific outcomes in patients with THRLBCL, patients with THRLBCL are managed similar to DLBCL. A recent study of the tumor microenvironment THRLBCL biopsy samples identified PD-1/PD-L1 signaling is likely the mechanism of immune escape[5]. A case series of 9 patients from 3 institutions with relapsed/refractory THRLBCL treated with Tisa-cel or Axi-cel showed 9/9 were refractory to CART[6]. This observation of poor responses to CART therapy in the THRLBCL cases in small case series require validation in a larger cohort. If patients with THRLBCL have poor outcomes with CART, it makes it even more important to study other therapies for this unique biological subtype.

Primary mediastinal (thymic) large B-cell lymphoma (PMBCL): PMBCL is rare (2-3% of NHL) and occurs predominantly in young adults. These lymphomas are often treated with chemo-immunotherapy +/- radiation in the frontline setting and similar to DLBCL in the relapsed/refractory setting. Pembrolizumab, a PD-1 inhibitor is approved for the treatment of PMBCL in the third line based on objective response rates 45-48% (CR rate 13-33%) and durable responses. Registration CART trials did include the PMBCL histology although subgroup analysis by histology was difficult to interpret due to small numbers and grouping with other histologies. Recently published real-world series from 5 academic medical centers of 33 patients with PMBCL showed comparable efficacy toxicity profile to that seen in the CART clinical trials which was not affected by the use of checkpoint blockade pre/post CART[7]. This study proposes a larger and more generalizable real-world validation of PMBCL outcomes through the larger CIBMTR database.

High grade B cell lymphoma (HGBCL with MYC and BCL2 and/or BCL6 rearrangements; HGBCL, NOS): These lymphomas are classified by the WHO as separate from DLBCL based on morphology and MYC gene rearrangements. They have an overall worse prognosis than DLBCL and are generally treated with more intensive immunochemotherapy upfront. In the relapsed/refractory setting, however, treatments are similar to DLBCL and a small number were included in the pivotal CART trials[1-3]. HGBCL have poor outcomes with autologous stem cell transplant[8] and therefore it is important to understand outcomes with CART studied in a larger cohort of the CIBMTR registry.

Transformed indolent NHL (tiNHL): Histologic transformation of indolent Non-Hodgkin lymphoma (iNHL) is usually associated with chemotherapy resistance and shorter survival after chemotherapy. There is no standard of care for transformed iNHL and therapy is mainly based on guidelines for de novo advanced DLBCL. The registrational CART trials[1-3] demonstrated that tFL have similar outcomes to de novo DLBL patients. However, the sample size of transformed iNHL patients was relatively small in these clinical trials. The goal of this CIBMTR study is to validate this data in the real-world setting with a larger cohort of transformed iNHL patients and assess outcomes compared to de novo DLBCL patients treated with CD19 CAR T.

Richter's transformation of CLL (RS): Although anti-CD19 CAR-T therapy was first studied in CLL, response rates in CLL are lower compared with DLBCL, which may be explained by CLL-induced impairment in T-cell activity. Patients with RS were excluded from the pivotal trials of axi-cel and tisagenlecleucel in DLBCL, and literature regarding the efficacy of approved CAR-T products in patients with RS is lacking. Kittai et al. have described experience with 9 RS cases treated with CART at a single institution[9]. All evaluable patients achieved an objective response including 5/8 patients with complete response (CR) and 3/8 patients with PR as best response. A case series from Israel included 8 patients with RS: All 71% (5/8) responders achieved complete response with DS1 in PET CT scan on day 28[10]. This CIBMTR study would evaluate RS outcomes with CART in a much larger cohort and will provide additional information to guide decision making for patients with RS along with recently published data on transplantation for RS from the CIBMTR[11].

X. Participant Selection Criteria

Inclusion criteria:

1. Adult patients (age ≥ 18 years of age) who underwent 1st infusion of commercially available CAR-T (Axi-cel and Tisa-cel) between 2015-2021
2. Diagnoses: THRBCL, PMBCL, HGBCL, NOS, transformed iNHL (FL, MZL, LPL), Richters transformation of CLL

Exclusion criteria: 2nd CART infusion

XI. Data Requirements

Patient related:

- Age at ASCT or CAR-T treatment
- Sex (Form 2400/2)
- Race (Form 2400/4)
- Ethnicity (Form 2400/3)
- ECOG performance status/Karnofsky performance status (Form 2018/80-81)
- HCT-CI (with component comorbidities where available)

Disease related:

- Diagnosis by WHO classification
- Date of diagnosis and relapse
- MYC-rearrangement (Form 2018/15-17)
- BCL2-rearrangement (Form 2018/6-8)
- BCL6-rearrangement (Form 2018/9-11)
- Ki-67 at diagnosis (Form 2018/20-22)
- LDH at diagnosis (Form 2018/67-68) and pre-CART/ASCT
- Extranodal involvement (Form 2018/75-76)
- Stage of organ involvement (Form 2018/78)
- Presence of B-symptoms (Form 2018/79)
- Prior lines of therapy (Form 2018/166-222) including prior SCT
- Primary refractory after first line of therapy

CART related:

- Date of ASCT/CAR-T
- Conditioning regimen for ASCT
- Disease status at ASCT/CART: CR vs PR vs SD vs PD
- CAR-T product (clinical trial/SOC; within/outside specification; cell dose)
- Bridging therapy pre-CART: yes/no
- Lymphodepleting drugs and dose
- Any concomitant therapy with CART

Follow-up

- Patient status at D100, 6 months, 1 year and last contact
- Best objective response (CR/PR/SD/PD)
- Time to neutrophil recovery (ANC 500)
- Time to platelet recovery (PLT 50)
- Maximum CRS grade (CAR-T only)
- Maximum ICANS grade (CAR-T only)
- Date of disease relapse /progression
- Cause of death

XII. Patient-Reported Outcome (PRO) Requirements: NA

XIII. Sample Requirements (if the study will use biologic samples from the CIBMTR Repository): NA

XIV. Non-CIBMTR Data Source, if applicable: NA

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XVI. Conflicts of Interest

None for all authors except mentioned below.

Alex Herrera:

Bristol Myers Squibb – research funding, consultancy

Genentech – research funding, consultancy

Merck – research funding, consultancy

Seattle Genetics - research funding, consultancy

KiTE Pharma - research funding

Gilead Sciences – research funding

AstraZeneca – research funding, consultancy

Karyopharm – consultancy

ADC Therapeutics – research funding, consultancy

Takeda – consultancy

Tubulis – consultancy

Table 1. Baseline characteristics for adult patients who underwent CAT-T therapy for rare subtypes between 2017 – 2021

Characteristic	N (%)
No. of patients	1242
No. of centers	113
Age at CT Treatment - median (min-max)	62.4 (18.5-90.8)
Age - no. (%)	
18-20	4 (0.3)
20-30	46 (3.7)
30-40	73 (5.9)
40-50	105 (8.5)
50-60	287 (23.1)
60-70	453 (36.5)
>=70	274 (22.1)
Gender - no. (%)	
Male	762 (61.4)
Female	480 (38.6)
Performance score prior to CT - no. (%)	
90-100	514 (41.4)
< 90	586 (47.2)
Not reported	142 (11.4)
HCT-CI - no. (%)	
0	386 (31.1)
1	251 (20.2)
2	178 (14.3)
3+	352 (28.3)
Not reported	75 (6.0)
Recipient race - no. (%)	
White	966 (77.8)
African American	57 (4.6)
Asian	67 (5.4)
Pacific Islander	2 (0.2)
Native American	1 (0.1)
More than one race	4 (0.3)
Unknown	70 (5.6)
Not reported	75 (6.0)
Recipient ethnicity - no. (%)	
Hispanic or Latino	119 (9.6)
Non-Hispanic or non-Latino	968 (77.9)
N/A - Not a resident of the U.S.	102 (8.2)
Unknown	53 (4.3)

Characteristic	**N (%)**
Disease type - no. (%)	
THRLBC	51 (4.1)
PMBCL	83 (6.7)
HGBCL	300 (24.2)
RS	91 (7.3)
Transformed follicular lymphoma	717 (57.7)
Disease status prior to CT - no. (%)	
CR	62 (5.0)
PR	268 (21.6)
Resistant	801 (64.5)
Untreated	59 (4.8)
Unknown	52 (4.2)
Product - no. (%)	
Kymriah	358 (28.8)
Yescarta	860 (69.2)
Breyanzi	24 (1.9)
Prior HCT - no. (%)	
No prior HCT	931 (75.0)
Allo	20 (1.6)
Auto	250 (20.1)
Allo and auto	1 (0.1)
Not reported	40 (3.2)
Prior line of therapies - no. (%)	
1	52 (4.2)
2	220 (17.7)
3+	830 (66.8)
Not reported	140 (11.3)
Bridging therapy - no. (%)	
No	762 (61.4)
Yes	292 (23.5)
Not reported	188 (15.1)
Time from diagnosis to CT - no. (%)	
0-12 months	658 (53.0)
>=12 months	584 (47.0)
Year of CT - no. (%)	
2017	1 (0.1)
2018	185 (14.9)
2019	335 (27.0)
2020	385 (31.0)
2021	336 (27.1)

Characteristic	**N (%)**
Follow-up - median (range)	12.7 (1.0-41.1)

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Bridging therapy - no. (%)	
No	762 (61.4)
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Not reported	188 (15.1)
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>=12 months	584 (47.0)
Year of CT - no. (%)	
2017	1 (0.1)
2018	185 (14.9)
2019	335 (27.0)
2020	385 (31.0)
2021	336 (27.1)
Follow-up - median (range)	12.7 (1.0-41.1)

Impact of CD19 directed CAR T-cell therapy on outcomes for primary and secondary central nervous system B-cell lymphomas

PRINICIPAL INVESTIGATORS:

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2. University of Utah
3. Medical University of South Carolina
4. Medical College of Wisconsin
5. MD Anderson Cancer Center

1.0 HYPOTHESIS:

With the increasing utilization of chimeric antigen receptor T (CAR-T) cell therapy for the treatment of central nervous system lymphoma (CNSL) in the past couple of years, we hypothesize that CAR-T cell therapy is safe and efficacious in patients with primary CNSL (PCNSL) and secondary CNSL (SCNSL).

2.0 SPECIFIC OBJECTIVES:

Primary Objective

- Overall Survival

Secondary Objectives

- Overall response rate (ORR) and complete response (CR) rate
- Cumulative incidence of non-relapse mortality (NRM);
- Cumulative incidence of disease relapse or progression;
- Progression-Free Survival;
- Neutrophil and platelet recovery;
- Cytokine release syndrome
- Neurotoxicity
- Cause of death

3.0 SCIENTIFIC JUSTIFICATION:

The involvement of CNS by recurrent diffuse-large B cell lymphoma (DLBCL) may be the result of either secondary CNS dissemination from systemic lymphoma (SCNSL) or relapsed PCNSL. The prognosis remains dismal in either case with no consensus regarding optimal salvage treatment (1, 2). While whole brain radiotherapy (WBRT) can improve survival by 10-16 months in recurrent PCNSL, it is associated with profound neurotoxicity (3-5). Different therapeutic strategies have been tried with modest success (6-10). Although one can rechallenge with HD MTX (in non-refractory cases), these patients tend to eventually relapse (11, 12). The outcomes of patients with SCNSL remains poor (13-15). Prospective and retrospective studies have shown that high-dose chemotherapy with CNS-penetrating agents should be considered for all young fit patients with CNS relapse of systemic lymphoma who demonstrate chemosensitive disease to high-dose methotrexate-based re-induction therapy. However, those who are older and or with co-morbidities or refractory to salvage regimen represents an unmet need (1, 16-19).

Axicabtagene ciloleucel (Axi-cel), Tisagenlecleucel (Tisa-cel), Lisocabtagene Maraleucel (Liso-cel), and Brexucabtagene Autoleucel (Brexu-cel) are currently approved CAR-T cell therapy products by the U.S. Food and Drug Administration, having demonstrated response rates of about 50-90% in B-cell non-Hodgkin lymphomas (20-23). This has revolutionized the management of relapsed/refractory DLBCL (20-22). However, majority of the clinical trials excluded patients with CNS involvement. Recently four studies (n>=5) showed the outcomes associated with CAR-T cell therapy in PCNSL and SCNSL patients in

the real-world setting (**Table 1**) (24-27). Three of them are in SCNSL (24-26) and one in PCNSL (27). In the largest of these studies (n=17) utilizing CAR-T (axicabtagene ciloleucel), the best ORR and ongoing responses at month 6 were 75% and 41%, respectively. The incidence of CRS and ICANS, of any grade or grade 3 or higher, were comparable between the CNS and non-CNS cohorts (25). The major limitation of all the studies is a small sample size and short follow-up.

Given the knowledge gap, analysis of a large retrospective cohort can provide valuable information to answer this question. Herein we propose a registry analysis using the CIBMTR database to study the impact of CART on outcomes in patients with PCNSL and SCNSL.

Table 1. CAR-T cell therapy for PCNSL and SCNSL (studies ≥5 patients)

Study	Study Design	CAR-T product	Patients (n)	Median age, years (range)
Frigault (24)	Single-center retrospective study	Tisa-cel	8	50 (17-79)
Bennani (25)	Multicenter retrospective cohort	Axi-cel	17	58 (48-69)
Ahmed (26)	Single-center retrospective study	Tisa-cel (n=4) Axi-cel (n=3)	7	50 (39-72)
Siddiqi (27)	Single-center retrospective study	Experimental*	5	49 (42-53)

Abbreviations: Tisa-cel: Tisagenlecleucel; Axi-cel: Axicabtagene Ciloleucel

* CD19 CART cells generated from autologous T naive/memory cells transduced with a CAR construct containing a CD28 costimulatory domain and co-expressing truncated epidermal growth factor receptor

4.0 STUDY POPULATION:

4.1 Inclusion criteria:

1. Adults (age ≥18 years) with CNSL who received CD19 CAR-T cell therapy between 2014-2021
2. Active CNS disease at the time of CART therapy
3. B-cell lymphoma subtypes to include DLBCL, transformed lymphoma, and MCL

4.2 Exclusion Criteria:

1. None

5.0 OUTCOMES*:*

Primary Outcome:

5.1 Overall survival (OS): time to death. Death from any cause will be considered an event. Surviving patients will be censored at the time of last follow-up.

Secondary Outcomes:

5.1 Progression-free survival: Survival following CART without relapse or progression. Relapse or progression of disease and death are considered events.
5.2 Non-relapse mortality: Cumulative incidence of NRM. NRM is defined as death without preceding disease relapse/progression. Relapse and progression are competing events.
5.3 Relapse/progression: Progressive disease or recurrences of disease would be counted as events. Treatment-related death, defined as death without relapse or progression, is the competing event. Those who survive without recurrence or progression would be censored at the time of last contact.
5.4 Neutrophil and platelet recovery
5.5 Cytokine release syndrome
5.6 Neurotoxicity: Determine incidence, grade, and usage of IL-6 antagonists/corticosteroid/anakinra for management of neurotoxicity
5.7 CNS complications: Development of CNS-related issues post CAR T-cell therapy other than those attributable to CRS/neurotoxicity or CNS relapse will be described. Events of interest includes cerebrovascular accidents (ischemia and/or hemorrhage), seizure beyond 2 months, dementia/memory loss, or other reported CNS events
5.8 Cause of death: descriptive only

6.0 VARIABLES TO BE DESCRIBED:

6.1 Patient related:

- Age at transplant or CAR-T: continuous, by decades
- Patient sex: female vs male
- Race: Caucasian, African American, Asian vs. others, missing
- KPS score pre HCT: 90-100 vs. <90 vs. missing

6.2 Disease related:

- LDH at diagnosis: normal, elevated, missing
- Number of lines of chemotherapy prior to CAR-T: 1 vs 2 vs 3 or more vs. missing
- Use of CNS directed therapy prior to CART; IT or RT or both
- Site of involvement: CNS only vs CNS and systemic
- CNS involvement: CSF vs parenchymal vs both
- Time from diagnosis to transplant: median, ≥12 months vs. <12 months
- Early chemoimmunotherapy Failure: No vs. Yes
- Primary refractory: No vs. Yes
- Prior autologous stem cell transplant: yes vs. no
- Prior allogeneic stem cell transplant: yes vs. no
- Disease status prior to CAR T-cell therapy: CR, PR, SD, or PD

6.3 CART related:

- Time from diagnosis to CAR T-cell therapy: continuous and categorical by months/years
- Time from autologous transplant to CAR T-cell therapy
- LDH at the time of CART infusion or LD chemotherapy: normal, elevated, missing
- CRP at the time of CART infusion or LD chemotherapy: normal, elevated, missing
- Use of bridging therapy: yes vs. no
- Type of bridging therapy used: corticosteroid vs. chemotherapy vs. Radiotherapy vs. chemoradiotherapy
- Type of lympho-depleting chemotherapy used: fludarabine/cyclophosphamide vs. others
- CAR T-cell product used: Axi-cel vs. Tisa-cel vs. Liso-cel vs Brexu-cel
- Maximum CRS grade
- Maximum ICANS grade
- Use of tocilizumab/corticosteroids/siltuximab/anakinra

7.0 STUDY DESIGN:

A retrospective multicenter study will be conducted utilizing CIBMTR dataset. Patients will be eligible if they satisfy the criteria detailed in the "Study population" section. The proposed study will evaluate the outcomes of CNSL patients who underwent CAR-T cell therapy.

Descriptive tables of patient, disease and CART-related factors will be created. All outcomes will be calculated relative to the CART date. Cumulative incidence function will be used to estimate relapse and NRM. Kaplan-Meier estimators will be used to estimate PFS and OS. Cox proportional hazard analysis will be used to identify prognostic factors for relapse, NRM, PFS, and OS using stepwise variable selection. The proportional hazards assumption will be checked. If a covariate violates the proportional hazards assumption, it will be added as a time-dependent covariate. The interactions between the main effect and significant covariates will also be examined. Results will be reported as hazard ratio (HR), 95% confidence interval for HR, and p-value. Where adequate numbers of patients are present to allow for statistically significant analysis, safety and efficacy outcomes can be compared amongst different CAR T-cell products. Safety and efficacy outcomes will be compared with historical cohorts of patients undergoing autologous and/or allogeneic stem hematopoietic stem cell transplant for primary and secondary CNS lymphoma.

8.0 REFERENCES

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Table 1. Baseline characteristics for adult patients who underwent CAT-T therapy for SCNSL between 2017 – 2021

Characteristic	N (%)
No. of patients	143
No. of centers	54
Age at CT Treatment - median (min-max)	60.9 (22.7-82.8)
Age - no. (%)	
18-30	4 (2.8)
30-40	9 (6.3)
40-50	18 (12.6)
50-60	36 (25.2)
60-70	54 (37.8)
>=70	22 (15.4)
Gender - no. (%)	
Male	91 (63.6)
Female	52 (36.4)
Performance score prior to CT - no. (%)	
90-100	49 (34.3)
< 90	81 (56.7)
Not reported	13 (9.1)
HCT-CI - no. (%)	
0	49 (34.3)
1	36 (25.2)
2	17 (11.9)
3+	33 (23.4)
Not reported	8 (5.6)
Recipient race - no. (%)	
White	111 (77.6)
African American	4 (2.8)
Asian	12 (8.4)
More than one race	1 (0.7)
Unknown	6 (4.2)
Not reported	9 (6.3)
Recipient ethnicity - no. (%)	
Hispanic or Latino	11 (7.7)
Non-Hispanic or non-Latino	113 (79.0)
N/A - Not a resident of the U.S.	13 (9.1)
Unknown	6 (4.2)
CNS involvement- no. (%)	
PCNSL	12 (9.2)
SCNSL	131 (90.8)

Characteristic	**N (%)**
CSF involvement	25 (19.1)
Brain involvement	94 (71.8)
Leptomingeal involvement	12 (9.1)
Lymphoma histology - no. (%)	
PCNSL	12 (8.4)
DLBCL	96 (67.1)
Transformed lymphoma	25 (17.5)
MCL	10 (7.0)
Disease status prior to CT - no. (%)	
CR	5 (3.5)
PR	36 (25.2)
Resistant	89 (62.2)
Untreated	9 (6.3)
Unknown	4 (2.8)
Product - no. (%)	
Kymriah	53 (37.1)
Yescarta	80 (55.9)
Tecartus	9 (6.3)
Breyanzi	1 (0.7)
Prior HCT - no. (%)	
No prior HCT	96 (67.1)
Allo	2 (1.4)
Auto	41 (28.7)
Not reported	4 (2.8)
Lines of therapy - no. (%)	
1	10 (7.0)
2	27 (18.9)
3+	105 (73.4)
Not reported	1 (0.7)
Bridging therapy - no. (%)	
No	97 (67.8)
Yes	38 (26.6)
Not reported	8 (5.6)
Time from diagnosis to CT - no. (%)	
<12 months	55 (38.5)
>=12 months	88 (61.5)
Year of CT - no. (%)	
2018	14 (9.8)
2019	35 (24.5)
2020	53 (37.1)
2021	41 (28.7)

Characteristic	**N (%)**
Follow-up - median (range)	12.1 (1.6-39.0)

Table 1. Baseline characteristics for adult patients who underwent CAT-T therapy for SCNSL between 2017 – 2021

Characteristic	N (%)
No. of patients	143
No. of centers	54
Age at CT Treatment - median (min-max)	60.9 (22.7-82.8)
Age - no. (%)	
18-30	4 (2.8)
30-40	9 (6.3)
40-50	18 (12.6)
50-60	36 (25.2)
60-70	54 (37.8)
>=70	22 (15.4)
Gender - no. (%)	
Male	91 (63.6)
Female	52 (36.4)
Performance score prior to CT - no. (%)	
90-100	49 (34.3)
< 90	81 (56.7)
Not reported	13 (9.1)
HCT-CI - no. (%)	
0	49 (34.3)
1	36 (25.2)
2	17 (11.9)
3+	33 (23.4)
Not reported	8 (5.6)
Recipient race - no. (%)	
White	111 (77.6)
African American	4 (2.8)
Asian	12 (8.4)
More than one race	1 (0.7)
Unknown	6 (4.2)
Not reported	9 (6.3)
Recipient ethnicity - no. (%)	
Hispanic or Latino	11 (7.7)
Non-Hispanic or non-Latino	113 (79.0)
N/A - Not a resident of the U.S.	13 (9.1)
Unknown	6 (4.2)
CNS involvement- no. (%)	
PCNSL	12 (9.2)
SCNSL	131 (90.8)
CSF involvement	25 (19.1)
Brain involvement	94 (71.8)

Characteristic	**N (%)**
Leptomingeal involvement	12 (9.1)
Lymphoma histology - no. (%)	
PCNSL	12 (8.4)
DLBCL	96 (67.1)
Transformed lymphoma	25 (17.5)
MCL	10 (7.0)
Disease status prior to CT - no. (%)	
CR	5 (3.5)
PR	36 (25.2)
Resistant	89 (62.2)
Untreated	9 (6.3)
Unknown	4 (2.8)
Product - no. (%)	
Kymriah	53 (37.1)
Yescarta	80 (55.9)
Tecartus	9 (6.3)
Breyanzi	1 (0.7)
Prior HCT - no. (%)	
No prior HCT	96 (67.1)
Allo	2 (1.4)
Auto	41 (28.7)
Not reported	4 (2.8)
Lines of therapy - no. (%)	
1	10 (7.0)
2	27 (18.9)
3+	105 (73.4)
Not reported	1 (0.7)
Bridging therapy - no. (%)	
No	97 (67.8)
Yes	38 (26.6)
Not reported	8 (5.6)
Time from diagnosis to CT - no. (%)	
<12 months	55 (38.5)
>=12 months	88 (61.5)
Year of CT - no. (%)	
2018	14 (9.8)
2019	35 (24.5)
2020	53 (37.1)
2021	41 (28.7)
Follow-up - median (range)	12.1 (1.6-39.0)

Outcome of patients with large cell lymphoma receiving ASCT vs. CAR-T therapy while in complete remission

Investigators (alphabetical order)

- **Mehdi Hamadani –** Medical College of Wisconsin, Milwaukee, WI
- **Antonio Jimenez, MD --** University of Miami, Miami, FL
- **Mazyar Shadman MD, MPH –** Fred Hutch, University of Washington, Seattle WA
- **Trent Wang, DO –** University of Miami, Miami, FL

Research question

In patients with large cell lymphoma who are in complete remission (CR) after salvage therapy, which treatment modality (ASCT vs. CAR-T) provides better clinical outcomes?

Research hypothesis

In patients with large cell lymphoma who are in complete remission (CR) after salvage therapy, ASCT provides superior clinical outcomes

Specific objectives/Outcomes to be investigated

1. To compare OS, PFS and relapse rate and NRM in patients who received ASCT vs. CAR-T therapy while in a CR
2. To compare cause of death in patients who received ASCT vs. CAR-T therapy while in a CR

Scientific Impact

With access to 3 different products, CAR-T therapy is sometimes used in patients who are in CR after receiving salvage therapy while these patients have been candidates for ASCT.(1) The 3 head-to-head ASCT vs. CAR-T trials randomized patients BEFORE starting salvage chemotherapy and are functionally salvage therapy vs. CAR-T studies.(2-4) Therefore, those studies will not answer the question that is being asked by this proposed study. This proposed CIBMTR analysis will complement the previously published CIBMTR study (ASCT vs. CAR-T in pts in PR) indicating superiority of ASCT in PR patients (5)and will guide day-to-day practice in how to best sequence treatment in patients with relapsed large cell lymphoma.

Scientific Justification

Patients with large cell lymphoma are considered transplant ineligible based on lack of response to prior chemotherapy. Some of these patients receive salvage chemotherapy before CAR-T therapy and achieve a CR. It is not clear if the bet course of action in these patients would be pursuing CAR-T or ASCT. This is question is particularly important because the recent publication by the CIBMTR group has shown that outcomes are superior after ASCT compared to CAR-T in patients in a PR after salvage therapy. (5)Also, the 3 head-to-head ASCT vs. CAR-T trials randomized patients BEFORE salvage chemotherapy and are

functionally salvage therapy vs. CAR-T studies. Therefore, they will not answer the question that is being asked by this proposed study.

Participant selection criteria

- All patients with large cell lymphoma (DLBCL,PMBCL) who received ASCT (2013-2019) or commercial CAR-T therapy (2018-2021) while in a CR
- Patients with a prior ASCT or CAR-T therapy are excluded

Data requirements

Baseline:

- Age at diagnosis
- Disease characteristics at diagnosis (IPI, Stage)
- Age at ASCT or CAR-T
- Sex
- Year of treatment
- Ethnicity
- Prior lines of treatment
    - Number
    - Type
- Pre-CAR-T LDH

Post CAR-T

- Cytokine-release syndrome (CRS) (yes/no, grade)
- Neurotoxicity (NT) (yes/no, grade)
- Response at first assessment (1 month) (CR,PR,SD,PD)
- Relapse (yes/no)
- Date of relapse
- Died (yes/no)
- Date of death
- Date of last contact

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Table 1. Baseline characteristics for adult patients who underwent CAT-T therapy or autoHCT (CRF) between for DLBCL in CR between 2016-2021

Characteristic	CAR-T	autoHCT
No. of patients	111	218
No. of centers	56	71
Age at CT Treatment - median (min-max)	64.5 (20.2-82.8)	59.5 (22.0-78.6)
Age - no. (%)		
18-30	3 (2.7)	5 (2.3)
30-40	5 (4.5)	10 (4.6)
40-50	10 (9.0)	28 (12.8)
50-60	20 (18.0)	68 (31.2)
60-70	38 (34.2)	76 (34.9)
>=70	35 (31.5)	31 (14.2)
Gender - no. (%)		
Male	63 (56.8)	142 (65.1)
Female	48 (43.2)	76 (34.9)
Performance score prior to CT - no. (%)		
90-100	45 (40.5)	124 (56.9)
< 90	48 (43.2)	89 (40.8)
Not reported	18 (16.2)	5 (2.3)
HCT-CI - no. (%)		
0	33 (29.7)	54 (24.8)
1	23 (20.7)	18 (8.3)
2	16 (14.4)	37 (17.0)
3+	34 (30.6)	108 (49.5)
Not reported	5 (4.5)	1 (0.0)
Recipient race - no. (%)		
White	79 (71.2)	142 (65.1)
African American	5 (4.5)	36 (16.5)
Asian	14 (12.6)	31 (14.2)
Pacific Islander	0 (0.0)	1 (0.5)
Native American	0 (0.0)	4 (1.8)
More than one race	6 (5.4)	0 (0.0)
Not reported	7 (6.3)	4 (1.8)
Recipient ethnicity - no. (%)		
Hispanic or Latino	9 (8.1)	20 (9.2)
Non-Hispanic or non-Latino	80 (72.1)	181 (83.0)
N/A - Not a resident of the U.S.	19 (17.1)	14 (6.4)
Not reported	3 (2.7)	3 (1.4)
Product - no. (%)		
Kymriah	60 (54.1)	N/A

Characteristic	**CAR-T**	**autoHCT**
Yescarta	46 (41.4)	N/A
Breyanzi	5 (4.5)	N/A
Prior lines of therapies - no. (%)		
2	23 (20.2)	140 (64.2)
3+	63 (55.3)	78 (35.8)
Not reported	25 (21.9)	0 (0)
Bridging therapy - no. (%)		
No	64 (57.7)	N/A
Yes	18 (16.2)	N/A
Missing	29 (26.1)	N/A
Time from diagnosis to CT - no. (%)		
0-12 months	28 (25.2)	56 (25.7)
>= 12 months	82 (73.9)	161 (73.9)
Not reported	1 (0.9)	1 (0.5)
Year of CT - no. (%)		
2016	0 (0.0)	56 (25.7)
2017	0 (0.0)	49 (22.5)
2018	8 (7.2)	55 (25.2)
2019	20 (18.0)	45 (20.6)
2020	35 (31.5)	13 (6.0)
2021	48 (43.2)	0 (0.0)
Follow-up - median (range)	12.2 (3.2-37.3)	26.1 (1.6-60.4)

Table 1. Baseline characteristics for adult patients who underwent CAT-T therapy or autoHCT (CRF) between for DLBCL in CR between 2016-2021

Characteristic	CAR-T	autoHCT
No. of patients	111	218
No. of centers	56	71
Age at CT Treatment - median (min-max)	64.5 (20.2-82.8)	59.5 (22.0-78.6)
Age - no. (%)		
18-30	3 (2.7)	5 (2.3)
30-40	5 (4.5)	10 (4.6)
40-50	10 (9.0)	28 (12.8)
50-60	20 (18.0)	68 (31.2)
60-70	38 (34.2)	76 (34.9)
>=70	35 (31.5)	31 (14.2)
Gender - no. (%)		
Male	63 (56.8)	142 (65.1)
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Performance score prior to CT - no. (%)		
90-100	45 (40.5)	124 (56.9)
< 90	48 (43.2)	89 (40.8)
Not reported	18 (16.2)	5 (2.3)
HCT-CI - no. (%)		
0	33 (29.7)	54 (24.8)
1	23 (20.7)	18 (8.3)
2	16 (14.4)	37 (17.0)
3+	34 (30.6)	108 (49.5)
Not reported	5 (4.5)	1 (0.0)
Recipient race - no. (%)		
White	79 (71.2)	142 (65.1)
African American	5 (4.5)	36 (16.5)
Asian	14 (12.6)	31 (14.2)
Pacific Islander	0 (0.0)	1 (0.5)
Native American	0 (0.0)	4 (1.8)
More than one race	6 (5.4)	0 (0.0)
Not reported	7 (6.3)	4 (1.8)
Recipient ethnicity - no. (%)		
Hispanic or Latino	9 (8.1)	20 (9.2)
Non-Hispanic or non-Latino	80 (72.1)	181 (83.0)
N/A - Not a resident of the U.S.	19 (17.1)	14 (6.4)
Not reported	3 (2.7)	3 (1.4)
Product - no. (%)		
Kymriah	60 (54.1)	N/A
Yescarta	46 (41.4)	N/A
Breyanzi	5 (4.5)	N/A

Characteristic	CAR-T	autoHCT
Prior lines of therapies - no. (%)		
2	23 (20.2)	140 (64.2)
3+	63 (55.3)	78 (35.8)
Not reported	25 (21.9)	0 (0)
Bridging therapy - no. (%)		
No	64 (57.7)	N/A
Yes	18 (16.2)	N/A
Missing	29 (26.1)	N/A
Time from diagnosis to CT - no. (%)		
0-12 months	28 (25.2)	56 (25.7)
>= 12 months	82 (73.9)	161 (73.9)
Not reported	1 (0.9)	1 (0.5)
Year of CT - no. (%)		
2016	0 (0.0)	56 (25.7)
2017	0 (0.0)	49 (22.5)
2018	8 (7.2)	55 (25.2)
2019	20 (18.0)	45 (20.6)
2020	35 (31.5)	13 (6.0)
2021	48 (43.2)	0 (0.0)
Follow-up - median (range)	12.2 (3.2-37.3)	26.1 (1.6-60.4)