Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
Honolulu, HI
Friday, February 14, 2025, 1:00 – 3:00 PM HST

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

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

3. **Presentations, Publications or Submitted papers**
   a. **LY22-01c** Wang TP, Ahn KW, Shadman M, Kaur M, Ahmed N, Bacher U, Cerny J, Chen A, Epperla N, Frigault M, Grover N, Haverkos B, Hill B, Hossain N, Iqbal M, Jain T, Krem MM, Maakaron J, Modi D, Alhaj Moustafa M, Riedell P, Savani B, Sica RA, Sureda A, Wudhikarn K, Herrera AF, Sauter C, Hamadani M, Jimenez Jimenez A. Chimeric antigen receptor T-cell infusion for large B-cell lymphoma in complete remission: A Center for International Blood and Marrow Transplant Research analysis. ***Leukemia. 2024 Jul 1; 38(7):1564-1569. doi:10.1038/s41375-024-02242-6. Epub 2024 May 15. PMC11271761.***
   b. **LY22-02a** Epperla N, Hashmi H, Ahn KW, Chen AI, Wirk B, Kanakry JA, Lekakis L, Lekakis L, Kharfan-Dabaja MA, Scordo M, Riedell PA, Jain T, Shadman M, Sauter C, Hamadani M, Herrera AF, Ahmed S. Outcomes of patients with secondary central nervous system lymphoma treated with chimeric antigen receptor T-cell therapy: A CIBMTR analysis. ***British Journal of Haematology. 2024 Sep 1; 205(3):1202-1207. doi:10.1111/bjh.19569. Epub 2024 May 26. PMC11499028.***
   c. **LY22-01a** Shadman M, Ahn KW, Kaur M, Lekakis L, Beitinjaneh A, Iqbal M, Ahmed N, Hill B, Hossain NM, Riedell P, Gopal AK, Grover N, Frigault M, Brammer J, Ghosh N, Merryman R, Lazaryan A, Ram R, Hertzberg M, Savani B, Awan F, Khimani F, Ahmed S, Kenkre VP, Ulrickson M, Shah N, Kharfan-Dabaja MA, Herrera A, Sauter C, Hamadani M. Autologous transplant vs. CAR-T therapy in patients

with DLBCL treated while in complete remission. ***Blood Cancer Journal. 14(1):108. doi:10.1038/s41408-024-01084-w. Epub 2024 Jul 8. PMC11231252.***

d. **LY22-01b** Pophali PA, Fein JA, Ahn KW, Allbee-Johnson M, Ahmed N, Awan FT, Farhan S, Grover NS, Hilal T, Iqbal M, Maakaron J, Modi D, Nasrollahi E, Schachter L, Sauter CS, Hamadani M, Herrera AF, Shouval R, Shadman M. CD19-directed CART therapy for T cell/histiocyte rich large B-cell lymphoma. ***Blood Advances. 2024 Oct 22; 8(20):5290-5296.doi:10.1182/bloodadvances.2024013863. Epub 2024 Jul 14. PMC11497379.***

e. **LY22-01a** Mercadal S, Ahn KW, Allbee-Johnson M, Ganguly S, Ramakrishnan Geethakumari P, Hong S, Malone A, Murthy H, Pawarode A, Sica AR, Solh M, Ustun C, Shadman M, Sauter CS, Hamadani M, Herrera AF, Lee CJ. Outcomes of patients with primary central nervous system lymphoma following CD19-targeted chimeric antigen receptor T-cell therapy. ***Haematologica. doi:10.3324/haematol.2024.285613. Epub 2024 Sep 5.***

f. **LY22-01b** Outcomes of autologous HCT and CD19 CAR-T in MYC+ large B-cell lymphoma patients. (M Hamadani/ F Furqan). ***Submitted.***

g. **LY20-02** Outcomes of allogeneic transplants in patients with hodgkin lymphoma in the era of checkpoint inhibitors: A joint CIBMTR and EBMT analysis. (M-A Perales/ A Sureda/ F Awan/ S Montoto). ***Submitted.***

4. Studies in progress (Attachment 3)

a. **LY22-02c** Efficacy and safety of CD19 directed CAR T-cell therapy for transferred follicular lymphoma (S Kambhampati/ K Nadiminti/ A Herrera). **Manuscript Preparation.**

b. **LY22-02d** Efficacy and safety of CD19 directed CAR T-cell therapy for Richter's transformation (M Shadman/ M Hamadani). **Manuscript Preparation.**

c. **LY22-02e** Efficacy and safety of CD19 directed CAR T-cell therapy for primary mediastinal B-cell lymphoma (J Gauthier/ A Herrera). **Manuscript Preparation.**

d. **LY22-02f** Efficacy and safety of CD19 directed CAR T-cell therapy for high grade B-cell lymphoma. (S Ahmed/ S Mercadal/ H Hashmi/ C Lee/ N Epperla). **Manuscript Preparation.**

e. **LY23-01** Efficacy of hematopoietic stem cell transplantation in patients with plasmablastic lymphoma (S Ahmed/ T Al-Juhaishi)**. Protocol Development.**

f. **LY24-01** Hematopoietic cell transplantation for rare mature T-cell lymphomas (M Hamadani/ A Herrera). **Protocol Development.**

5. Future/proposed studies

a. **PROP 2410-44; 2410-168** Axi-cel vs. Liso-cel in Second line in DLBCL (A Mian/ B T. Hill/ D Reef/ N Grover) (Attachment 4)

b. **PROP 2410-66** A Matching Adjusted Indirect Comparison (MAIC) Analysis Comparing the Clinical Outcomes of Patients with Follicular Lymphoma Treated with Anti-CD19 Chimeric Antigen Receptor T Cell Therapy (CART) and Bispecific T Cell Engager (M Di/ M Shadman) (Attachment 5)

c. **PROP 2410-67** Real-world Outcomes Following Axicabtagene Ciloleucel and Lisocabtagene Maraleucel in Older Patients with Large B Cell Lymphoma (M Di/ M Shadman) (Attachment 6)

d. **PROP 2410-72; 2410-239** Brux-cel in older MCL patients (S Gupta/ V Bachanova/ P Jain/ A Lionel) (Attachment 7)

e. **PROP 2410-100** Incidence and Risk factors for Non-relapse Mortality after anti-CD19 CAR T-cell therapy for Lymphoma (D Modi) (Attachment 8)

f. **PROP 2410-120; 2410-194** AutoHCT in Secondary CNS lymphoma (B Gattas/ U Gergis/ A Kidwell/ N N. Shah) (Attachment 9)

Proposed studies; not accepted for consideration at this time.

g. **PROP 2401-01** Impact of mogamulizumab on GVHD in patients receiving post-transplantation cyclophosphamide based GVHD prophylaxis (C Sterling). ***Dropped due to small sample size.***
h. **PROP 2407-01** Outcome of CART therapy post allogenic HSCT (J L Wagner). ***Dropped due to low scientific impact.***
i. **PROP 2408-07** Real world outcomes of second chimeric antigen receptor T cell (CAR T-cell) therapy for lymphoma (J Joseph). ***Dropped due to low scientific impact.***
j. **PROP 2409-13** Autologous stem cell transplant vs chimeric antigen receptor T-cell therapy in older patients with chemosensitive late relapsed diffuse large B-cell lymphoma (A Tun/ P Johnston). ***Dropped due to low scientific impact.***
k. **PROP 2409-14** Autologous stem cell transplant vs chimeric antigen receptor T-cell therapy in follicular lymphoma with early treatment failure (A Tun/ C Sauter). ***Dropped due to low scientific impact.***
l. **PROP 2409-32** The impact of TP53 genomic alterations in large B-cell lymphoma treated with CD19-CAR-T (R Shouval). ***Dropped due to supplemental data needed.***
m. **PROP 2410-12** Outcomes of HIV+ Lymphoma treated with Chimeric Antigen Receptor T-Cell Therapy (M Iqbal/ H Murthy). ***Dropped due to overlap with current study/publication.***
n. **PROP 2410-13** Outcomes and Utilization Trends of Autologous Hematopoietic Cell Transplantation for Classical Hodgkin Lymphoma (M Iqbal/ M Kharfan-Dabaja). ***Dropped due to low scientific impact.***
o. **PROP 2410-15** Evaluating Outcomes of Allogeneic Hematopoietic Cell Transplantation in Cutaneous T Cell Lymphoma in the Contemporary Era (M Iqbal/ M Kharfan-Dabaja). ***Dropped due to low scientific impact.***
p. **PROP 2410-19** Use of PD1 Inhibitors as Salvage Therapy Prior to Autologous Stem Cell Transplantation (ASCT) in Hodgkin Lymphoma (Y Berry/ S Farhan). ***Dropped due to low scientific impact.***
q. **PROP 2410-42** Outcomes of CAR-T in DLBCL Based on Remission Status (A Sindel). ***Dropped due to low scientific impact.***
r. **PROP 2410-64** Real world comparison of efficacy of bispecific antibodies (BsAbs) and chimeric antigen receptor T-cell therapies (CART) in large B-cell lymphoma (LBCL) (T Zhuang/ P Strati). ***Dropped due to small sample size.***
s. **PROP 2410-65** Impact of checkpoint inhibitors on outcomes after autologous stem cell transplant for relapsed Hodgkin's lymphoma (P Pophali/ D Trotier). ***Dropped due to low scientific impact.***
t. **PROP 2410-68** CD19 Directed CAR-T therapy Outcomes in Patients with Relapsed/Refractory Diffuse Large B Cell Lymphoma (DLBCL) as Determined by Tumor Size (& burden) and Lactate Dehydrogenase Enzyme (LDH) (A Desai/ R Maziarz). ***Dropped due to overlap with current study/publication.***
u. **PROP 2410-83** The impact of novel therapies and modern antiretroviral therapy on outcomes after autologous stem cell transplant in patients with relapsed and refractory HIV-associated lymphoma (K Lurain/ A Herrera). ***Dropped due to overlap with current study/publication.***
v. **PROP 2410-88** Predictive Modeling for CAR-T Therapies in Relapsed/Refractory Follicular Lymphoma Using Machine Learning (N Ahmed/ S Irfan). ***Dropped due to low scientific impact.***
w. **PROP 2410-98** Outcomes of Hematopoietic Cell Transplantation and CAR T-Cell Therapy for Denovo CD5+ Diffuse Large B-Cell Lymphoma (B Wirk). ***Dropped due to small sample size.***

x. **PROP 2410-105** Outcomes of CD3/CD20 bispecific antibodies and other targeted therapies post CD19 CAR T therapy in relapsed refractory diffuse large B-cell lymphoma (S Thiruvengadam/ A Herrera). ***Dropped due to small sample size.***

y. **PROP 2410-108** Outcomes of R/R large B-cell lymphoma patients treated with CD19 CAR T cell therapy previously exposed to bispecific antibody with propensity score matching comparison to those naïve to bispecific antibody (S Thiruvengadam/ A Herrera). ***Dropped due to small sample size.***

z. **PROP 2410-110** Outcomes of R/R FL patients treated with CD19 CAR T cell therapy previously exposed to bispecific antibody with propensity score matching comparison to those naïve to bispecific antibody (S Thiruvengadam/ A Herrera). ***Dropped due to small sample size.***

aa. **PROP 2410-112** Comparative efficacy of CD19+CAR-T vs autoHCT in 2L DLBCL based on the putative cell of origin (ABC vs GCB) (M Abid/ S Ahmed). ***Dropped due to low scientific impact.***

bb. **PROP 2410-113** Efficacy of a second CAR-T infusion in patients with relapsed/refractory B-cell malignancies (M Abid/ S Ahmed). ***Dropped due to low scientific impact.***

cc. **PROP 2410-114** Outcomes of Burkitt lymphoma Patients Undergoing Autologous and Allogeneic hematopoientic cell transplantation: A contemporary analysis (I Muhsen/ M Aljurf). ***Dropped due to low scientific impact.***

dd. **PROP 2410-115** Real-World Outcomes of CD19+CAR-T and Comparison of Axi-cel vs Tisa-cel for Relapsed/refractory Follicular Lymphoma (M Abid/ S Ahmed). ***Dropped due to low scientific impact.***

ee. **PROP 2410-116** Efficacy of Autologous Stem Cell Transplant in DLBCL Patients Who Relapse After CAR T-Cell Therapy (M Abid/ S Ahmed). ***Dropped due to low scientific impact.***

ff. **PROP 2410-117** Analysis of Commercial CD19+CAR-T Therapy for Patients with relapsed/refractory Aggressive Large B Cell Lymphoma in the real-world third line Setting (M Abid/ S Ahmed). ***Dropped due to low scientific impact.***

gg. **PROP 2410-127** Real-world non-relapse mortality and early mortality after brexucabtagene autoleucel (brexu-cel) CAR T-cell therapy for mantle cell lymphoma (P Jain/ A Lionel). ***Dropped due to low scientific impact.***

hh. **PROP 2410-132** Comparative outcome analysis of patients with primary refractory or early relapsed aggressive B-cell lymphoma treated with axicabtagene ciloleucel versus lisocabtagene maraleucel (X Bi/ U Gergis). ***Dropped due to low scientific impact.***

ii. **PROP 2410-150** Outcomes of autologous stem cell transplantation in DLBCL relapsed/refractory to CD19 CAR T (S Thiruvengadam/ E Bezerra). ***Dropped due to low scientific impact.***

jj. **PROP 2410-162** A comparison of the safety and efficacy of anti-CD19 CAR T-cell therapy versus autologous stem cell transplantation (ASCT) in follicular lymphoma experiencing early therapy failure (POD12 and POD24) (H Wolfe/ P Ramakrishnan). ***Dropped due to low scientific impact.***

kk. **PROP 2410-164** Outcomes of subsequent transplant or cellular therapy for relapse after CD19 autologous CAR T-cell therapy in large B-cell lymphoma (H Cherniawsky/ R J Stubbins). ***Dropped due to low scientific impact.***

ll. **PROP 2410-166** Real-world Outcomes Following Lisocabtagene Maraleucel in Patients with Mantle Cell Lymphoma (J Huang/ M Shadman). ***Dropped due to small sample size.***

mm. **PROP 2410-170** Optimizing CAR-T in Follicular Lymphoma: Identifying the Best Line of Therapy to Maximize Survival (D Reef/ N Grover). ***Dropped due to low scientific impact.***

nn. **PROP 2410-171** Effect of Prior CD19-Targeted Therapies and CD3xCD20 Bispecific Antibodies on Subsequent Anti-CD19 CAR T-Cell Therapy Outcomes in Diffuse Large B-cell Lymphoma (E Yilmaz/ F Awan). ***Dropped due to small sample size.***

oo. **PROP 2410-185** Efficacy and Toxicity of CAR T-Cell Therapy in Patients with Large B-Cell Lymphoma Previously Treated with Bispecific Antibodies (J Huang/ M Shadman). ***Dropped due to small sample size.***

pp. **PROP 2410-189** Efficacy of a second CAR T-cell therapy in patients with Relapse/Refractory B-cell non-Hodgkin lymphoma (A Kidwell/ N Shah). ***Dropped due to low scientific impact.***

qq. **PROP 2410-197** Efficacy and safety of CD19 CAR T cell therapy in EBV-positive diffuse large B-cell lymphoma (M Alhomoud/ M Scordo). ***Dropped due to small sample size.***

rr. **PROP 2410-198** Evaluating outcomes of Hematopoietic Cell Transplantation in Hepatosplenic T Cell Lymphoma (M Iqbal/ H Murthy). ***Dropped due to overlap with current study/publication.***

ss. **PROP 2410-215** Real-world efficacy of anti-CD19-chimeric antigen receptor T cell therapy in the second-line setting for late-relapsed large B cell lymphoma (S Ahmed/ K Chohan). ***Dropped due to low scientific impact.***

tt. **PROP 2410-216** Post-autologous stem cell transplant outcomes of primary mediastinal B-cell lymphoma patients with prior exposure to checkpoint inhibitors (S Larson/ J Timmerman). ***Dropped due to overlap with current study/publication.***

uu. **PROP 2410-219** Outcomes of chimeric antigen receptor T-cell therapy (CAR-T) for patients with relapsed/refractory large B cell lymphoma with testicular involvement – an efficacy analysis of CAR-T for a rare sanctuary site (G Hildebrandt/ M Yasir). ***Dropped due to small sample size.***

vv. **PROP 2410-226** A Matched Adjusted Indirect Comparision of Safety and Efficacy of CD20-directed BiTE therapy versus CD19-directed CAR-T therapy in LBCL (K Chetlapalli/ L Gowda). ***Dropped due to low scientific impact.***

ww. **PROP 2410-236** Real-world analysis of brexucabtagene autoleucel as compared to allogeneic transplant for patients with high-risk mantle cell lymphoma (S Ahmed/ K Chohan). ***Dropped due to low scientific impact.***

xx. **PROP 2410-238** Outcomes of Subsequent CD19-directed CAR-T infusion after relapse from prior CAR-T cell therapy for B cell malignancies (S Mirza/ L Gowda). ***Dropped due to low scientific impact.***

yy. **PROP 2410-243** Efficacy and toxicity of allogeneic transplantation post-chimeric antigen receptor T cell therapy failure in large B cell lymphoma Cri (S Ahmed/ K Chohan). ***Dropped due to low scientific impact.***

zz. **PROP 2410-244** Impact of BTK Inhibitor Maintenance Therapy on Outcomes Following CAR T-Cell Therapy in Mantle Cell Lymphoma (O Jarallah/ S Mirza). ***Dropped due to supplemental data needed.***

aaa. **PROP 2410-252** Outcomes and toxicity of autologous stem cell transplant for patients with Primary CNS Lymphoma associated with HIV (L Schachter/ J Cleveland). ***Dropped due to small sample size.***

bbb. **PROP 2410-263** Survival Outcomes of Allogeneic Transplants (allo-SCT) in comparison to Chimeric Antigen Receptor (CAR T) therapy for Relapsed Refractory Mantle Cell lymphoma (MCL) (S Naik/ C Annageldiyev). ***Dropped due to low scientific impact.***

6. Other business

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
San Antonio, TX
Wednesday, February 21, 2024, 1:00 - 3:00 PM CT

Co-Chair:	**Alex Herrera, MD; City of Hope National Medical Center, Duarte, CA; Telephone: 626-256-4673; E-mail: aherrera@coh.org**
Co-Chair:	**Mazyar Shadman, MD, MPH; Fred Hutchinson Cancer Center, Seattle, WA; E-mail: mshadman@fredhutch.org**
Incoming Co-Chair:	**Cameron Turtle, MBBS, PhD; Fred Hutchinson Cancer Research Center, Seattle, WA; E-mail: cturtle@fredhutch.org**
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Scientific Director:	**Mehdi Hamadani, MD; CIBMTR® (Center for International Blood and Marrow Transplant Research), Medical College of Wisconsin, Milwaukee, WI; Telephone: 414-805-0700; E-mail: mhamadani@mcw.edu**
Statistical Director:	**Kwang Woo Ahn, PhD; CIBMTR® (Center for International Blood and Marrow Transplant Research), Medical College of Wisconsin, Milwaukee, WI; Telephone: 414-456-7387; E-mail: kwooahn@mcw.edu**
Statistician:	**Keming Zhan, MS; CIBMTR® (Center for International Blood and Marrow Transplant Research), Medical College of Wisconsin, Milwaukee, WI; Telephone: 414-805-0711; E-mail: kezhan@mcw.edu**

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1. Introduction

The CIBMTR Lymphoma Working Committee was called to order at 1 pm on Wednesday, February 21, 2024, by Dr. Craig Sauter, who introduced the working committee leadership, and highlighted leadership's conflict of interest disclosures per CIBMTR policy. He indicated the availability of publicly available dataset for secondary analyses and explained the difference between the TED and CRF data collection forms. Dr. Craig Sauter emphasized the process of becoming a Working Committee member and outlined the Working Committee goals, expectations, limitations, and the voting guidelines. In addition, rules of authorship were emphasized: 1) substantial and timely contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; 3) final approval for the version to be published. He encouraged junior faculty, fellows, and assistant professors to collaborate actively with the Lymphoma Writing Committee. Dr. Hamadani provided gratitude to outgoing chair - Dr. Craig Sauter for his contributions to LYWC on behalf of CIBMTR. Dr. Hamadani provided an update on the Working Committee productivity including publications, presentations at international conferences and went over the three studies in progress and detailed the goals for these studies.

2. Presentations, published or submitted papers

(a) **LY22-01a** Outcomes of CD19 CAR-T in patients who achieve complete remission prior to lymphodepletion in patients with aggressive non-Hodgkins lymphoma (Mazyar Shadman / Mehdi Hamadani). ***Oral presentation at ASH 2023; Manuscript under review.***

(b) **LY22-01c** Outcomes of CD19 CAR-T in patients who achieve complete remission prior to lymphodepletion in patients with aggressive non-Hodgkins lymphoma (Trent Wang / Antonio martin Jimenez Jimenez). ***Oral presentation ASH 2023; Manuscript under review.***

(c) **LY22-02a** Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with primary and secondary central nervous system involvement (Narendranath Epperla / Hamza Hashmi / Sairah Ahmed / Santiago Mercadal / Catherine Lee). ***Oral presentation at Tandem 2024; currently in manuscript preparation phase.***

(d) **LY22-02b** Efficacy and safety of CD19 directed CAR T-cell therapy for T-cell rich histiocyte rich B-cell lymphoma (Priyanka Pophali / Roni Shouval /Mazyar Shadman). ***Poster presentation, Tandem Meetings 2024; Manuscript circulated within writing committee.***

3. Studies in progress

(a) **LY20-02** Outcomes of allogeneic transplants in patients with hodgkin lymphoma in the era of checkpoint inhibitors: A joint CIBMTR and EBMT analysis (Miguel-Angel Perales/Ana Maria Sureda). **Manuscript preparation.**

(b) **LY22-01b** Outcomes of autologous HCT and CD19 CAR-T in MYC+ large B-cell lymphoma patients (Fateeha Furqan / Mehdi Hamadani). **Data File Preparation.**

(c) **LY22-02c** Efficacy and safety of CD19 directed CAR T-cell therapy for transferred follicular lymphoma (Swetha Kambhampati / Kalyan Nadiminti / Alex Herrera). **Waiting hours assignment.**

(d) **LY22-02d** Efficacy and safety of CD19 directed CAR T-cell therapy for Richter's transformation. Data File preparation (Mazyar Shadman / Mehdi Hamadani). **Waiting hours assignment.**

(e) **LY22-02e** Efficacy and safety of CD19 directed CAR T-cell therapy for primary mediastinal B-cell lymphoma (Jordan Gauthier / Alex Herrera). **Waiting hours assignment.**

(f) **LY22-02f** Efficacy and safety of CD19 directed CAR T-cell therapy for high grade B-cell lymphoma (Nasheed Hossain / Alex Herrera). **Waiting hours assignment.**

(g) **LY23-01** Efficacy of hematopoietic stem cell transplantation in patients with plasmablastic lymphoma. **Protocol Development.**

4. Research Datasets Available for Secondary Analysis, Introduction to TED (Transplant Essential Data) vs CRF (Comprehensive Report Form)

Dr. Mehdi Hamadani emphasized the availability of published datasets freely available to the public for secondary analysis. Also, explained the difference between the TED and CRF databases. It was emphasized that CRF is a subset of the TED database, and that the CRF forms collect all disease specific information such as lines of therapy, extranodal involvement, and prior radiation. If a study needs any of this information, CRF level data is needed on the study. Then Dr. Hamadani detailed the LYWC study life cycle and introduced PRO data collection effort of CIBMTR to audience followed by encouragement to propose studies that can encompass PRO data.

Dr. Hamadani finished the introduction slides by inviting the members to attend the Collaborative Study Proposal Session.

5. Future/proposed studies

Dr. Alex Herrera presented the first three proposed concepts and emphasized that all presentations are in-person. Finally encourage the virtual attendants to submit their questions on the chat.

(a) **Mazyar Shadman:** A matching adjusted indirect comparison (MAIC) analysis comparing the clinical outcomes of patients with follicular lymphoma treated with anti CD19 directed CAR-T therapy vs the bispecific antibody, mosunetuzumab (Mazyar Shadman/Mehdi Hamadani)

Dr Shadman presented the concept in-person. The proposed study wants to look at comparative efficacy and safety profile of cases treated with commercial CAR-T product axi-cel and bispecific agent - mosunetuzumab. CAR-T data will be obtained from CIBMTR registry and mosunetuzumab data will be obtained from GO29781 study followed by matching reweighting.
The proposal was opened for questions from the audience. A clarification was requested on matching of the 2 cohorts based on sample size which was responded as in following approach of careful consideration of number of variables for matching to find the balance as higher number of variables leads to over-adjustment in some instances. Statistical director of LYWC also contributed in answering the question and added propensity score calculation approach followed by weight application to create balance among CIBMTR and published data. Another question was raised regarding consideration of tisa-cel in the study and was answered that enrollment of tisa-cel for this particular indication is very slow and adding these cases into study will add heterogeneity to analysis. Additionally, follow-up of tisa-cell cases will not be long enough to be considered into analysis. A suggestion was also received to include ZUMA5 clinical trial cases as control to make study stronger. Another question was raised related to impact of transformation which was answered by providing the criteria of exclusion of reported transformed cases. Another suggestion was received to add hematopoietic recovery data as outcome. However, published data doesn't reported this outcome because of which this outcome cannot be compared among 2 cohorts. Last question was if CIBMTR collects data related to bispecific agents in registry. Dr. Hamadani responded that CIBMTR registry collects data mainly related to cellular therapies, however, there might be industry funded venues within CIBMTR where bispecific agents are compared with cellular therapies reported to CIBMTR.

(b) **Aung Tun**: Autologous stem cell transplant vs chimeric antigen receptor T-cell therapy (CAR-T) in patients with diffuse large B-cell lymphoma who relapsed or progressed in central nervous system (Aung Tun / Stephen Ansell)

Dr. Tun presented the proposal on behalf of study group. The proposed study hypothesizes that autologous stem cell transplantation is associated with superior progression-free survival (PFS) than CAR-T in patients with chemo-sensitive relapsed secondary Nervous System lymphoma (SCNSL). It also hypothesizes that CAR-T therapy is reasonably safe with a manageable toxicity profile in patients with SCNSL.
The proposal was opened for questions from the audience. A member of audience asked if bridging therapy or use of other modalities like ibrutinib will be captured in the study. Dr. Tun responded that reporting use of other modalities and bridging therapy will be helpful in the study even though this data is under-reported due to its complexity. A clarification was requested regarding criteria of conditioning regimen in transplant cohort which was answered by Dr. Tun

that all conditioning regimens will be looked on including BEAM. A suggestion was provided by a member of audience that comparing outcomes among primary/refractory cases and relapsed cases among these cohorts will be a better comparison to avoid potential biases in this study. Another suggestion was also received related to exclusion of CAR-T cases who received any prior autologous stem cell transplant to avoid overlapping.

(c) **Caroline Lee:** Real-world outcomes of second-line CD19 CAR T-cell therapy for large B-cell lymphoma (Caroline Lee / Saurabh Dahiya / Mazyar Shadman / Swetha Kambhampati / Alex Herrera / Maria Silvina Odstrcil Bobillo / Catherine Joy Lee)

Dr. Lee presented the proposal on behalf of study group. The rational of the study is that safety and efficacy of standard-of-care (SOC) second-line CD19 CAR T-cell therapy are unknown in the real-world population which includes patients with high-risk disease and/or comorbid conditions excluded from the registrational trials. The proposal hypothesize that the real-world safety and efficacy outcomes are similar to those reported in the registrational trials: ZUMA-7, TRANSFORM, and PILOT.
Study was opened for questions. A suggestion was received to parse out the patients who contact transplant centers after receiving treatment from primary physicians as it does not lead to a case where all the therapies received by patient are known to the center. Dr. Hamadani explained this as a complicated concept as data for bridging therapy is determined by CIBMTR and is not reported by centers as it is, however, it can be looked upon with handful data. Another suggestion was also received related to consideration of time to lines of therapies which can help determine intent, early therapy failure, and bridging therapy prior to infusion. Dr. Pasquini explained issues in determination of time of lines of therapies as centers sometimes do not report timings of lines of therapies and also have misunderstandings about definition of bridging therapy because of which a question related to collection of bridging therapy provision is not introduced on CIBMTR forms directly.

Dr. Shadman presented last 3 proposal concepts.

(d) **Mehdi Hamadani:** Hematopoietic cell transplantation for rare mature T-cell lymphomas. A Basket – mentoring study proposal (Mehdi Hamadani / Mazyar Shadman / Craig Sauter / Cameron Turtle / Alex Herrera)

Dr. Hamadani presented the proposal having objective of looking at survival outcomes, non-relapse mortality, relapse/progression and toxicity measures post HCT for rare mature T-cell lymphomas. Another goal of the study is to involve multiple junior investigators in leading a registry project. He also mentioned if LYWC members receives the proposal positively, the LYWC will seek guidance from CIBMTR Foster group for a fair way of identifying junior faculty to lead sub-projects.
The proposal was opened for questions. A suggestion was received to look on a cohort separately having cases which were treated with consolidation intent within 6 months of induction therapy for this study. Dr. Hamadani reflected the numbers of feasible cases among sub-diseases and agreed on looking consolidated cases separately. Another question was raised related to lumping of other DLI proposals having same criteria and objectives with this proposal. Dr. Hamadani responded that due to limited granularity of information for these sub-diseases data, lumping of

other DLI proposals is not that easy. However, publicly available datasets can be used to analyze such data if someone is interested.

(e) **Evandro Bezerra:** Outcomes of autologous stem cell transplant in large B-cell lymphoma related/refractory to CART19 (Evandro Bezerra / Samantha Jaglowski / Swetha Kambhampati / Alexa Herrera / Baldeep Wirk)

Dr. Bezzera presented the concept to the audience on behalf of group. The study hypothesizes that autologous stem cell transplant (ASCT) is feasible and safe if relapsed/refractory large B-cell lymphoma after CART 19, and may be effective in subset of patients. The study will determine the feasibility, safety, and effectiveness of ASCT post-CART19. If ASCT post-CART19 is proven to be feasible, safe, and effective, it may increase access to ASCT for a population for which currently the only curative therapy option is allogeneic stem cell transplant which is associated with high morbid-mortality.
The proposal was opened for questions. A question was raised if cases who receive pseudo bridging therapy can be separated from cases who receive real bridging therapy prior to infusion. Dr. Bezzera responded that just because study looks at autologous transplant post CAR-T infusion so lines of therapies prior to CAR-T infusion will not be looked upon. Another question was raised on feasibility of the study which was responded with conduction of descriptive analysis only. A clarification was requested if those cases will be included in the study who had autologous transplant prior to CAR-T and Dr. Bezzerra clarified by mentioning exclusion of those cases. Another clarification was made related to lines of therapies if CAR-T has to be given as second line post autologous transplant which was responded as CAR-T given in any line of therapies post-autologous stem cell transplant will be included in the study.

(f) **Mengyang Di:** Comparative effectiveness of glofitamab and axicabtagene ciloleucel in large B cell lymphoma: A CIBMTR-based matching-adjusted indirect comparison analysis (Mengyang Di / Mazyar Shadman)

Dr. Di presented the concept to the audience. The study hypothesizes better efficacy of axi-cel than glofitamab in lines of therapies. Matching-adjusted indirect comparison analysis will be performed for selecting patients from CIBMTR database. The results of study will cover the gap of knowledge pertaining to relative efficacy between CAR-Ts and bispecific agents and can lead to changes in clinical practice.
The proposal was opened for questions. A question was raised related to ways to deal with cases from glofitamab cohort that has received prior CAR-T which was responded by Dr. Di as one of the limitations. She also mentioned that progress-free survival at 2 years follow-up on 2 cohorts where one received prior CAR-T and other did not was similar in one of studies presented at ASH meeting. So, it is assumed that this factor will not impact the findings considering the caveat of comparing real-world data and clinical trial data. Another question was raised in regard to consideration of only one drug – glofitamab in the bispecific cohort which was answered as it was the first approved bispecific agent for the large B cell lymphoma indication and thus is the primary reason to be included solely in the study. Another question raised was related to finding out ways of unsuccessful CAR-T infusions due to factors like prolonged manufacturing where clinicians prefer to opt CAR-T infusion but change the treatment due to some factors as this is one of the biasing in the real-world clinical practice. Dr. Di mentioned this as one of the other

limitations of the study. An online question was also addressed related to explanation of results pertaining to sequencing of therapies. Dr. Di explained that based on hypothesis, axi-cel treatment should be more efficacious than glofitamab in the clinical settings. If axi-cel leads to more durable progression-free survival, it can be given prior to bispecific agents for large B cell lymphoma in second or greater line of therapy settings.

Proposed studies; not accepted for consideration at this time

Dr. Hamadani thanked all the investigators who submitted their concepts but were not accepted for presentation.

a. **PROP 2305-02** Autologous and Allogeneic Hematopoietic Cell Transplantation for ALK+ Diffuse Large B-Cell Lymphoma. *Dropped – low scientific impact.*
b. **PROP 2305-06** Chimeric Antigen Receptor T-Cell Therapy vs. Autologous Transplant in Relapsed DLBCL After Complete Remission. *Dropped – overlap with current study/publication.*
c. **PROP 2309-03** Clinical Outcome and Impact of Fludarabine Lymphodepletion Dose Prior to CD19 CAR T Cell Therapy in Aggressive Non-Hodgkin's Lymphoma Patients. *Dropped – low scientific impact.*
d. **PROP 2309-04** Impact of Donor age on Post-SCT Outcomes in Patients with Acute Myeloid Leukemia. *Dropped – low scientific impact.*
e. **PROP 2309-05** Outcomes of Haplo vs MUD vs Umbilical Cord vs Matched Related Allogeneic Stem Cell Transplant in Patients with Cutaneous T-Cell Lymphomas. *Dropped – low scientific impact.*
f. **PROP 2309-08** Role of Induction Chemotherapy Regimen in Relapse Free Survival Following Autologous Bone Marrow Transplant Among Mantle Cell Lymphoma Patients. *Dropped – low scientific impact.*
g. **PROP 2309-14** The Impact of Salvage Therapy on Outcomes After Autologous Stem Cell Transplant in Patients with Relapsed and Refractory Hodgkin Lymphoma. *Dropped – low scientific impact.*
h. **PROP 2309-16** Fludarabine Lymphodepletion Exposure as a Driver of Outcomes After Car-T. *Dropped – supplemental data needed.*
i. **PROP 2310-16** Incidence of Second Primary Malignancies and Related Survival Outcomes in Lymphoma Patients Undergoing CAR-T Therapy. *Dropped – supplemental data needed.*
j. **PROP 2310-20** Real-World Outcomes of CD19 CAR T for Relapsed/Refractory Follicular Lymphoma. *Dropped – low scientific impact.*
k. **PROP 2310-22** Real-World Outcomes of Novel Therapies Post CD19 CAR T Therapy in Relapsed Refractory Diffuse Large B-Cell Lymphoma. *Dropped – low scientific impact.*
l. **PROP 2310-51** Evaluating Outcomes of Hematopoietic Cell Transplantation in Hepatosplenic T Cell Lymphoma. *Dropped – low scientific impact.*
m. **PROP 2310-70** Efficacy and Safety of CD19-Directed CAR-T Cell Therapy in NHL Patients Who Did Not Meet Clinical Trial Criteria for Second-Line or Third-Line Setting, Including Those with Prior CD19 Therapy Exposure. *Dropped – low scientific impact.*
n. **PROP 2310-76** Real-Word Efficacy of Lisocabtagene Maraleucel (Liso-cel) Therapy in Patients with Relapsed or Refractory Large B Cell Lymphoma. *Dropped – low scientific impact.*
o. **PROP 2310-77** Optimal Monitoring Period for Lymphoma Patients Who Are Recipients of Commercial CD19 CAR-T Therapy. *Dropped – low scientific impact.*

p. **PROP 2310-85** Outcomes of HIV-Associated Large B-Cell Lymphoma Treated with Chimeric Antigen Receptor T-Cell Therapy. *Dropped – low scientific impact.*
q. **PROP 2310-100** Autologous Transplant vs Chimeric Antigen Receptor T-Cell Therapy for DLBCL Achieving a Partial Remission to Frontline Chemoimmunotherapy. *Dropped – low scientific impact.*
r. **PROP 2310-108** Real World Outcomes of Axi-cel and Tisa-Cel in Patients with Relapsed/Refractory Follicular Lymphoma. *Dropped – low scientific impact.*
s. **PROP 2310-112** Effect of Diabetes on the Outcomes of Diffuse Large B Cell Lymphoma Patients Treated with CAR T-Cells. *Dropped – low scientific impact.*
t. **PROP 2310-134** Determination of the Optimal Conditioning Regimen for Non-Hodgkin Lymphoma with Secondary CNS Involvement. *Dropped – low scientific impact.*
u. **PROP 2310-135** Comparative Outcomes Analysis of Patients with Aggressive B- Cell Lymphoma Treated with Axicabtagene Ciloleucel vs. Lisocabtagene Maraleucel. *Dropped – low scientific impact.*
v. **PROP 2310-137** Impact of Lymphodepleting Chemotherapy on Outcomes After CAR-T Cell Therapy for Relapsed Refractory Non-Hodgkin's Lymphoma. *Dropped – low scientific impact.*
w. **PROP 2310-139** Can the Outcome of a CAR T-Cell Treatment be Predicted Before the Treatment Starts? *Dropped – low scientific impact.*
x. **PROP 2310-145** Outcomes of CAR-T Therapy in Large B-Cell Lymphoma Patients with History of CNS Involvement. *Dropped – low scientific impact.*
y. **PROP 2310-151** A Comparison of Chemotherapy versus Non-chemotherapy-based Salvage regimens Leading to Autologous Hematopoietic Cell Transplant (autoHCT) for the Treatment of Relapsed/Refractory Hodgkin Lymphoma. *Dropped – supplemental data needed.*
z. **PROP 2310-153** A Comparison Between Chemotherapy-Based and Non-Chemotherapy-Based Salvage Regimens for Large B Cell Lymphomas (LBCL) Prior to Autologous Stem Cell Transplantation. *Dropped – supplemental data needed.*
aa. **PROP 2310-156** The Predictive Role of Cytopenia Recovery on Outcome Following CAR-T Cell Therapy in Lymphoma. *Dropped – overlap with current study/publication.*
bb. **PROP 2310-162** Outcomes of Hematopoietic Stem Cell Transplantation (HSCT) in Rare T Cell Lymphoma (TCL) Subtypes – Hepatosplenic TCL (HSTCL) and Enteropathy Associated TCL (EATL). *Dropped – low scientific impact.*
cc. **PROP 2310-165** Impact of Novel Agent-Based Salvage Therapies on Outcomes in Classical Hodgkin Lymphoma Patients Undergoing Autologous Hematopoietic Cell Transplantation. *Dropped – supplemental data needed.*
dd. **PROP 2310-167** Impact of prior cellular immunotherapy on outcomes post CD19 CAR-T cell therapy for relapsed refractory NHL. *Dropped – low scientific impact.*
ee. **PROP 2310-182** The Impact of Conditioning Regimens on Outcomes of Autologous Hematopoietic Stem Cell Transplantation (HSCT) in Peripheral T Cell Lymphomas (PTCL). *Dropped – low scientific impact.*
ff. **PROP 2310-191** Risk Factors and Outcomes of Patients with Lymphoid Malignancies Receiving out of Specification Autologous Cell Therapy Products. *Dropped – low scientific impact.*
gg. **PROP 2310-193** Comparative Efficacy of CD19 CAR-T Cell Therapy in Extra-Nodal versus Nodal-Only Large B-Cell Lymphoma. *Dropped – supplemental data needed.*
hh. **PROP 2310-197** Outcomes in Late Relapse Aggressive B-Cell Lymphoma. *Dropped – low scientific impact.*
ii. **PROP 2310-204** Efficacy of a Second CAR T-Cell Therapy in Patients with Relapse/Refractory B-Cell Malignancies. *Dropped – low scientific impact.*

jj. **PROP 2310-220** Chimeric Antigen Receptor T (CAR T) Cell Therapy in Non-Hodgkin's B Cell Lymphoma Patients with Pre-Existing Active Autoimmune Rheumatological Diseases – Safety and Efficacy Analysis. *Dropped – supplemental data needed.*

kk. **PROP 2310-223** CAR-T and Allogeneic Transplant in Relapsed Mantle Cell Lymphoma: A Contemporary Real-World Data in the Era of Novel Drugs. *Dropped – low scientific impact.*

ll. **PROP 2310-230** Comparing the Efficacy and the Safety of CD19 CAR T Cell Therapy in EBV-Positive versus EBV-Negative Diffuse Large B-Cell Lymphoma. *Dropped – low scientific impact.*

mm. **PROP 2310-234** Prognostic Impact of Corticosteroids Following CAR-T Cell Therapy in Large B-Cell Lymphoma: Assessing Infection Risk and Clinical Outcomes. *Dropped – low scientific impact.*

nn. **PROP 2310-238** Outcomes of Donor Lymphocyte Infusion in Patients with Hodgkin Lymphoma that Received Checkpoint Inhibitors. *Dropped – low scientific impact.*

oo. **PROP 2310-252** Comparative Outcomes of Large B Cell Lymphoma Patients Treated with Lisocabtagene Maraleucel (liso-cel) Compared to Axicabtagene Ciloleucel (axi-cel). *Dropped – low scientific impact.*

pp. **PROP 2310-253** Impact of Pre-Existing Autoimmune Disease on Outcomes After CAR-T Cell Therapy. *Dropped – supplemental data needed.*

qq. **PROP 2310-256** Outcomes of Bispecific Immune Effector Engager Antibodies BITEs Before and After CD19 CAR-T for Patients with Large B-Cell Lymphomas. *Dropped – low scientific impact.*

rr. **PROP 2310-259** Comparative Outcomes of Patients with Follicular Lympyhoma Treated with Lisocabtagene Maraleucel (liso-cel) Compared to Axicabtagene Ciloleucel (axi-cel). *Dropped – low scientific impact.*

ss. **PROP 2310-265** CAR-T cell therapy versus salvage/auto-transplant for patients with primary refractory Mantle Cell Lymphoma. *Dropped – low scientific impact.*

tt. **PROP 2310-267** Liso-Cabtagene Comparison to Axi-Cel and Tisa-Cel. *Dropped – low scientific impact.*

7. Other Business

After the proposals were presented, the voting process was reiterated, and the working committee leadership invite the attendees to rate each new proposal using the Tandem App. Without additional comments, the meeting was adjourned.

Working Committee Overview Plan 2024-2025		
Study number and title	**Current Status**	**Chairs Priority**
LY20-02: Outcomes of allogeneic transplants in patients with hodgkin lymphoma in the era of checkpoint inhibitors: A joint CIBMTR and EBMT analysis.	Manuscript preparation	1
LY22-01: Outcomes of CD19 CAR-T in patients who achieve complete remission prior to lymphodepletion in patients with aggressive nonHodgkins lymphoma.	Data file preparation	2
LY22-02: Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with primary and secondary central nervous system involvement.	Protocol development	3
LY23-01: Efficacy of hematopoietic stem cell transplantation in patients with plasmablastic lymphoma.	Protocol development	4
LY24-01: Hematopoietic cell transplantation for rare mature T-cell lymphomas.	Protocol Development	5

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2025						
	HLA-Identical Sibling		Alternative Donor		Autologous	
	TED only	Research	TED only	Research	TED Only	Research
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Anaplastic large cell	346	60	557	187	2260	215
PIF	65 (18.8)	9 (15.0)	91 (16.3)	34 (18.2)	296 (13.1)	21 (9.8)
CR1	52 (15.0)	11 (18.3)	77 (13.8)	28 (15.0)	1030 (45.6)	93 (43.3)
Rel 1	31 (9.0)	10 (16.7)	40 (7.2)	12 (6.4)	185 (8.2)	24 (11.2)
CR2	105 (30.3)	17 (28.3)	190 (34.1)	50 (26.7)	522 (23.1)	52 (24.2)
Other/Unknown	93 (26.9)	13 (21.7)	159 (28.5)	63 (33.7)	227 (10.0)	25 (11.6)
Burkitt/small non-cleaved	206	59	154	112	738	157
PIF	37 (18.0)	8 (13.6)	18 (11.7)	21 (18.8)	118 (16.0)	32 (20.4)
CR1	45 (21.8)	15 (25.4)	34 (22.1)	16 (14.3)	261 (35.4)	62 (39.5)
Rel 1	28 (13.6)	7 (11.9)	18 (11.7)	16 (14.3)	60 (8.1)	14 (8.9)
CR2	51 (24.8)	21 (35.6)	55 (35.7)	39 (34.8)	187 (25.3)	38 (24.2)
Other/Unknown	45 (21.8)	8 (13.6)	29 (18.8)	20 (17.9)	112 (15.2)	11 (7.0)
Diffuse large cell/immunoblastic	1825	332	1987	911	22230	2630
PIF	418 (22.9)	90 (27.1)	466 (23.5)	268 (29.4)	3861 (17.4)	455 (17.3)
CR1	197 (10.8)	54 (16.3)	297 (14.9)	101 (11.1)	4026 (18.1)	494 (18.8)
Rel 1	280 (15.3)	44 (13.3)	207 (10.4)	88 (9.7)	3782 (17.0)	476 (18.1)
CR2	251 (13.8)	32 (9.6)	335 (16.9)	113 (12.4)	6499 (29.2)	774 (29.4)
Other/Unknown	679 (37.2)	112 (33.7)	682 (34.3)	341 (37.4)	4062 (18.3)	431 (16.4)
Follicular	1471	519	1325	731	5374	926
PIF	250 (17.0)	94 (18.1)	228 (17.2)	147 (20.1)	785 (14.6)	108 (11.7)
CR1	109 (7.4)	38 (7.3)	95 (7.2)	43 (5.9)	641 (11.9)	115 (12.4)
Rel 1	199 (13.5)	106 (20.4)	157 (11.8)	103 (14.1)	952 (17.7)	171 (18.5)
CR2	194 (13.2)	73 (14.1)	183 (13.8)	80 (10.9)	1409 (26.2)	218 (23.5)
Other/Unknown	719 (48.9)	208 (40.1)	662 (50.0)	358 (49.0)	1587 (29.5)	314 (33.9)
Lymphoblastic	172	49	125	106	266	35
PIF	18 (10.5)	7 (14.3)	8 (6.4)	12 (11.3)	14 (5.3)	1 (2.9)
CR1	50 (29.1)	11 (22.4)	21 (16.8)	18 (17.0)	118 (44.4)	19 (54.3)
Rel 1	28 (16.3)	8 (16.3)	10 (8.0)	16 (15.1)	23 (8.6)	1 (2.9)
CR2	32 (18.6)	12 (24.5)	35 (28.0)	34 (32.1)	32 (12.0)	6 (17.1)
Other/Unknown	44 (25.6)	11 (22.4)	51 (40.8)	26 (24.5)	79 (29.7)	8 (22.9)
Mantle	943	205	1157	486	9906	998

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2025						
PIF	172 (18.2)	44 (21.5)	161 (13.9)	83 (17.1)	1392 (14.1)	132 (13.2)
CR1	193 (20.5)	40 (19.5)	215 (18.6)	78 (16.0)	7007 (70.7)	687 (68.8)
Rel 1	138 (14.6)	34 (16.6)	159 (13.7)	80 (16.5)	261 (2.6)	34 (3.4)
CR2	182 (19.3)	30 (14.6)	335 (29.0)	94 (19.3)	483 (4.9)	61 (6.1)
Other/Unknown	258 (27.4)	57 (27.8)	287 (24.8)	151 (31.1)	763 (7.7)	84 (8.4)
Marginal	98	25	110	40	418	43
PIF	16 (16.3)	8 (32.0)	32 (29.1)	10 (25.0)	74 (17.7)	13 (30.2)
CR1	9 (9.2)	3 (12.0)	19 (17.3)	5 (12.5)	74 (17.7)	4 (9.3)
Rel 1	11 (11.2)	1 (4.0)	12 (10.9)	6 (15.0)	55 (13.2)	3 (7.0)
CR2	14 (14.3)	3 (12.0)	12 (10.9)	4 (10.0)	90 (21.5)	10 (23.3)
Other/Unknown	48 (49.0)	10 (40.0)	35 (31.8)	15 (37.5)	125 (29.9)	13 (30.2)
NK T cell	295	51	434	120	874	88
PIF	70 (23.7)	11 (21.6)	99 (22.8)	27 (22.5)	153 (17.5)	16 (18.2)
CR1	80 (27.1)	13 (25.5)	137 (31.6)	46 (38.3)	404 (46.2)	40 (45.5)
Rel 1	25 (8.5)	6 (11.8)	26 (6.0)	8 (6.7)	64 (7.3)	5 (5.7)
CR2	58 (19.7)	5 (9.8)	94 (21.7)	28 (23.3)	134 (15.3)	14 (15.9)
Other/Unknown	62 (21.0)	16 (31.4)	78 (18.0)	11 (9.2)	119 (13.6)	13 (14.8)
T cell	1052	260	1763	649	4380	463
PIF	345 (32.8)	100 (38.5)	560 (31.8)	276 (42.5)	712 (16.3)	68 (14.7)
CR1	216 (20.5)	55 (21.2)	409 (23.2)	126 (19.4)	2592 (59.2)	249 (53.8)
Rel 1	116 (11.0)	26 (10.0)	182 (10.3)	65 (10.0)	288 (6.6)	45 (9.7)
CR2	161 (15.3)	32 (12.3)	330 (18.7)	76 (11.7)	436 (10.0)	52 (11.2)
Other/Unknown	214 (20.3)	47 (18.1)	282 (16.0)	106 (16.3)	352 (8.0)	49 (10.6)
NHL not specified	180	24	102	120	857	44
PIF	15 (8.3)	4 (16.7)	7 (6.9)	31 (25.8)	92 (10.7)	8 (18.2)
CR1	13 (7.2)	0 (0.0)	5 (4.9)	13 (10.8)	107 (12.5)	11 (25.0)
Rel 1	28 (15.6)	2 (8.3)	7 (6.9)	18 (15.0)	63 (7.4)	5 (11.4)
CR2	15 (8.3)	2 (8.3)	18 (17.6)	19 (15.8)	111 (13.0)	5 (11.4)
Other/Unknown	109 (60.6)	16 (66.7)	65 (63.7)	39 (32.5)	484 (56.5)	15 (34.1)
Other	810	205	1402	441	11252	1063
PIF	204 (25.2)	61 (29.8)	371 (26.5)	118 (26.8)	2059 (18.3)	203 (19.1)
CR1	162 (20.0)	38 (18.5)	345 (24.6)	131 (29.7)	3787 (33.7)	384 (36.1)
Rel 1	78 (9.6)	19 (9.3)	120 (8.6)	36 (8.2)	1302 (11.6)	98 (9.2)
CR2	118 (14.6)	16 (7.8)	261 (18.6)	57 (12.9)	3190 (28.4)	256 (24.1)
Other/Unknown	248 (30.6)	71 (34.6)	305 (21.8)	99 (22.4)	914 (8.1)	122 (11.5)

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2025						
Hodgkin	1382	364	1674	1288	21849	2527
PIF	259 (18.7)	63 (17.3)	297 (17.7)	185 (14.4)	3947 (18.1)	553 (21.9)
CR1	76 (5.5)	28 (7.7)	126 (7.5)	115 (8.9)	2980 (13.6)	347 (13.7)
Rel 1	162 (11.7)	56 (15.4)	184 (11.0)	145 (11.3)	3813 (17.5)	463 (18.3)
CR2	154 (11.1)	55 (15.1)	229 (13.7)	189 (14.7)	7272 (33.3)	762 (30.2)
Other/Unknown	731 (52.9)	162 (44.5)	838 (50.1)	654 (50.8)	3837 (17.6)	402 (15.9)
Graft type	8780	2153	10790	5191	80404	9189
BM	878 (10.0)	194 (9.0)	1745 (16.2)	1047 (20.2)	715 (0.9)	72 (0.8)
PB	7840 (89.3)	1954 (90.8)	8429 (78.1)	3500 (67.4)	78936 (98.2)	9058 (98.6)
Other/Unknown	62 (0.7)	5 (0.2)	616 (5.7)	644 (12.4)	753 (0.9)	59 (0.6)

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TO: Lymphoma Working Committee Members

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

RE: 2024-2025 Studies in Progress Summary

LY22-02c Efficacy and safety of CD19 directed CAR T-cell therapy for transferred follicular lymphoma (S Kambhampati/ K Nadiminti/ A Herrera) This study evaluates outcomes of patients undergoing CAR-T for follicular lymphoma.

Status: **Manuscript Preparation** Goal: **Submission**

LY22-02d Efficacy and safety of CD19 directed CAR T-cell therapy for Richter's transformation (M Shadman/ M Hamadani) This study evaluates outcomes of patients undergoing CAR-T for Richter's transformation.

Status: **Manuscript Preparation** Goal: **Submission**

LY22-02e Efficacy and safety of CD19 directed CAR T-cell therapy for primary mediastinal B-cell lymphoma (J Gauthier/ A Herrera) This study evaluates outcomes of patients undergoing CAR-T for primary mediastinal B-cell lymphoma.

Status: **Manuscript Preparation** Goal: **Submission**

LY22-02f Efficacy and safety of CD19 directed CAR T-cell therapy for high grade B-cell lymphoma. (S Ahmed/ S Mercadal/ H Hashmi/ C Lee/ N Epperla) This study evaluates outcomes of patients undergoing CAR-T for high grade B-cell lymphoma.

Status: **Manuscript Preparation** Goal: **Submission**

LY23-01 Efficacy of hematopoietic stem cell transplantation in patients with plasmablastic lymphoma (S Ahmed/ T Al-Juhaishi) This study will evaluate outcomes of autologous and allogenic HCT with plasmablastic lymphoma.

Status: **Protocol Development** Goal: **Submission**

LY24-01a Hematopoietic cell transplantation for rare mature T-cell lymphomas (Madiha Iqbal / Aung Tun) This study will evaluate outcomes of HCT with rare peripheral T-cell lymphoma (PTCL) subtypes such as hepatosplenic T-cell lymphoma (HSTCL)

Status: **Protocol Development** Goal: **Submission**

LY24-01b Hematopoietic cell transplantation for rare mature T-cell lymphomas (Daniel Reef / Niloufer Khan) This study will evaluate outcomes of HCT with rare peripheral T-cell lymphoma (PTCL) subtypes such as subcutaneous panniculitis-like T-cell lymphoma (SPTCL).

Status: **Protocol Development** Goal: **Submission**

LY24-01c Hematopoietic cell transplantation for rare mature T-cell lymphomas (Alejandro Sica / Robert Stuver) This study will evaluate outcomes of HCT with rare peripheral T-cell lymphoma (PTCL) subtypes such as adult T-cell leukemia/lymphoma (ATLL)

Status: **Protocol Development** Goal: **Submission**

LY24-01d Hematopoietic cell transplantation for rare mature T-cell lymphomas (Taylor Brooks / Yifan Pang) This study will evaluate outcomes of HCT with rare peripheral T-cell lymphoma (PTCL) subtypes such as monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)/ (EATL)

Status: **Protocol Development** Goal: **Submission**

LY24-01e Hematopoietic cell transplantation for rare mature T-cell lymphomas (Amrita Desai / Kamil Rechache) This study will evaluate outcomes of HCT with rare peripheral T-cell lymphoma (PTCL) subtypes such as extra-nodal NK/T-cell lymphoma, nasal type (NKTCL)

Status: **Protocol Development** Goal: **Submission**

LY24-01f Hematopoietic cell transplantation for rare mature T-cell lymphomas (Ibrahim Muhsen / Christina Poh) This study will evaluate outcomes of HCT with rare peripheral T-cell lymphoma (PTCL) subtypes such as non-angioimmunoblastic T-cell lymphoma nodal T-follicular helper cell lymphoma (non AITL T-FHCL)

Status: **Protocol Development** Goal: **Submission**

Field	Response
Proposal Number	2410-44-MIAN
Proposal Title	Comparative Outcomes Analysis of Patients with Aggressive B-Cell Lymphoma Treated with Axicabtagene Ciloleucel vs. Lisocabtagene maraleucel.
Key Words	CAR T cell therapy, axi-cel, liso-cel, dlbcl, follicular lymphoma
Principal Investigator #1: - First and last name, degree(s)	Agrima Mian, MD
Principal Investigator #1: - Email address	miana@ccf.org
Principal Investigator #1: - Institution name	Cleveland Clinic
Principal Investigator #1: - Academic rank	Fellow PGY-V, Hematology and Medical Oncology
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Brian T. Hill, MD, PhD
Principal Investigator #2 (If applicable): - Email address:)	hillb2@ccf.org
Principal Investigator #2 (If applicable): - Institution name:	Cleveland Clinic
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	BRIAN T. HILL
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	-
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	CRAIG SAUTER

Field	Response
RESEARCH QUESTION:	In patients with relapsed or refractory aggressive B-cell lymphoma, is there a significant difference between the comparative survival outcomes and toxicities in those treated with axicabtagene ciloleucel (axi-cel) versus lisocabtagene maraleucel (liso-cel)?
RESEARCH HYPOTHESIS:	Currently, axi-cel and liso-cel share essentially the same indications for treatment of relapsed or refractory (r/r) large B-cell lymphoma, and no direct comparison of these products has been performed so far. The hypothesis of this study is that patients with r/r aggressive B-cell lymphoma have similar rates of durable remissions when treated with anti-CD19 directed chimeric antigen receptor (CAR) T-cell using axi-cel or liso-cel.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Outcome To compare Progression free survival (PFS) assessed at 6 months in patients with r/r LBCL treated with axi-cel vs. liso-cel. (As shown in the two pivotal trials ZUMA-1 and TRANSCEND NHL 001 (1,2), for patients treated with both axi-cel and liso-cel, the PFS curves reach a plateau at 6 months, indicating that majority of patients who are free from progression/relapse at 6 months will not eventually relapse/progress.) Secondary Outcomes To compare the overall survival (OS) in patients with r/r LBCL treated with axi-cel vs. liso-cel. To compare the best objective response rate (ORR), complete remission (CR), partial remission (PR) rates and incidence of relapse/progression in patients with r/r LBCL treated with axi-cel vs. liso-cel. To compare the incidence and severity of cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS) in patients with r/r LBCL treated with axi-cel vs. liso-cel. To compare treatment-related mortality (TRM) and primary cause of death in patients with r/r LBCL treated with axi-cel vs. liso-cel.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Results of this study will immediately inform clinical practice as currently all approved anti-CD19 CAR T-cell therapies essentially share the same indication for use in r/r LBCL population, and the selection of the type of product is based on institutional preference, manufacturing availability and/or perceived efficacy and tolerability of these agents.

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.	Although diffuse large B-cell lymphoma (DLBCL) is a curable illness, approximately 30-40% patients experience relapse or may fail initial therapy. Fewer than 50% of patients with relapsed or refractory (r/r) LBCL achieve a response to subsequent treatment after second line salvage regimens and autologous stem cell transplant (ASCT) (3,4). Particularly worse outcomes are seen in those with chemotherapy refractory disease, early relapse (<1 year) or those who relapse after ASCT (median overall survival of 6 months) (5). At present, three anti-CD19 directed chimeric antigen receptor (CAR) T-cell therapy products are commercially available for patients with r/r LBCL, who have failed prior systemic therapy or transplant. These have remarkable clinical activity and can potentially achieve durable remissions. In a single center, retrospective, study of 215 patients with r/r LBCL, outcomes of those treated with (any) anti-CD19 CAR T-cell therapy compared with a historical population treated with alternate therapies, demonstrated a superior CR rate (52% vs 22%; P< 0.001), median PFS (5.2 vs 2.3 months; P=0.1), and median OS (19.3 vs 6.5 months; P=0.006), irrespective of number of lines of prior therapy (6). Two seminal studies lead to the FDA approval of axi-cel and tisagenlecleucel for this patient population (1,7). Lisocabtagene maraleucel (liso-cel), a novel anti-CD19 CAR T-cell (with a 4-1BB co-stimulatory domain administered as sequential infusions of equal target doses of CD8 and CD4 CAR T-cells) received FDA approval for r/r LBCL and follicular lymphoma grade 3b, after results from the TRANSCEND NHL 001 study (2). Compared to the seminal CAR T-cell studies, this study enrolled a broad range of patients with diverse histological features and other high-risk features such as low creatinine clearance, poor cardiac function and secondary CNS involvement. At present, there is paucity of data on comparative efficacy and toxicity of the three commercial CAR T-cell products in the real-world scenario. There are limited reports, but no conclusive evidence, to suggest that axi-cel may have superior disease control and higher toxicity, than tisa-cel (8,9). Recently, a matching-adjusted indirect comparison of the patient population in the JULIET vs. TRANSCEND NHL-001 study indicated no differences in the OS, PFS and CR rate between patients treated with tisa-cel vs liso-cel (10). Our previously proposed CIBMTR study to compare outcomes of patients treated with axi-cel vs. tisa-cel is currently in progress. With the FDA approval of liso-cel, which essentially shares the same indication for treatment as the prior two CAR T-cell products, “real-world” data to compare their efficacy and toxicity is warranted. A CIBMTR study is the most reasonable

Field	Response
	methodology to address this clinical question, since head-to-head comparison in randomized controlled trials seems unlikely in the near future.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria Patients ≥ 18 years who have undergone treatment with axi-cel or liso-cel at a CIBMTR center between 2018-2022. Patients with the following diagnosis: DLBCL with or without transformation from indolent lymphoma, high-grade B-cell lymphoma (including double-hit or triple-hit lymphoma), primary mediastinal B-cell lymphoma and Grade 3b Follicular lymphoma. Exclusion Criteria Patients who have received prior cellular therapy (for any indication) will be excluded.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	disease less likely to be seen in pediatric age group
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Data captured in the baseline demographics will include gender, age of diagnosis, performance status, time from diagnosis to relapse, response to most recent therapy (chemosensitive or chemoresistant), disease status at the last evaluation prior to CAR-T cell therapy and hematopoietic cell transplantation comorbidity index (HCT-CI). Details (and number) of prior treatments will include systemic chemotherapies (including bridging therapy), monoclonal antibodies or check point inhibitor therapy and prior hematopoietic stem cell transplant. Details of response and survival outcomes will include best response, time to best response, time to relapse/progression and overall survival. Details of toxicities will include severity of CRS and ICANS (using ASTCT consensus grading), specific therapies given for treatment of CRS and ICANS, peripheral blood cytopenia, hypogammaglobinemia, tumor lysis syndrome, clinically significant infections, subsequent malignancies or other Grade ¾ toxicities. These data will be procured from CIBMTR data collection forms: 4000 (Pre-Cellular Therapy Essential Data), 4003 (Cell Therapy Product), 4006 (Cellular Therapy Infusion) and 4100 (Cellular Therapy Essential Data Follow-Up Form) No supplemental data form will be required.
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	-

Field	Response
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	-
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	-
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.	-

REFERENCES:	1. Neelapu SS, Locke FL, Bartlett NL, Lekakis LJ, Miklos DB, Jacobson CA, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. N Engl J Med. 2017 28;377(26):2531–44. 2. Abramson JS, Palomba ML, Gordon LI, Lunning MA, Wang M, Arnason J, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. Lancet. 2020 Sep 19;396(10254):839–52. 3. Gisselbrecht C, Glass B, Mounier N, Singh Gill D, Linch DC, Trneny M, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. J Clin Oncol. 2010 Sep 20;28(27):4184–90. 4. Van Den Neste E, Schmitz N, Mounier N, Gill D, Linch D, Trneny M, et al. Outcome of patients with relapsed diffuse large B-cell lymphoma who fail second-line salvage regimens in the International CORAL study. Bone Marrow Transplant. 2016 Jan;51(1):51–7. 5. Crump M, Neelapu SS, Farooq U, Van Den Neste E, Kuruvilla J, Westin J, et al. Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study. Blood. 2017 19;130(16):1800–8. 6. Sermer D, Batlevi C, Palomba ML, Shah G, Lin RJ, Perales M-A, et al. Outcomes in patients with DLBCL treated with commercial CAR T cells compared with alternate therapies. Blood Advances. 2020 Oct 1;4(19):4669–78. 7. Schuster SJ, Bishop MR, Tam CS, Waller EK, Borchmann P, McGuirk JP, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019 03;380(1):45–56. 8. Riedell PA, Walling C, Nastoupil LJ, Pennisi M, Maziarz RT, McGuirk JP, et al. A Multicenter Retrospective Analysis of Clinical Outcomes, Toxicities, and Patterns of Use in Institutions Utilizing Commercial Axicabtagene Ciloleucel and Tisagenlecleucel for Relapsed/Refractory Aggressive B-Cell Lymphomas. Blood. 2019 Nov 13;134(Supplement_1):1599–1599. 9. Nastoupil LJ, Jain MD, Feng L, Spiegel JY, Ghobadi A, Lin Y, et al. Standard-of-Care Axicabtagene Ciloleucel for Relapsed or Refractory Large B-Cell Lymphoma: Results From the US Lymphoma CAR T Consortium. J Clin Oncol. 2020 Sep 20;38(27):3119–28. 10. Schuster SJ, Zhang J, Yang H, Agarwal A, Tang W, Martinez-Prieto M, et al. Comparative efficacy of tisagenlecleucel (tisa-cel) and lisocabtagene maraleucel (liso-cel) in patients with

Field	Response
	relapsed/refractory diffuse large B-cell lymphoma (r/r DLBCL). JCO. 2021 May 20;39(15_suppl):7535–7535.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	Yes, I have conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	Brian T. Hill has received research funding from Kite Pharma (a Gilead Company) and has served as a consultant to Kite Pharma as well as Novartis and Juno Therapeutics (a Celgene/Bristol-Myers Squibb Company).

Field	Response
Proposal Number	2410-168-REEF
Proposal Title	Axicabtagene ciloleucel (axi-cel) versus lisocabtagene maraleucel (liso-cel) as second-line therapy for relapsed/refractory diffuse large B-cell lymphoma: Individualized patient outcome prediction
Key Words	Diffuse large B-cell lymphoma, DLBCL, CAR-T, axi-cel, axicabtagene ciloleucel, liso-cel, lisocabtagene maraleucel, machine learning, artificial intelligence, heterogeneous treatment effects
Principal Investigator #1: - First and last name, degree(s)	Daniel Reef, MD
Principal Investigator #1: - Email address	daniel.reef@unchealth.unc.edu
Principal Investigator #1: - Institution name	UNC Lineberger Comprehensive Cancer Center
Principal Investigator #1: - Academic rank	Hematology/Oncology Fellow
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Natalie Grover, MD
Principal Investigator #2 (If applicable): - Email address:)	natalie_grover@med.unc.edu
Principal Investigator #2 (If applicable): - Institution name:	UNC Lineberger Comprehensive Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Daniel Reef
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	N/A
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-

Field	Response
RESEARCH QUESTION:	How will an individual patient with early relapsed or primary refractory diffuse large B-cell lymphoma after 1st-line therapy respond to 2nd-line axi-cel or liso-cel?
RESEARCH HYPOTHESIS:	For individual patients with early relapsed or primary refractory diffuse large B-cell lymphoma after 1st-line therapy, we will be able to use causal machine learning tools to accurately quantify the impact of 2nd-line axi-cel and liso-cel on outcomes assessing efficacy and toxicity.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	We aim to estimate individualized treatment effects among patients with early relapsed or primary refractory diffuse large B-cell lymphoma after 1st-line therapy treated with either 2nd-line axi-cel or liso-cel. Specific outcomes to assess include: 1. Overall survival 2. Progression-free survival 3. Complete response: Probability 4. Cytokine release syndrome: Probability of grade ≥3 5. Immune effector cell-associated neurotoxicity syndrome: Probability of grade ≥2, Probability of grade ≥3 6.Clinically significant infection: Probability 7. Clinically significant COVID-19 infection: Probability 8. Organ toxicity: Probability of grade ≥3 9. Absolute neutrophil count ≤500 at day 30 after CAR-T infusion: Probability 10. Absolute neutrophil count ≤500 at day 90 after CAR-T infusion: Probability 11. Platelet count ≥20 at day 30 after CAR-T infusion (if initial platelet count ≥20): Probability 12. Platelet count ≥20 at day 90 after CAR-T infusion (if initial platelet count ≥20): Probability

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Axi-cel and liso-cel are both indicated for adults with diffuse large B-cell lymphoma refractory to 1st-line chemoimmunotherapy or relapsed within 12 months of 1st-line chemoimmunotherapy. Studies of patients with relapsed/refractory diffuse large B-cell lymphoma using matching-adjusted indirect comparisons of trial data or real-world data have suggested that in terms of efficacy, axi-cel is either superior to or similar to liso-cel. These studies have also suggested that there is a higher incidence of severe adverse events with axi-cel than with liso-cel. This has created a paradigm whereby clinicians typically recommend axi-cel for younger, healthier patients and liso-cel for older patients with a greater burden of frailty and/or comorbidity. However, clinicians lack tools to make quantitative comparisons between the two options for individual patients which can make it difficult to make optimal decisions, particularly in edge cases where it is not clear whether to prioritize efficacy or safety. Additionally, the studies comparing outcomes with axi-cel and liso-cel included either patients with ≥2 prior lines of therapy or any number of prior lines of therapy; they do not directly inform use of CAR-T for 2nd-line therapy. We aim to develop a tool to better inform decisions between using axi-cel or liso-cel for adults with diffuse large B-cell lymphoma refractory to 1st-line chemoimmunotherapy or relapsed within 12 months of 1st-line chemoimmunotherapy.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	The ZUMA-7 and TRANSFORM trials demonstrated superior efficacy for axi-cel and liso-cel over standard-of-care platinum-based chemoimmunotherapy as 2nd-line therapy in primary refractory and early relapsed diffuse large B-cell lymphoma [1,2]. Indirect comparison of the trials shows similar event-free survival hazard ratios, while grade ≥3 cytokine release syndrome and immune cell-associated neurotoxicity syndrome were both more common with axi-cel than with liso-cel; incidence of severe infections is difficult to compare; and prolonged cytopenias may have been less common with axi-cel than with liso-cel [1,2]. While indirect comparison of trial results is often necessary for decision-making in clinical practice, a more direct comparison between axi-cel and liso-cel as 2nd-line therapy in primary refractory and early relapsed diffuse large B-cell lymphoma would help to make more informed decisions. Two studies have used matching-adjusted indirect comparison of axi-cel and liso-cel as 3rd or later line therapy for relapsed or refractory diffuse large B-cell lymphoma [3,4]. Both used data from the TRANSCEND NHL 001 and ZUMA-1 studies [3,4]. Maloney et al. found similar efficacy between axi-cel and liso-cel, but higher odds of grade ≥3 CRS and neurological events with axi-cel than with liso-cel [3]. Oluwole et al. found superior overall survival and progression-free survival for axi-cel over liso-cel and, like Maloney et al., found higher odds of grade ≥3 cytokine release syndrome and neurological events with axi-cel over liso-cel [3,4]. A single-center, real-world study comparing outcomes with axi-cel and liso-cel in patients with diffuse large B-cell lymphoma after any number of prior lines of therapy treated at the Fred Hutchinson Cancer Center demonstrated similar efficacy for axi-cel and liso-cel with a higher incidence of any-grade cytokine release syndrome and immune effector-associated neurotoxicity syndrome with axi-cel than with liso-cel [5]. The matching-adjusted indirect comparison and real-world studies are inconsistent in the comparative efficacy of axi-cel and liso-cel, but consistent in comparing the therapies' safety profiles. None of these studies directly inform choosing between axi-cel and liso-cel as 2nd-line therapy for patients with primary refractory or early relapsed diffuse large B-cell lymphoma. Indeed, to our knowledge there is no such study that has been published to date. With this in mind, we aim to use CIBMTR data to develop a tool to predict individualized efficacy and safety outcomes for patients treated with axi-cel or liso-cel in the 2nd-line setting for relapsed or refractory diffuse large B-cell lymphoma.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	- Age ≥18 years at start of 2nd-line therapy - Diagnosis of diffuse large B-cell lymphoma - Treatment with either axi-cel or liso-cel as 2nd-line therapy for early relapsed or primary refractory diffuse large B-cell lymphoma
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	We aim to optimize use of axi-cel and liso-cel for their FDA-approved indications in 2nd-line treatment of DLBCL. They are only approved for use in adults.
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Forms: Form F2400 (CTED) Form F2402 (CTED) Form F2900 (CTED) Form F4000 (CTED) Form F4003 (CTED) Form F4006 (CTED) Form F4100 (CTED) Form F2018 (CRF) – Only required to confirm early relapse for patients relapsing >1 year after diagnosis. Not required to confirm early relapse for patients relapsing < 1 year after diagnosis or for patients with primary induction failure. Baseline characteristics: - Age at CAR-T infusion - Sex - Comorbidities - Prior solid organ transplant (yes/no) - Prior COVID-19 vaccination - Prior COVID-19 booster - Pre-exposure drugs given for COVID-19 - Baseline platelet count - Karnofsky performance status and/or ECOG performance status - Large B-cell lymphoma subtype - Transformation from different lymphoma histology - Baseline LDH (and upper limit of normal) - Baseline PET Deauville score - Baseline disease status (ie, 1st relapse – untreated, primary induction failure – resistant, etc.) - Prior bridging therapy and best response to bridging (*optional, requires CRF data) Intervention: - Cellular therapy product - Product out of specification (yes/no) - Lymphodepletion (yes/no) - Date of cell product collection (to calculate vein-to-vein time) - Date of CAR-T infusion - Total number of cells administered Efficacy outcomes: - Vital status at last follow-up - Date of last follow-up - Relapse or progression (yes/no) - Date of relapse or progression - Best response Safety outcomes: - Maximum grade of cytokine release syndrome - Maximum grade of immune cell-associated neurotoxicity syndrome - Clinically significant infection (yes/no) - Death from infection - Grade 3-5 organ toxicity - Absolute neutrophil count recovery to ≥500 (yes/no with date of recovery) - Platelet count recovery to ≥20 (yes/no with date of recovery)
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)

Field	Response
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	This study will use causal machine learning approaches to quantify individualized treatment effects.
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	N/A
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A
REFERENCES:	1. Locke FL, Miklos DB, Jacobson CA, et al. Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma. N. Engl. J. Med. 2022;386(7):640–654. 2. Abramson JS, Solomon SR, Arnason J, et al. Lisocabtagene maraleucel as second-line therapy for large B-cell lymphoma: primary analysis of the phase 3 TRANSFORM study. Blood. 2023;141(14):1675–1684. 3. Maloney DG, Kuruvilla J, Liu FF, et al. Matching-adjusted indirect treatment comparison of liso-cel versus axi-cel in relapsed or refractory large B cell lymphoma. J. Hematol. Oncol.J Hematol Oncol. 2021;14(1):140. 4. Oluwole OO, Chen JMH, Chan K, et al. Matching-adjusted indirect comparison of axi-cel and liso-cel in relapsed or refractory large B-cell lymphoma. Leuk. Lymphoma. 2022;63(13):3052–3062. 5. Portuguese AJ, Albittar A, Huang JJ, et al. Real-World Comparison of Lisocabtagene Maraleucel (Liso-Cel) and Axicabtagene Ciloleucel (Axi-Cel): Efficacy & Toxicity. Transplant. Cell. Ther. 2024;30(2):S192
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	Yes, I have conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	Daniel Reef: Owns stock in Regeneron Pharmaceuticals. Natalie Grover: Received honoraria from BMS and Kite, is on a data safety monitoring committee for Novartis, and receives research funding from BMS. Remuneration is <$5000 annually.

Characteristics of adults with DLBCL treated with Axi-cel or Liso-cel CAR-T infusion reported to the CIBMTR between 2018-2023

Characteristic	Axicabtagene ciloleucel	Lisocabtagene maraleucel	Total
No. of patients	383	139	522
No. of centers	91	46	97
Age group - no. (%)			
Median (min-max)	64.2 (19.5-86.0)	72.8 (29.2-85.4)	67.0 (19.5-86.0)
60+	242 (63.2)	117 (84.2)	359 (68.8)
Recipient Sex - no. (%)			
Male	254 (66)	79 (57)	333 (64)
Female	129 (34)	60 (43)	189 (36)
Recipient race - no. (%)			
White	300 (78)	122 (88)	422 (81)
Black or African American	21 (5)	7 (5)	28 (5)
Asian	25 (7)	3 (2)	28 (5)
Native Hawaiian or other Pacific Islander	0 (0)	1 (1)	1 (0)
Other	1 (0)	1 (1)	2 (0)
More than one race	21 (5)	4 (3)	25 (5)
Missing	15 (4)	1 (1)	16 (3)
Ethnicity - no. (%)			
Hispanic or Latino	38 (10)	6 (4)	44 (8)
Non-Hispanic or Latino	321 (84)	129 (93)	450 (86)
Non-resident of the U.S.	13 (3)	0 (0)	13 (2)
Not reported	11 (3)	4 (3)	15 (3)
Karnofsky performance score prior to CT - no. (%)			
90-100	160 (42)	52 (37)	212 (41)
80	119 (31)	46 (33)	165 (32)
< 80	73 (19)	20 (14)	93 (18)
Not reported	31 (8)	21 (15)	52 (10)
HCT-CI Score - no. (%)			
0	132 (34)	35 (25)	167 (32)
1	88 (23)	38 (27)	126 (24)
2	55 (14)	19 (14)	74 (14)
3+	107 (28)	46 (33)	153 (29)
Not reported	1 (0)	1 (1)	2 (0)
Disease status prior to CT for lymphoma - no. (%)			

Characteristic	Axicabtagene ciloleucel	Lisocabtagene maraleucel	Total
CR	16 (4)	16 (12)	32 (6)
PR	94 (25)	35 (25)	129 (25)
Resistant	240 (63)	59 (42)	299 (57)
Untreated	16 (4)	17 (12)	33 (6)
Unknown	17 (4)	12 (9)	29 (6)
Time from initial diagnosis to CT - no. (%)			
>= 0 to < 6 months	42 (11)	9 (6)	51 (10)
>= 6 to < 12 months	233 (61)	68 (49)	301 (58)
>= 12 months	108 (28)	62 (45)	170 (33)
Bridging therapy - no. (%)			
No	147 (38)	42 (30)	189 (36)
Yes	228 (60)	96 (69)	324 (62)
Not reported	8 (2)	1 (1)	9 (2)
Number of lines of therapy (accounting for bridging - no. (%)			
1	383 (100)	139 (100)	522 (100)
Prior HCT - no. (%)			
No	383 (100)	139 (100)	522 (100)
Year of CT - no. (%)			
2022	222 (58)	23 (17)	245 (47)
2023	161 (42)	116 (83)	277 (53)
Follow-up among survivors - median (range)	12.5 (1.7-26.4)	12.1 (1.0-24.5)	12.3 (1.0-26.4)

Field	Response
Proposal Number	2410-66-DI
Proposal Title	A Matching Adjusted Indirect Comparison (MAIC) Analysis Comparing the Clinical Outcomes of Patients with Follicular Lymphoma Treated with Anti-CD19 Chimeric Antigen Receptor T Cell Therapy (CART) and Bispecific T Cell Engager.
Key Words	Follicular lymphoma, CAR-T therapy, Bispecific antibody
Principal Investigator #1: - First and last name, degree(s)	Mengyang Di, MD PhD
Principal Investigator #1: - Email address	mydi@fredhutch.org
Principal Investigator #1: - Institution name	Fred Hutchinson Cancer Center
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Mazyar Shadman, MD MPH
Principal Investigator #2 (If applicable): - Email address:)	mshadman@fredhutch.org
Principal Investigator #2 (If applicable): - Institution name:	Fred Hutchinson Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Mengyang Di
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	NA
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Mehdi Hamadani

Field	Response
RESEARCH QUESTION:	In patients with FL who received 2 or more prior lines of treatment, are clinical outcomes different in patients treated with commercial CD19 directed CAR-T versus (vs) in those who received the CD20/CD3 bispecific antibody (Mosunetuzumab-axgb [mosun] or Epcoritamab-bysp [epcor])?
RESEARCH HYPOTHESIS:	We hypothesize that CD19 directed CAR-T is associated with an improved clinical efficacy compared to bispecific antibodies (mosun or epcor) in patients with r/r FL after 2 or more prior lines of treatment. Given that the trial data on mosun is more mature (median follow-up 3.5 years for the latest data (1)), our proposed analyses will be focused on the comparison of CART and mosun.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary objective: To compare the progression-free survival (PFS) between CART and mosun. Secondary objectives 1) To compare the PFS between CART and epcor. 2) To compare the overall survival (OS) between CART and mosun. 3) To compare the OS between CART and epcor. 4) To compare the rate of infections between CART and mosun. 5) To compare the rate of infections between CART and epcor. 6) To compare the rate of cytokine release syndrome (CRS) between CART and mosun. 7) To compare the rate of CRS between CART and epcor. 8) To compare the rate of non-relapse mortality (NRM) between CART and mosun. 9) To compare the rate of NRM between CART and epcor. 10) To compare causes of death between CART and mosun. 11) To compare causes of death between CART and epcor.

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Both CAR-T therapy (Axicabtagene Ciloleucel [axi-cel], Tisagenlecleucel [tisa-cel], or Lisocabtagene Maraleucel [liso-cel]) (2-4) and bispecific antibody (mosun and epcor) (1, 5, 6) have been approved for treatment in patients with FL after 2 or prior lines of treatment. Both approaches have high efficacy with the current follow-up based on single arm studies. However, there is no prior, ongoing, or planned head-to-head clinical trial to compare the clinical efficacy and safety between the 2 treatment modalities. CIBMTR has collected detailed and high-quality clinical data in a large number of patients receiving CART. This provides a unique opportunity to perform a Matching Adjusted Indirect Comparison (MAIC) analysis (7) to compare the two treatment modalities by using the patient level data from the CIBMTR and the published data from the trials on mosun and epcor, respectively. The results will be important and informative for clinical practice. Findings may indicate clinical benefit for one of the two modalities and potentially impact the clinical practice.
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.	This analysis is justified as there is no clinical trial that compares CAR-T and bispecific antibodies in patients with FL. There are very unlikely such studies to allow direct comparisons in foreseeable future to the best of our knowledge. On the other hand, it is crucial to make the best effort to examine the relative efficacy and safety. Results will very likely inform how to sequence the two treatment modalities in relapsed/refractory FL. CIBMTR is in a unique position for this MAIC analysis and can potentially provide a relatively large sample for adjustment of confounders. The latter may not be possible to achieve for the lymphoma community.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	1) Patients with a diagnosis of FL 2) Treatment with tisa-cel, axi-cel, and liso-cel 3) At least 2 prior lines of treatment 4) No history of histologic transformation 5) No prior history of other CAR-T therapy
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	The therapies of interest are only approved in adult population thus far.

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Following patient characteristics are required for patients: a. Age b. Sex c. Ethnicity d. ECOG at treatment e. Ann arbor stage at treatment f. Bulky disease at treatment g. FLIPI risk factor if available at treatment h. Number of prior lines of therapy i. Prior autologous transplant j. Refractoriness to last previous therapy k. Refractoriness to previous anti-CD20 therapy (if available) l. Refractoriness to previous alkylator therapy (if available) m. Progressive disease withing 24 months from first line of therapy Using the CIBMTR database, a cohort of patients with FL will be selected after matching with the published baseline characteristics of patients who were treated with mosun or epcor on the pivotal clinical trials, respectively (1, 5, 6). One cohort will be selected to include patients who received axi-cel, tisa-cel, or liso-cel for their FL. There is no plan to compare among the three CAR-T cohorts. The selected CART cohort using the patient level data will be compared to the aggregate published data on each of the bispecific antibodies. The baseline characteristics and outcomes are described above.
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	-
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	-
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	-
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.	-

Field	Response
REFERENCES:	1. Budde LE, Assouline S, Sehn LH, Schuster SJ, Yoon SS, Yoon DH, et al. Durable Responses With Mosunetuzumab in Relapsed/Refractory Indolent and Aggressive B-Cell Non-Hodgkin Lymphomas: Extended Follow-Up of a Phase I/II Study. J Clin Oncol. 2024;42(19):2250-6. 2. Dreyling M, Fowler NH, Dickinson M, Martinez-Lopez J, Kolstad A, Butler J, et al. Durable response after tisagenlecleucel in adults with relapsed/refractory follicular lymphoma: ELARA trial update. Blood. 2024;143(17):1713-25. 3. Morschhauser F, Dahiya S, Palomba ML, Martin Garcia-Sancho A, Reguera Ortega JL, Kuruvilla J, et al. Lisocabtagene maraleucel in follicular lymphoma: the phase 2 TRANSCEND FL study. Nat Med. 2024;30(8):2199-207. 4. Neelapu SS, Chavez JC, Sehgal AR, Epperla N, Ulrickson M, Bachy E, et al. Three-year follow-up analysis of axicabtagene ciloleucel in relapsed/refractory indolent non-Hodgkin lymphoma (ZUMA-5). Blood. 2024;143(6):496-506. 5. Budde LE, Sehn LH, Matasar M, Schuster SJ, Assouline S, Giri P, et al. Safety and efficacy of mosunetuzumab, a bispecific antibody, in patients with relapsed or refractory follicular lymphoma: a single-arm, multicentre, phase 2 study. Lancet Oncol. 2022;23(8):1055-65. 6. Linton KM, Vitolo U, Jurczak W, Lugtenburg PJ, Gyan E, Sureda A, et al. Epcoritamab monotherapy in patients with relapsed or refractory follicular lymphoma (EPCORE NHL-1): a phase 2 cohort of a single-arm, multicentre study. Lancet Haematol. 2024;11(8):e593-e605. 7. Signorovitch JE, Sikirica V, Erder MH, Xie J, Lu M, Hodgkins PS, et al. Matching-adjusted indirect comparisons: a new tool for timely comparative effectiveness research. Value Health. 2012;15(6):940-7.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	Yes, I have conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	Mengyang Di: Consulting: BeiGene, Genetech; Research funding: Schrodinger, BeiGene. Mazyar Shadman: Consulting, Advisory Boards, steering committees or data safety monitoring committees: Abbvie, Genentech, Genmab, AstraZeneca, Beigene, Bristol Myers Squibb, Morphosys/Incyte, Kite Pharma, Eli Lilly, Fate therapeutics. Research Funding: Mustang Bio, Celgene, Bristol Myers Squibb, Pharmacyclics, Gilead, Genentech, AbbVie, TG Therapeutics, Beigene, AstraZeneca, Genmab, Morphosys/Incyte, Vincerx. Employment (spouse): BMS.

Characteristics of adults with LBCL treated with axi-cel, and liso-cel CAR-T infusion reported to the CIBMTR

Characteristic	Axicabtagene ciloleucel	Lisocabtagene maraleucel	Total
No. of patients	1203	162	1365
No. of centers	121	43	123
Age group - no. (%)			
Median (min-max)	74.1 (70.0-90.8)	75.2 (70.0-91.2)	74.2 (70.0-91.2)
70-80	1108 (92.1)	137 (84.6)	1245 (91.2)
80+	95 (7.9)	25 (15.4)	120 (8.8)
Recipient Sex - no. (%)			
Male	768 (64)	98 (60)	866 (63)
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Not reported	1 (0)	0 (0)	1 (0)
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White	944 (78)	142 (88)	1086 (80)
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More than one race	46 (4)	5 (3)	51 (4)
Missing	103 (9)	2 (1)	105 (8)
Ethnicity - no. (%)			
Hispanic or Latino	90 (7)	11 (7)	101 (7)
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Non-resident of the U.S.	116 (10)	2 (1)	118 (9)
Not reported	35 (3)	7 (4)	42 (3)

Characteristic	Axicabtagene ciloleucel	Lisocabtagene maraleucel	Total
Karnofsky performance score prior to CT - no. (%)			
90-100	384 (32)	55 (34)	439 (32)
80	433 (36)	45 (28)	478 (35)
< 80	259 (22)	44 (27)	303 (22)
Not reported	127 (11)	18 (11)	145 (11)
HCT-CI Score - no. (%)			
0	298 (25)	38 (23)	336 (25)
1	198 (16)	25 (15)	223 (16)
2	167 (14)	20 (12)	187 (14)
3+	519 (43)	75 (46)	594 (44)
Not reported	21 (2)	4 (2)	25 (2)
Disease status prior to CT for lymphoma - no. (%)			
CR	82 (7)	13 (8)	95 (7)
PR	275 (23)	32 (20)	307 (22)
Resistant	709 (59)	102 (63)	811 (59)
Untreated	75 (6)	6 (4)	81 (6)
Unknown	62 (5)	9 (6)	71 (5)
Time from initial diagnosis to CT - no. (%)			
>= 0 to < 6 months	140 (12)	19 (12)	159 (12)
>= 6 to < 12 months	343 (29)	37 (23)	380 (28)
>= 12 months	719 (60)	106 (65)	825 (60)
Not reported	1 (0)	0 (0)	1 (0)
No. of lines of prior therapies (including HCT and CT) - no. (%)			
1	61 (5)	5 (3)	66 (5)
2	304 (25)	36 (22)	340 (25)

Characteristic	Axicabtagene ciloleucel	Lisocabtagene maraleucel	Total
>= 3	515 (43)	109 (67)	624 (46)
Not reported	323 (27)	12 (7)	335 (25)
Prior HCT - no. (%)			
No	1033 (86)	148 (91)	1181 (87)
Yes	168 (14)	14 (9)	182 (13)
Not reported	2 (0)	0 (0)	2 (0)
Year of CT - no. (%)			
2017	2 (0)	0 (0)	2 (0)
2018	61 (5)	0 (0)	61 (4)
2019	141 (12)	0 (0)	141 (10)
2020	172 (14)	0 (0)	172 (13)
2021	143 (12)	58 (36)	201 (15)
2022	286 (24)	93 (57)	379 (28)
2023	299 (25)	8 (5)	307 (22)
2024	99 (8)	3 (2)	102 (7)
Follow-up among survivors - median (range)	13.9 (1.0-75.4)	24.1 (3.1-38.0)	22.6 (1.0-75.4)

Field	Response
Proposal Number	2410-67-DI
Proposal Title	Real-world Outcomes Following Anti-CD19 Chimeric Antigen Receptor T Cell Therapy in Older Patients with Large B Cell Lymphoma.
Key Words	Large B cell lymphoma, CAR-T therapy, geriatric
Principal Investigator #1: - First and last name, degree(s)	Mengyang Di, MD PhD
Principal Investigator #1: - Email address	mydi@fredhutch.org
Principal Investigator #1: - Institution name	Fred Hutchinson Cancer Center
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Mazyar Shadman, MD MPH
Principal Investigator #2 (If applicable): - Email address:)	mshadman@fredhutch.org
Principal Investigator #2 (If applicable): - Institution name:	Fred Hutchinson Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Mengyang Di
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	NA
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Mehdi Hamadani

Field	Response
RESEARCH QUESTION:	What is the efficacy and safety of using anti-CD19 chimeric antigen receptor T cell therapy (CART; Axicabtagene Ciloleucel [axi-cel], Tisagenlecleucel [tisa-cel], Lisocabtagene Maraleucel [liso-cel]) in patients ≥75 years old with large B cell lymphoma (LBCL) outside the clinical trial setting, compared to the younger group (younger than 75 years old)?
RESEARCH HYPOTHESIS:	Compared to younger patients (younger than 75 years old), the clinical efficacy and risk of cytokine release syndromes of anti-CD19 CAR-T (axi-cel, tisa-cel, or liso-cel) are respectively similar in patients with LBCL ≥75 years old. However, the risks of immune effector cell-associated neurotoxicity syndrome and infection are higher in the older population (≥75 years old).
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary objective: To compare the progression-free survival (PFS) following each anti-CD19 CAR-T product (axi-cel, tisa-cel, or liso-cel) in patients with LBCL ≥75 years old, using those aged younger than 75 as reference. Secondary objectives 1) To compare the overall survival (OS) following each anti-CD19 CAR-T product in patients with LBCL ≥75 years old, using those aged younger than 75 as reference. 2) To compare the rate of infections following each anti-CD19 CAR-T product in patients with LBCL ≥75 years old, using those aged younger than 75 as reference. 3) To compare the rate of cytokine release syndrome (CRS) following each anti-CD19 CAR-T product in patients with LBCL ≥75 years old, using those aged younger than 75 as reference. 4) To compare the rate of immune effector cell-associated neurotoxicity syndrome (ICANS) following each anti-CD19 CAR-T product in patients with LBCL ≥75 years old, using those aged younger than 75 as reference. 5) To compare the rate of non-relapse mortality (NRM) following each anti-CD19 CAR-T product in patients with LBCL ≥75 years old, using those aged younger than 75 as reference. 6) To compare causes of death following each anti-CD19 CAR-T product in patients with LBCL ≥75 years old, using those aged younger than 75 as reference.

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Due to the prevalent frailty and comorbidity, management of LBCL in older patients has been challenging (1, 2), particularly in the relapsed/refractory (r/r) setting where the curative therapy often includes stem cell transplant. The approval of anti-CD19 CAR-T (tisa-cel, axi-cel, and liso-cel) in LBCL provides very promising curative-intent treatment options for older patients (3-10). However, it remains unclear whether CAR-T provides similar efficacy in older patients, particularly those ≥75 years old, compared to their younger counterparts (11-16). In addition, complications of CAR-T, including CRS, ICANS, and infection, may be barriers of fully adopting this therapy modality in older patients (11-16). Whether there should an age limit remains unanswered. CIBMTR has collected detailed, high-quality clinical data in a large number of patients with LBCL receiving anti-CD19 CART, across all age groups. This provides a unique opportunity to examine the relative efficacy and safety of CART in older patients (≥75 years old), compared to the younger group. The results of this study will possibly provide further guidance on use of CART in older patients with LBCL.
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.	This CIBMTR-based analysis is justified, as previous similar studies have shown inconsistent results on the relative efficacy and safety of anti-CD19 CAR-T in older patients with LBCL (11-16); there is no or very sparse data on using CAR-T in patients ≥75 years old. Importantly, these studies each have their own limitations in answering this important question, including small sample size, suboptimal reference groups (e.g., using patients 65-69 years old as the control), not reflecting the real-world experience (e.g., subgroup analyses from ZUMA-1 trial), and lack of granular clinical data (e.g., no data on CRS or ICANS in the Medicare-based analyses). CIBMTR includes a large number of patients with LBCL receiving anti-CD19 CART and has collected detailed, high-quality clinical data from primarily the routine practice. Patients included in the database are across all age groups. These advantages help overcome most of the limitations discussed above. This CIBMTR-based analysis has the potential of providing a more definitive answer to the relative outcomes of using CAR-T in older patients with LBCL.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	1) Patients with a diagnosis of LBCL, including diffuse large B cell lymphoma, high grade B cell lymphoma, primary mediastinal B cell lymphoma, LBCL arising from indolent lymphoma, and follicular lymphoma grade 3B. 2) Treatment with tisa-cel, axi-cel, or liso-cel 3)At least 1 prior line of treatment 4) No prior history of other CAR-T therapy
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	The therapies of interest are only approved in adult patients thus far.
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Following patient characteristics are required for patients: a. Age b. Sex c. Ethnicity d. ECOG at treatment e. Ann arbor stage at treatment f. Bulky disease at treatment g. Number of prior lines of therapy h. Prior autologous transplant i. Refractoriness to last previous therapy j. Primary refractoriness k. Refractoriness to previous anti-CD20 therapy (if available) l. Refractoriness to previous alkylator therapy (if available) m. Comorbidity profile Using the CIBMTR database, a cohort of patients with LBCL will be selected. Three separate cohorts will be selected from the patients who received axi-cel, tisa-cel, and liso-cel. There is no plan to compare among the three CAR-T cohorts. In each cohort, we will compare the outcomes of interest in older patients (≥75 years old) and in the younger group (<75 years old). Multivariable Cox regression models will be used for time to event outcomes (e.g., OS). Multivariable competing risk analyses will be applied for outcomes, such as, NRM (relapse or mortality due to relapse as competing events) and toxicities (mortality as competing events). The baseline characteristics for multivariable adjustment and outcomes are described above.
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	-
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	-

Field	Response
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	-
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.	-

REFERENCES:	1. Di M, Keeney T, Belanger E, Huntington SF, Olszewski AJ, Panagiotou OA. Functional status and therapy for older adults with diffuse large B-cell lymphoma in nursing homes: A population-based study. J Am Geriatr Soc. 2023;71(7):2239-49. 2. Di M, Keeney T, Belanger E, Panagiotou OA, Olszewski AJ. Global Risk Indicator and Therapy for Older Patients With Diffuse Large B-Cell Lymphoma: A Population-Based Study. JCO Oncol Pract. 2022;18(3):e383-e402. 3. Abramson JS, Palomba ML, Gordon LI, Lunning MA, Wang M, Arnason J, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. Lancet. 2020;396(10254):839-52. 4. Abramson JS, Solomon SR, Arnason J, Johnston PB, Glass B, Bachanova V, et al. Lisocabtagene maraleucel as second-line therapy for large B-cell lymphoma: primary analysis of the phase 3 TRANSFORM study. Blood. 2023;141(14):1675-84. 5. Bishop MR, Dickinson M, Purtill D, Barba P, Santoro A, Hamad N, et al. Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma. N Engl J Med. 2022;386(7):629-39. 6. Neelapu SS, Jacobson CA, Ghobadi A, Miklos DB, Lekakis LJ, Oluwole OO, et al. Five-year follow-up of ZUMA-1 supports the curative potential of axicabtagene ciloleucel in refractory large B-cell lymphoma. Blood. 2023;141(19):2307-15. 7. Schuster SJ, Bishop MR, Tam CS, Waller EK, Borchmann P, McGuirk JP, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019;380(1):45-56. 8. Schuster SJ, Tam CS, Borchmann P, Worel N, McGuirk JP, Holte H, et al. Long-term clinical outcomes of tisagenlecleucel in patients with relapsed or refractory aggressive B-cell lymphomas (JULIET): a multicentre, open-label, single-arm, phase 2 study. Lancet Oncol. 2021;22(10):1403-15. 9. Sehgal A, Hoda D, Riedell PA, Ghosh N, Hamadani M, Hildebrandt GC, et al. Lisocabtagene maraleucel as second-line therapy in adults with relapsed or refractory large B-cell lymphoma who were not intended for haematopoietic stem cell transplantation (PILOT): an open-label, phase 2 study. Lancet Oncol. 2022;23(8):1066-77. 10. Westin JR, Oluwole OO, Kersten MJ, Miklos DB, Perales MA, Ghobadi A, et al. Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma. N Engl J Med. 2023;389(2):148-57. 11. Dreger P, Holtick U, Subklewe

Field	Response
	M, von Tresckow B, Ayuk F, Wagner E, et al. Impact of age on outcome of CAR-T cell therapies for large B-cell lymphoma: the GLA/DRST experience. Bone Marrow Transplant. 2023;58(2):229-32. 12. Ram R, Grisariu S, Shargian-Alon L, Amit O, Bar-On Y, Stepensky P, et al. Toxicity and efficacy of chimeric antigen receptor T-cell therapy in patients with diffuse large B-cell lymphoma above the age of 70 years compared to younger patients - a matched control multicenter cohort study. Haematologica. 2022;107(5):1111-8. 13. Chihara D, Liao L, Tkacz J, Franco A, Lewing B, Kilgore KM, et al. Real-world experience of CAR T-cell therapy in older patients with relapsed/refractory diffuse large B-cell lymphoma. Blood. 2023;142(12):1047-55. 14. Johnson PC, Neckermann I, Sadrzadeh H, Newcomb R, El-Jawahri AR, Frigault MJ. Clinical Outcomes and Toxicity in Older Adults Receiving Chimeric Antigen Receptor T Cell Therapy. Transplant Cell Ther. 2024;30(5):490-9. 15. Shouse G, Danilov AV, Artz A. CAR T-Cell Therapy in the Older Person: Indications and Risks. Curr Oncol Rep. 2022;24(9):1189-99. 16. Neelapu SS, Jacobson CA, Oluwole OO, Munoz J, Deol A, Miklos DB, et al. Outcomes of older patients in ZUMA-1, a pivotal study of axicabtagene ciloleucel in refractory large B-cell lymphoma. Blood. 2020;135(23):2106-9.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	Yes, I have conflicts of interest pertinent to this proposal
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2	167 (14)	20 (12)	187 (14)
3+	519 (43)	75 (46)	594 (44)
Not reported	21 (2)	4 (2)	25 (2)
Disease status prior to CT for lymphoma - no. (%)			
CR	82 (7)	13 (8)	95 (7)
PR	275 (23)	32 (20)	307 (22)
Resistant	709 (59)	102 (63)	811 (59)
Untreated	75 (6)	6 (4)	81 (6)
Unknown	62 (5)	9 (6)	71 (5)
Time from initial diagnosis to CT - no. (%)			
>= 0 to < 6 months	140 (12)	19 (12)	159 (12)
>= 6 to < 12 months	343 (29)	37 (23)	380 (28)
>= 12 months	719 (60)	106 (65)	825 (60)
Not reported	1 (0)	0 (0)	1 (0)
No. of lines of prior therapies (including HCT and CT) - no. (%)			
1	61 (5)	5 (3)	66 (5)
2	304 (25)	36 (22)	340 (25)

Characteristic	Axicabtagene ciloleucel	Lisocabtagene maraleucel	Total
>= 3	515 (43)	109 (67)	624 (46)
Not reported	323 (27)	12 (7)	335 (25)
Prior HCT - no. (%)			
No	1033 (86)	148 (91)	1181 (87)
Yes	168 (14)	14 (9)	182 (13)
Not reported	2 (0)	0 (0)	2 (0)
Year of CT - no. (%)			
2017	2 (0)	0 (0)	2 (0)
2018	61 (5)	0 (0)	61 (4)
2019	141 (12)	0 (0)	141 (10)
2020	172 (14)	0 (0)	172 (13)
2021	143 (12)	58 (36)	201 (15)
2022	286 (24)	93 (57)	379 (28)
2023	299 (25)	8 (5)	307 (22)
2024	99 (8)	3 (2)	102 (7)
Follow-up among survivors - median (range)	13.9 (1.0-75.4)	24.1 (3.1-38.0)	22.6 (1.0-75.4)

Field	Response
Proposal Number	2410-72-GUPTA
Proposal Title	Real-World Comparison of Safety, Efficacy and Outcomes of Brexucabtagene Autoleucel versus Lisocabtagene Maraleucel for Relapsed or Mantle Cell Lymphoma
Key Words	CAR-T, Lisocabtagene maraleucel, Brexucabtagene Autoleucel, CAR-T cell, Mantle Cell Lymphoma, Real World Outcomes
Principal Investigator #1: - First and last name, degree(s)	Supriya Gupta, MD
Principal Investigator #1: - Email address	gupt0509@umn.edu
Principal Investigator #1: - Institution name	University of Minnesota
Principal Investigator #1: - Academic rank	Asssistant Professor of Medicine
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Veronika Bachanova, MD, PhD
Principal Investigator #2 (If applicable): - Email address:)	bach0173@umn.edu
Principal Investigator #2 (If applicable): - Institution name:	University of Minnesota
Principal Investigator #2 (If applicable): - Academic rank:	Professor of Medicine
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Supriya Gupta
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
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	SG: Real-world comparison of anti-BCMA CAR-T cell therapy in relapsed/refractory multiple myeloma (Plasma Cell Committee) - co-PI VB: Co-Chair of CIBMTR Acute Leukemia Working Committee
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No

Field	Response
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-
RESEARCH QUESTION:	Does the safety and efficacy of Brexucabtagene autoleucel and Lisocabtagene maraleucel for the treatment of relapsed or refractory mantle cell lymphoma differ in the real-world setting?
RESEARCH HYPOTHESIS:	Treatment of relapsed or refractory mantle cell lymphoma with CD19-directed CAR-T cell therapy with Brexucabtagene autoleucel and Lisocabtagene maraleucel have similar response rates, disease control and survival, but Brexucabtagene autoleucel has higher rates of treatment-related adverse events.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary aim: 1. To compare the overall survival and progression-free survival of patients treated with Brexucabtagene autoleucel versus Lisocabtagene maraleucel. 2. To compare the overall response rates and complete response rates of Brexucabtagene autoleucel and Lisocabtagene maraleucel 3. To compare the rates of cytokine release syndrome and immune effector cell associated neurotoxicity syndrome Secondary aim: 1. To evaluate the outcomes of treatment with Brexucabtagene autoleucel and Lisocabtagene maraleucel among different patient subsets, including those with higher risk disease features, greater tumor burden, elderly patients and those with co-morbidities that would have precluded their participation in the ZUMA-2 and TRANSCEND NHL 001 (Mantle Cell Cohort) clinical trials due to the stringent inclusion criteria. 2. To compare rates of treatment-related mortality associated with each CAR-T cell therapy. 3. To describe the rates of other adverse events not specified in the primary outcomes.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	There are currently two FDA-approved CAR-T cell therapies for relapsed mantle cell lymphoma: Brexucabtagene autoleucel and Lisocabtagene maraleucel. There have been no head-to-head comparisons between the two. This study will provide valuable insight into the different safety and efficacy of treatment with Brexucabtagene autoleucel and Lisocabtagene maraleucel in the real-world, non-trial population, and in different patient subgroups. This will allow for predictive modeling of factors that impact safety, response and survival outcomes with each of these CAR-T products and ultimately inform treatment selection in patients with various different baseline demographic and clinical characteristics.

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.	Patients with mantle cell lymphoma who experience disease progression after treatment with Bruton tyrosine kinase inhibitor (BTKi) have historically poor outcomes with subsequent therapy, including conventional chemotherapy, with an objective response rate of approximately 30%, and median overall survival of 6-10 months. [1-3] This led to the emergence of novel immunotherapeutic agents, including chimeric antigen receptor T (CAR-T) cells targeting the CD19 antigen. To this date, Brexucabtagene autoleucel (Brexu-cel) and Lisocabtagene maraleucel (Liso-cel) are the only two CD19-directed CAR-T products to receive FDA approval for the treatment of relapsed or refractory mantle cell lymphoma. [4, 5] The first CAR-T cell therapy to be approved in mantle cell lymphoma was Brexu-cel based on the results of the phase 2 ZUMA-2 clinical trial. [4] This study included 74 patients with relapsed or refractory disease who had a median of 3 (range, 1-5) prior therapies, including BTK inhibitor therapy. In the treated population, 93% in the primary efficacy analysis had an objective response, and 67% had a complete response. At a median follow-up of 12.3 months (range, 7 to 32.3), 57% of the patients were in remission. At 12 months, the estimated progression-free survival (PFS) and overall survival (OS) were 61% and 83%, respectively. The incidence of cytokine release syndrome was 91% (24% grade 3 or higher and no grade 5). The incidence of neurological events was 63% (32% grade 3 or higher and no grade 5 events). The most common adverse events of grade 3 or higher were cytopenias (94%) and infections (32%). All-cause mortality with Brexu-cel was 24%, primarily from progressive disease (21%). Two patients (3%) had grade 5 adverse events due to infections. At the 3-year follow-up of ZUMA-2, the objective response rate was 91%, with a complete response rate of 68% at a median follow-up of 35.6 months. [6] The median duration of response (DOR), PFS and OS were 28.2 months, 25.8 months, and 46.6 months, respectively. The objective response rates and ongoing response rates were consistent among prespecified subgroups by prior BTKi exposure or high-risk characteristics such as TP53 mutation and blastoid morphology. Real world outcomes of Brexu-cel from the CIBMTR registry were similar to those seen on the ZUMA-2 clinical trials with an objective response rate was 89% and complete response rate of 78%. [7] At a 6-month follow-up, the incidence of relapse or progressive disease was 21%. The DOR, PFS and OS were 76%, 73% and 83%, respectively. CRS occurred in 94% of patients (9% grade 3 or higher). Neurotoxicity occurred in 79% (27% grade 3

Field	Response
	or higher). Non-relapse mortality at day 100 and day 180 were 3% and 6%, respectively, mainly due to infections. The MCL cohort of the phase 1 TRANSCEND study demonstrated that Liso-cel had an objective response rate of 83% and a complete response rate of 72% in a heavily pretreated population with relapsed or refractory disease. [5] The median DOR and PFS were 15.7 months and 15.3 months, respectively at a median follow-up of 16.1 months. The incidence of CRS was 61% (1% grade 3 or higher and no grade 5), and neurotoxicity was 31% (9% grade 3 or higher and no grade 5). Grade 3 or higher rates of infections and prolonged cytopenias were 15% and 40%, respectively. Both studies demonstrated deep and durable responses. The TRANSCEND trial reported lower incidences of treatment-related adverse events like CRS, ICANS, cytopenias, and infections with Liso-cel, suggesting there may be key differences in the safety profiles of these two therapies. However, the designs of these two trials were not identical - ZUMA-2 permitted a maximum of five prior lines of therapy, while TRANSCEND included 30% of patients who had received more than five prior lines. Furthermore, TRANSCEND allowed patients with moderate renal or cardiac dysfunction and secondary CNS involvement, which were excluded in ZUMA-2. Therefore, no strong conclusions can be drawn based on direct comparison of the two trials. Additionally, both trials enrolled highly selected patients, which may limit the generalizability of the results in the real-world setting. There remains a critical need for real-world evidence to assess the applicability of these therapies to a broader patient population, and to understand the predictors of response and adverse events associated with these therapies. This in turn would guide clinicians in selecting the most appropriate CAR-T product for patients, and characterize which patient subsets derive the most benefit from these therapies. To this date, there are no published or planned head-to-head trials to compare the safety and efficacy of treating relapsed or refractory mantle cell lymphoma with Brexu-cel versus Liso-cel. Therefore, we aim to study the differences in the performance between these CAR-T products in the real-world setting among different patient populations captured by the CIBMTR database.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: 1. Patients who have received standard-of-care treatment with either Brexucabtagene autoleucel or Lisocabtagene maraleucel for relapsed or refractory mantle cell lymphoma and who have at least one follow-up timepoint or experienced mortality before the first follow-up. Exclusion Criteria: 1. Patients with relapsed or refractory mantle cell lymphoma treated with Brexucabtagene autoleucel or Lisocabtagene maraleucel on a registered clinical trial or expanded-access program.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	Mantle cell lymphoma is uncommon in the pediatric patient population.

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Patient and disease-related factors: Age at treatment Sex Race/Ethnicity ECOG performance status/Karnofsky Performance Status Comorbidities HCT-CI score prior to CAR-T Baseline CBC Baseline LDH Baseline eGFR Baseline cardiac function HIV, Hepatitis B and Hepatitis C serostatus Number of prior lines of therapy Disease stage Disease status at the time of CAR-T Bone marrow morphology Cytogenetics and molecular profile TP53 mutation status Ki67% Exposure to and number of previous non-covalent BTK inhibitors Exposure to and number of previous covalent BTK inhibitors Prior stem cell transplantation CAR-T related factors: Lymphodepleting regimen used prior to CAR-T Bridging therapy used prior to CAR-T Specific CAR-T product used Inpatient versus outpatient administration Cytokine release syndrome occurrence (Y/N) Cytokine release syndrome maximum grade Cytokine release syndrome duration ICANS occurrence (Y/N) ICANS maximum grade ICANS duration Steroids administered Tocilizumab administered Anakinra administered Occurrence of infectious complications post-CAR-T CBC parameters post-CAR-T at first follow-up Ferritin post-CAR-T at first follow-up Overall Response Rate: Defined as the proportion of patients who achieved a partial response or better as defined by the Lugano Response Criteria for Non-Hodgkin Lymphoma Complete Response Rate: Defined as the proportion of patients who achieved a complete response as defined by the Lugano Response Criteria for Non-Hodgkin Lymphoma Progression-Free Survival: Defined as the duration from the date of infusion to progressive disease, or death from any cause, whichever occurred first. Patients will be censored at the time of last follow-up. Overall Survival: Defined as the time from infusion to the date of death due to any cause Patients will be censored at the time of last follow-up. Cause of death (if applicable) We aim to perform matched comparison of both products, and characterize the differential outcomes and toxicity. If this proposal is accepted, we will work closely with a CIBMTR statistician after receiving the initial set of data to better identify how to define and categorize these variables in univariate and multivariate analyses.
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)

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

Field	Response
REFERENCES:	1. Cheah CY, Chihara D, Romaguera JE, et al: Patients with mantle cell lymphoma failing ibrutinib are unlikely to respond to salvage chemotherapy and have poor outcomes. Ann Oncol 26:1175-1179, 2015 2. Martin P, Maddocks K, Leonard JP, et al: Postibrutinib outcomes in patients with mantle cell lymphoma. Blood 127:1559-1563, 2016 3. Jain P, Kanagal-Shamanna R, Zhang S, et al: Long-term outcomes and mutation profiling of patients with mantle cell lymphoma (MCL) who discontinued ibrutinib. Br J Haematol 183:578-587, 2018 4. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med. 2020;382(14):1331-1342. doi:10.1056/NEJMoa1914347 5. Wang M, Siddiqi T, Gordon LI, et al. Lisocabtagene Maraleucel in Relapsed/Refractory Mantle Cell Lymphoma: Primary Analysis of the Mantle Cell Lymphoma Cohort From TRANSCEND NHL 001, a Phase I Multicenter Seamless Design Study. J Clin Oncol. 2024;42(10):1146-1157. doi:10.1200/JCO.23.02214 6. Wang M, Munoz J, Goy A, et al. Three-Year Follow-Up of KTE-X19 in Patients With Relapsed/Refractory Mantle Cell Lymphoma, Including High-Risk Subgroups, in the ZUMA-2 Study. J Clin Oncol. 2023;41(3):555-567. doi:10.1200/JCO.21.02370 7. Kambhampati S. et al, Real-world outcomes of brexucabtagene autoleucel (brexu-cel) for relapsed or refractory (R/R) mantle cell lymphoma (MCL): A CIBMTR subgroup analysis by prior treatment. JCO 41, 7507-7507(2023). DOI: 10.1200/JCO.2023.41.16_suppl.7507
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	-

Field	Response
Proposal Number	2410-239-JAIN
Proposal Title	Real-world efficacy and safety of lisocabtagene maraleucel (liso-cel) and brexucabtagene autoleucel (brexu-cel) CAR T-cell therapy for mantle cell lymphoma
Key Words	Mantle cell lymphoma, CAR T-cell, liso-cel, brexu-cel
Principal Investigator #1: - First and last name, degree(s)	Preetesh Jain, MD, PhD, DM
Principal Investigator #1: - Email address	pjain@mdanderson.org
Principal Investigator #1: - Institution name	MD Anderson Cancer Center
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Anath Lionel, MD, PhD
Principal Investigator #2 (If applicable): - Email address:)	aclionel@mdanderson.org
Principal Investigator #2 (If applicable): - Institution name:	MD Anderson Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Fellow
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Preetesh Jain
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	None
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-

Field	Response
RESEARCH QUESTION:	What is the real-world evidence for clinical efficacy and safety profile of lisocabtagene maraleucel (liso-cel) in r/r MCL and how does this compare with real-world data from brexucabtagene autoleucel (brexu-cel)?
RESEARCH HYPOTHESIS:	We hypothesize that comparison of the real world evidence for clinical efficacy and safety profile of liso-cel and brexu-cel will assist in identifying the optimal CAR T-cell product for r/r MCL in different clinical contexts taking into account relevant characteristics from patients and their disease.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary outcomes: Compare clinical efficacy metrics between liso-cel and brexu-cel including overall survival (OS), progression free survival (PFS), objective response rate (ORR) and complete response rate (CRR). Secondary outcomes: Compare mortality rates after brexu-cel and liso-cel including early mortality within 30 days after infusion and total non-relapse mortality after infusion. Compare toxicity profile metrics between liso-cel and brexu-cel including frequency and severity grades of complications after CAR T-cell therapy such as cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome (IEC-HS), infections, and prolonged cytopenias.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Completion of this project will enhance our understanding of the comparative efficacy and safety profiles of liso-cel and brexu-cel which in turn will help guide patient selection for each of these SOC CART products for RR-MCL. By identifying differing toxicities with brexu-cel or liso-cel, we can achieve this aim. This project will also advance understanding of CAR T-cell therapy in r/r MCL by providing the first real-world evidence of efficacy and safety for liso-cel and providing a comparison with brexu-cel.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	The recently published TRANSCEND MCL phase 1 trial (Wang et al. 2024) found liso-cel to have high CR (72%) and ORR (83%) rates and lower rates than brexu-cel of treatment-related toxicities such as severe ICANS and CRS. These results led to FDA approval of liso-cel for the indication of r/r MCL. However, there have been no real-world analyses of the safety and efficacy of liso-cel for MCL. Our research aims to analyze real-world CIBMTR data to compare the efficacy and safety profiles of liso-cel and brexu-cel in r/r MCL. We will also examine patient demographic information (such as age, performance status, ethnicity) and disease characteristics (high-risk features such as TP53 mutations, CNS involvement, Ki-67 proliferative index, morphology, prior lines of treatment) to determine if there are certain sub-groups of patients who might be at higher risk from treatment related toxicities from brexu-cel and who might therefore be recommended to receive liso-cel. Our results will aid clinicians in the selection of the optimal CAR T-cell product for r/r MCL considering relevant characteristics from patients and their disease.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: Adult patients who received standard of care CAR T-cell therapy with either liso-cel or brexu-cel for MCL Exclusion criteria: 1. Pediatric patients (< 18 years of age)
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	Since this study investigates standard of care FDA approved CAR T-cell therapy for MCL, and this is only approved in adult patients, the study will focus on adult patients.

DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Patient Variables: Ethnicity Race ECOG score HCT-CI comorbidity score Height at start of lymphodepleting therapy Weight at start of lymphodepleting therapy Date of admission for cellular therapy Date of discharge from admission for cellular therapy Date of last follow-up of patient Survival status at time of last-follow-up Date of death if patient is dead Cause of death if patient is dead Disease Variables: Most recent LDH within 30 days of lymphodepleting therapy and LDH upper limit of normal for institution Most recent CBC before lymphodepletion therapy Most recent ferritin before lymphodepletion therapy Most recent CRP before lymphodepletion therapy Most recent creatinine before lymphodepletion therapy Best response to cellular therapy Date of best response Was disease relapse or progression detected Date of relapse or progression New malignancy after cellular therapy Lymphoma histology Ki-67 from tissues Cyclin D1 SOCX11 Cytogenetics (karyotyping) WBC at diagnosis ALC TP53 deletion or mutation Other mutations Morphology type of MCL BM onvolvement at diagnosis and pre and post CART GI involvement at diagnosis and pre and post CART Hemoglobin at diagnosis LDH at diagnosis Nodal involvement Extranodal involvement and sites Stage at diagnosis Systemic therapies before CART including dates started and stopped Number of lines of prior theapies POD-24 after first line treatment Bendamustine exposure prior to CART and dates BTKi refractory prior to CART BTKi type before CART BTKi intolerant prior to CART Allo-SCT before CART Auto-SCT before CART CNS involvement before CART Radiation therapy before CART Best response for each therapy Date of best response assessment for each therapy Date of relapse or progression after each line of therapy Systemic therapies after CART including dates started and stopped Disease status at time of evaluation for last report to CIBMTR Infusion Variables: Was this infusion received within the context of a clinical trial? Was this infusion received outside the context of a clinical trial? Is this the first time the recipient is being treated using a cellular therapy? Name of cellular therapy product What was the primary indication for performing treatment with cellular therapy? Was lymphodepletion therapy given prior to the infusion Setting of cell therapy infusion i.e. inpatient or outpatient Drugs that were part of lymphodepletion

Field	Response
	regimen Cumulative dose of steroids given Therapy given for prevention of CRS Therapy given for prevention of neurotoxicity Did patient experience CRS Date CRS started Maximum grade of CRS Therapy given for CRS Symptoms of CRS Therapy given for hypotension Was MAS/HLH present Therapy given for MAS/HLH Did patient experience neurotoxicity Therapy given for neurotoxicity Lowest ICE score Maximum grade of ICANS Did patient receive IVIG Clinically significant infection after infusion
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	None
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	No
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	No
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	None

Field	Response
REFERENCES:	Cordas Dos Santos DM, Tix T, Shouval R, et al. A systematic review and meta-analysis of nonrelapse mortality after CAR T cell therapy. Nat Med. 2024 Sep;30(9):2667-2678. Iacoboni G, Rejeski K, Villacampa G, et al. Real-world evidence of brexucabtagene autoleucel for the treatment of relapsed or refractory mantle cell lymphoma. Blood Adv. 2022 Jun 28;6(12):3606-3610. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-cell therapy in relapsed or refractory mantle-cell lymphoma. N Engl J Med. 2020;382(14):1331-1342. Wang M, Siddiqi T, Gordon LI, et al. Lisocabtagene Maraleucel in Relapsed/Refractory Mantle Cell Lymphoma: Primary Analysis of the Mantle Cell Lymphoma Cohort From TRANSCEND NHL 001, a Phase I Multicenter Seamless Design Study. J Clin Oncol. 2024 Apr 1;42(10):1146-1157. Wang Y, Jain P, Locke FL, et al. Brexucabtagene autoleucel for relapsed or refractory mantle cell lymphoma in standard-of-care practice: results from the US lymphoma CAR T consortium. J Clin Oncol. 2023;41(14):2594-2606.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	Yes, I have conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	Dr. Preetesh Jain has received research funding from Astra Zeneca, Kite, Beigene; honoraria from Aptitude Health, Pharmacy times, Dava Oncology, Adaptive Biotech, Eli Lilly, Beigene and advisory board funding from Eli Lilly, Kite, LOXO Oncology, Incyte and Janssen-PCYC.

Characteristics of patents (Age>=60) with mantle cell lymphoma treated with Brexucabtagene autoleucel CAR-T infusion reported to the CIBMTR

Characteristic	60-70	70+	Total
No. of patients	382	309	691
No. of centers	92	83	107
Age group - no. (%)			
Median (min-max)	65.4 (60.0-70.0)	74.3 (70.0-90.5)	69.4 (60.0-90.5)
Recipient Sex - no. (%)			
Male	290 (76)	251 (81)	541 (78)
Female	92 (24)	58 (19)	150 (22)
Recipient race - no. (%)			
White	318 (83)	269 (87)	587 (85)
Black or African American	18 (5)	7 (2)	25 (4)
Asian	9 (2)	7 (2)	16 (2)
American Indian or Alaska Native	3 (1)	0 (0)	3 (0)
Other	1 (0)	0 (0)	1 (0)
More than one race	14 (4)	12 (4)	26 (4)
Missing	19 (5)	14 (5)	33 (5)
Ethnicity - no. (%)			
Hispanic or Latino	28 (7)	19 (6)	47 (7)
Non-Hispanic or Latino	326 (85)	262 (85)	588 (85)
Non-resident of the U.S.	13 (3)	14 (5)	27 (4)
Not reported	15 (4)	14 (5)	29 (4)
Karnofsky performance score prior to CT - no. (%)			
90-100	154 (40)	97 (31)	251 (36)
80	117 (31)	112 (36)	229 (33)
< 80	61 (16)	65 (21)	126 (18)
Not reported	50 (13)	35 (11)	85 (12)
HCT-CI Score - no. (%)			
0	118 (31)	68 (22)	186 (27)
1	81 (21)	58 (19)	139 (20)
2	52 (14)	38 (12)	90 (13)
3+	131 (34)	142 (46)	273 (40)
Not reported	0 (0)	3 (1)	3 (0)
Disease status prior to CT for lymphoma - no. (%)			
CR	26 (7)	18 (6)	44 (6)
PR	77 (20)	63 (20)	140 (20)

Characteristic	60-70	70+	Total
Resistant	235 (62)	195 (63)	430 (62)
Untreated	21 (5)	10 (3)	31 (4)
Unknown	23 (6)	23 (7)	46 (7)
Time from initial diagnosis to CT - no. (%)			
>= 0 to < 6 months	26 (7)	8 (3)	34 (5)
>= 6 to < 12 months	30 (8)	31 (10)	61 (9)
>= 12 months	325 (85)	270 (87)	595 (86)
Not reported	1 (0)	0 (0)	1 (0)
Product - no. (%)			
Brexucabtagene autoleucel	382 (100)	309 (100)	691 (100)
No. of lines of prior therapies (including HCT and CT) - no. (%)			
1	14 (4)	8 (3)	22 (3)
2	67 (18)	46 (15)	113 (16)
>= 3	247 (65)	205 (66)	452 (65)
Not reported	54 (14)	50 (16)	104 (15)
Prior HCT - no. (%)			
No	229 (60)	239 (77)	468 (68)
Yes	153 (40)	70 (23)	223 (32)
Year of CT - no. (%)			
2020	24 (6)	22 (7)	46 (7)
2021	108 (28)	85 (28)	193 (28)
2022	107 (28)	85 (28)	192 (28)
2023	106 (28)	94 (30)	200 (29)
2024	37 (10)	23 (7)	60 (9)
Follow-up among survivors - median (range)	22.7 (2.7-48.8)	21.3 (2.0-39.8)	22.6 (2.0-48.8)

Field	Response
Proposal Number	2410-100-MODI
Proposal Title	Incidence and Risk factors for Non-relapse Mortality after anti-CD19 CAR T-cell therapy for Lymphoma
Key Words	Diffuse large B cell lymphoma, Follicular lymphoma, Mantle cell lymphoma, CAR T-cell therapy, Axi-cel, Lisa-cel, Tisa-cel, Brexu-cel, Non-relapse mortality
Principal Investigator #1: - First and last name, degree(s)	Dipenkumar Modi, MD
Principal Investigator #1: - Email address	modid@karmanos.org
Principal Investigator #1: - Institution name	Karmanos Cancer Institute, Wayne State University
Principal Investigator #1: - Academic rank	Associate Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	-
Principal Investigator #2 (If applicable): - Email address:)	-
Principal Investigator #2 (If applicable): - Institution name:	-
Principal Investigator #2 (If applicable): - Academic rank:	-
Junior investigator status (defined as ≤5 years from fellowship)	-
Do you identify as an underrepresented/minority?	-
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:	-
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	-
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-

Field	Response
RESEARCH QUESTION:	To evaluate risk factors and incidence of non-relapse mortality following anti-CD19 CAR T-cell therapy for lymphoma
RESEARCH HYPOTHESIS:	CAR T-cell therapy may be associated with high rate of infection-related death.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary objectives: - To estimate cumulative incidence of NRM at 1-year - To evaluate association of NRM with different CAR T-cell products (axi-cel, liso-cel, tisa-cel, brexu-cel) - To identify timing of NRM following CAR T-cell therapy (early vs late) - To identify etiology of NRM - To identify risk factors associated with NRM Secondary Objectives: - To evaluate 1-year progression-free and overall survival - To evaluate rate of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS)
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	CAR T-cell therapy has transformed landscape of lymphoma, however, NRM remains the most common cause of death after disease progression. Identifying etiology and risk factors of NRM will be very critical in developing preventative strategies and indirectly to improve post-CAR T-cell therapy outcomes. The CIBMTR will provide the largest database of patients undergoing CAR T-cell therapy which would be helpful in identifying causes of NRM.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Anti-CD19 directed CAR T-cell therapy is increasingly used for B-cell non-Hodgkin lymphoma. Although it has demonstrated significant anti-lymphoma activity, it is associated with characteristic toxicities including cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), pancytopenia, and B-cell aplasia leading to hypogammaglobinemia. Besides disease progression, non-relapse morality (NRM) following CAR T-cell therapy is the most common cause of death. Several factors could contribute to NRM such as T-cell depletion and severe neutropenia from use of lymphodepleting chemotherapy, profound immunosuppression from systemic corticosteroids for CRS and ICANS, and hypogammaglobulinemia from B-cell aplasia. In addition, secondary malignancy, particularly myeloid neoplasm and T-cell lymphoma have been reported after CAR T-cell therapy (1, 2). Previous trials have reported NRM rate of 0-6% (3-11). However, these studies are limited by sample size. Furthermore, detailed analysis on etiology, risk factors, and timing of NRM was not mentioned. Therefore, information about risk factors associated with NRM after CAR T-cell therapy is not well known. Identifying timing and risk factors for NRM is very important as it will help develop prevention strategies which could improve long-term outcomes.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: a. All patients aged >18 years with B-cell non-Hodgkin lymphoma b. First commercial anti-CD19 CAR T-cell infusion between 2017-2023 in the US c. At least 3 months follow up Exclusion criteria: d. No consent for research e. Clinical trial CAR-T, including out of specification products f. Non-CD19 CAR-T
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	CAR T-cell therapy is not approved for pediatric population.

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Patient-related: - Age at CAR-T, years: - Sex: male vs. Female - Race: white, African American, Asian, Pacific Islander, Native American - Ethnicity: Hispanic, Non-Hispanic, N/A (Not a US resident), Unknown - Hematopoietic cell transplantation co-morbidity index (HCT-CI) - Karnofsky performance score prior to CT: 90-100, 80, <80 - ECOG performance status - Baseline cytopenia Disease-related: - NHL Disease classification (DLBCL, FL, MCL, Others) - Stage at diagnosis I/II/III/IV - LDH prior to infusion: normal or elevated - CNS involvement Y/N - Number of prior lines of therapy: 1, 2, >=3, missing - Disease status at CAR T cell infusion: CR, PR, resistant, untreated, unknown CAR-T related: - CAR-T product (axi-cel, tisa-cel, liso-cel, brexu-cel) - Time from diagnosis to CAR T - Time from leukapheresis to CAR T - Ferritin: elevated or normal (prior to CAR T cell infusion) - CRP: elevated or normal (prior to CAR T cell infusion) - Bridging therapy: Yes vs No - Type of bridging used: systemic, intrathecal, intraocular, radiation, surgery - Lymphodepletion: Fludarabine-based - Year of CAR T cell infusion: 2017-2023
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	-
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	-
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	-
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.	-

Field	Response
REFERENCES:	1. Ghilardi G, Fraietta JA, Gerson JN, Van Deerlin VM, Morrissette JJD, Caponetti GC, et al. T cell lymphoma and secondary primary malignancy risk after commercial CAR T cell therapy. Nat Med. 2024;30(4):984-9. 2. Storgard R, Rejeski K, Perales MA, Goldman A, Shouval R. T-Cell Malignant Neoplasms After Chimeric Antigen Receptor T-Cell Therapy. JAMA Oncol. 2024;10(6):826-8. 3. Neelapu SS, Locke FL, Bartlett NL, Lekakis LJ, Miklos DB, Jacobson CA, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. N Engl J Med. 2017;377(26):2531-44. 4. Schuster SJ, Bishop MR, Tam CS, Waller EK, Borchmann P, McGuirk JP, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019;380(1):45-56. 5. Abramson JS, Palomba ML, Gordon LI, Lunning MA, Wang M, Arnason J, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. Lancet. 2020;396(10254):839-52. 6. Nastoupil LJ, Jain MD, Feng L, Spiegel JY, Ghobadi A, Lin Y, et al. Standard-of-Care Axicabtagene Ciloleucel for Relapsed or Refractory Large B-Cell Lymphoma: Results From the US Lymphoma CAR T Consortium. J Clin Oncol. 2020;38(27):3119-28. 7. Jacobson CA, Hunter BD, Redd R, Rodig SJ, Chen PH, Wright K, et al. Axicabtagene Ciloleucel in the Non-Trial Setting: Outcomes and Correlates of Response, Resistance, and Toxicity. J Clin Oncol. 2020;38(27):3095-106. 8. Pasquini MC, Hu ZH, Curran K, Laetsch T, Locke F, Rouce R, et al. Real-world evidence of tisagenlecleucel for pediatric acute lymphoblastic leukemia and non-Hodgkin lymphoma. Blood Adv. 2020;4(21):5414-24. 9. Kwon M, Iacoboni G, Reguera JL, Corral LL, Morales RH, Ortiz-Maldonado V, et al. Axicabtagene ciloleucel compared to tisagenlecleucel for the treatment of aggressive B-cell lymphoma. Haematologica. 2023;108(1):110-21. 10. Cordas Dos Santos DM, Tix T, Shouval R, Gafter-Gvili A, Alberge JB, Cliff ERS, et al. A systematic review and meta-analysis of nonrelapse mortality after CAR T cell therapy. Nat Med. 2024;30(9):2667-78. 11. Lemoine J, Bachy E, Cartron G, Beauvais D, Gastinne T, Di Blasi R, et al. Nonrelapse mortality after CAR T-cell therapy for large B-cell lymphoma: a LYSA study from the DESCAR-T registry. Blood Adv. 2023;7(21):6589-98.

Field	Response
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	-

Characteristics of adults with B-cell non-Hodgkin lymphoma treated with axi-cel or liso-cel or tisa-cel or brexu-cel CAR-T infusion reported to the CIBMTR between 2017 and 2023

Characteristic	N (%)
No. of patients	6879
No. of centers	159
Age group - no. (%)	
Median (min-max)	64.7 (18.0-91.2)
18-20	6 (0.1)
20-30	95 (1.4)
30-40	236 (3.4)
40-50	554 (8.1)
50-60	1410 (20.5)
60-70	2585 (37.6)
>=70	1993 (29.0)
Recipient Sex - no. (%)	
Male	4470 (65)
Female	2408 (35)
Not reported	1 (0)
Recipient race - no. (%)	
White	5342 (78)
Black or African American	330 (5)
Asian	353 (5)
Native Hawaiian or other Pacific Islander	10 (0)
American Indian or Alaska Native	29 (0)
Other	33 (0)
More than one race	322 (5)
Missing	460 (7)
Ethnicity - no. (%)	
Hispanic or Latino	680 (10)
Non-Hispanic or Latino	5348 (78)
Non-resident of the U.S.	638 (9)
Not reported	213 (3)
Karnofsky performance score prior to CT - no. (%)	
90-100	2759 (40)
80	2054 (30)
< 80	1322 (19)
Not reported	744 (11)
Specify ALL classification - no. (%)	

Characteristic	N (%)
NHL follicular,predominantly small cleaved cell:	69 (1)
NHL follicular,mixed,small cleaved and large cell:	193 (3)
NHL diffuse, large B-cell:	1419 (21)
NHL mantle cell:	791 (11)
Other B-cell, spec:	24 (0)
Follicular, predominantly large cell Grade IIIA (2400v4):	141 (2)
Follicular, predominantly large cell Grade IIIB (2400v4):	57 (1)
Follicular unknown grade:	83 (1)
Follicular, predominantly large cell (Grade IIIA vs IIIB not specified)	20 (0)
Diffuse, large B-cell lymphoma- Germinal center B-cell type	2309 (34)
Diffuse, large B-cell lymphoma- Activated B-cell type	1702 (25)
EBV+ DLBCL, NOS (1823)	67 (1)
DLBCL associated with chronic inflammation (1825)	2 (0)
HHV8+ DLBCL, NOS (1826)	2 (0)
HCT-CI Score - no. (%)	
0	2047 (30)
1	1404 (20)
2	945 (14)
3+	2408 (35)
Not reported	75 (1)
Disease status prior to CT for lymphoma - no. (%)	
CR	397 (6)
PR	1422 (21)
Resistant	4222 (61)
Untreated	427 (6)
Unknown	408 (6)
Not reported	3 (0)
Time from initial diagnosis to CT - no. (%)	
>= 0 to < 6 months	675 (10)
>= 6 to < 12 months	1760 (26)
>= 12 months	4439 (65)
Not reported	5 (0)
Product - no. (%)	
Tisagenlecleucel	1191 (17)
Axicabtagene ciloleucel	4621 (67)
Brexucabtagene autoleucel	777 (11)
Lisocabtagene maraleucel	290 (4)
No. of lines of prior therapies (including HCT and CT) - no. (%)	

Characteristic	N (%)
1	289 (4)
2	1594 (23)
>= 3	3816 (55)
Not reported	1180 (17)
Prior HCT - no. (%)	
No	5276 (77)
Yes	1590 (23)
Unknown	2 (0)
Not reported	11 (0)
Year of CT - no. (%)	
2017	5 (0)
2018	390 (6)
2019	794 (12)
2020	1010 (15)
2021	1384 (20)
2022	1683 (24)
2023	1613 (23)
Follow-up among survivors - median (range)	24.2 (0.8-76.3)

Field	Response
Proposal Number	2410-120-GATTAS
Proposal Title	Outcomes of autologous stem cell transplantation for patients with DLBCL with secondary CNS involvement in the contemporary era
Key Words	Diffuse large B-cell lymphoma; DLBCL; LBCL; secondary CNSL; Autologous stem cell transplant; auto-HCT
Principal Investigator #1: - First and last name, degree(s)	Boula Gattas, MD
Principal Investigator #1: - Email address	Boula.gattas@jefferson.edu
Principal Investigator #1: - Institution name	Thomas Jefferson University
Principal Investigator #1: - Academic rank	-
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Usama Gergis, MD MBA
Principal Investigator #2 (If applicable): - Email address:)	Usama.gergis@jefferson.edu
Principal Investigator #2 (If applicable): - Institution name:	Thomas Jefferson University
Principal Investigator #2 (If applicable): - Academic rank:	Professor of Medical Oncology
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	-
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	N/A
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Dr. Usama Gergis, MD, MBA

Field	Response
RESEARCH QUESTION:	Does consolidative autologous stem cell transplantation improve outcomes for patients with DLBCL with secondary CNS involvement in the contemporary era?
RESEARCH HYPOTHESIS:	In patients with diffuse large B-cell lymphoma (DLBCL) and secondary CNS involvement who achieve a complete response (CR) with chemoimmunotherapy, consolidative autologous stem cell transplantation (ASCT) improves progression-free survival (PFS) and overall survival (OS) by reducing the risk of both systemic and CNS relapse compared to patients who do not undergo ASCT.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary objectives 1. Overall survival (OS) at 5-year Time to death. Death from any cause will be considered an event. Surviving patients will be censored at time of last follow-up. 2. Progression-free survival (PFS) at 5-year Survival without disease progression or relapse from CR. Progression, relapse, and death are considered events. Patients who are alive and in remission are censored at time of last follow-up. Secondary objectives 1. CNS-Specific Relapse-Free Survival: · Time until CNS relapse, focusing on the efficacy of ASCT in preventing relapse specifically in the CNS. 2. Systemic Relapse-Free Survival: · Time until systemic (non-CNS) relapse, assessing how well ASCT prevents relapse outside the CNS. 3. Non-Relapse Mortality (NRM): · Deaths not related to lymphoma relapse, measuring the risks of ASCT-associated complications such as infections, organ damage, or secondary malignancies. 4. Cumulative incidence of relapse
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	DLBCL with CNS involvement is associated with a poorer prognosis compared to DLBCL without CNS involvement. The blood-brain barrier makes treatment more challenging, as many systemic therapies have limited penetration into the CNS. Achieving a complete response (CR) with chemoimmunotherapy, such as high-dose methotrexate or rituximab-based regimens, is effective, but the risk of CNS relapse remains high without further intervention. Recent studies and real-world data have started to show positive outcomes for patients with secondary CNS involvement who undergo ASCT after achieving CR, but the results are still being validated through clinical trials. Using the CIBMTR database, our study aims to evaluate outcomes of ASCT for DLBCL with CNS involvement in the contemporary era

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Secondary CNS lymphoma (SCNSL) is a rare and challenging condition linked to poor outcomes, frequently seen DLBCL and other aggressive lymphoma (1,2). While there is no consensus on the best treatment for secondary CNS involvement in lymphoma, therapies targeting CNS lesions, such as high-dose methotrexate-based regimens used for primary CNS lymphoma, have been widely employed. However, most patients are not cured, as responses are often short-lived and disease progression is common (3,4). Chimeric antigen receptor T cells were not sufficiently studied in SCNSL(5,6). However, for transplant-eligible patients, prior phase II studies have shown ASCT to be a feasible consolidative (7,8). However, these studies are limited by small and heterogeneous populations. Observational data suggest that ASCT with high dose busulfan/thiotepa conditioning may offer a prolonged response in a subset of patients, but real-world data on its effectiveness are needed (9). Patients who received ASBMT before 2005 with SCNSL were compared to patients without CNS involvement in a CIBMTR study. There was no significant differences in 5-year progression-free and overall survival between the two groups. (10). In MARIETTA phase II trial, MATRix plus RICE followed by ASCT included 79 patients up to 70 years old with secondary CNS DLBCL. Fifty-eight percent achieved PFS at one year. However, grade 3-4 hematological toxicities were common, leading to a treatment-related mortality rate of 5% (11). In a multicenter Phase II Trial, 39 patients with SCNSL were treated with high-dose methotrexate and cytarabine, followed by R-HDS and ASCT. The 2 – year PFS was 42%.(12). In a largest real-world data from CIMBTR analysis of 144 patients receiving CAR-T therapy, the 2-year progression-free survival (PFS) was 21% and overall survival (OS) was 34%. KPS <90% was linked to worse OS, with 81% of deaths due to disease recurrence or progression, and non-relapse mortality (NRM) was 5% (13). Our proposal is timely, given the lack of data on the efficacy of ASCT in patients with SCNSL in the contemporary era.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: Adult patients ≥18 years old with DLBCL and secondary CNSL who undergo ASCT after 2005. Exclusion criteria: Other types of Lymphoma, Relapsed/ refractory DBCL, Isolated CNSL, Primary CNS Lymphoma.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	-

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Patient characteristics: age, gender, race, ethnicity, performance status, comorbidities. Disease characteristics: disease status at ASCT, stage, IPI score, LDH level, type of lymphoma, double hit/triple hit. Transplant related: conditioning regimen, prior radiation.
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	N/A
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A

REFERENCES:	1. Alderuccio JP, Nayak L, Cwynarski K. How I treat secondary CNS involvement by aggressive lymphomas. Blood [Internet]. 2023 Nov 23 [cited 2024 Oct 4];142(21):1771–83. Available from: https://ashpublications.org/blood/article/142/21/1771/497854/How-I-treat-secondary-CNS-involvement-by 2. Ferreri AJM, Assanelli A, Crocchiolo R, Ciceri F. Central nervous system dissemination in immunocompetent patients with aggressive lymphomas: incidence, risk factors and therapeutic options. Hematol Oncol [Internet]. 2009 Jun [cited 2024 Oct 4];27(2):61–70. Available from: https://onlinelibrary.wiley.com/doi/10.1002/hon.881 3. Tomita N, Kodama F, Kanamori H, Motomura S, Ishigatsubo Y. Secondary Central Nervous System Lymphoma. Int J Hematol [Internet]. 2006 Aug 1 [cited 2024 Oct 4];84(2):128–35. Available from: http://link.springer.com/10.1532/IJH97.06091 4. Kim SJ, Oh SY, Kim JS, Kim H, Lee GW, Won JH, et al. Secondary central nervous system (CNS) involvement in patients with diffuse large B-cell lymphoma: a therapeutic dilemma. Ann Hematol [Internet]. 2011 May [cited 2024 Oct 4];90(5):539–46. Available from: http://link.springer.com/10.1007/s00277-010-1104-0 5. Abramson JS, Solomon SR, Arnason J, Johnston PB, Glass B, Bachanova V, et al. Lisocabtagene maraleucel as second-line therapy for large B-cell lymphoma: primary analysis of the phase 3 TRANSFORM study. Blood [Internet]. 2023 Apr 6 [cited 2024 Oct 4];141(14):1675–84. Available from: https://ashpublications.org/blood/article/141/14/1675/493847/Lisocabtagene-maraleucel-as-second-line-therapy 6. Westin JR, Oluwole OO, Kersten MJ, Miklos DB, Perales MA, Ghobadi A, et al. Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma. N Engl J Med [Internet]. 2023 Jul 13 [cited 2024 Oct 4];389(2):148–57. Available from: http://www.nejm.org/doi/10.1056/NEJMoa2301665 7. Korfel A, Elter T, Thiel E, Hanel M, Mohle R, Schroers R, et al. Phase II study of central nervous system (CNS)-directed chemotherapy including high-dose chemotherapy with autologous stem cell transplantation for CNS relapse of aggressive lymphomas. Haematologica [Internet]. 2013 Mar 1 [cited 2024 Oct 4];98(3):364–70. Available from: http://www.haematologica.org/cgi/doi/10.3324/haematol.2012.077917 8. Ferreri AJM, Doorduijn JK, Re A, Cabras MG, Smith J, Ilariucci F, et al. MATRix–RICE therapy and autologous haematopoietic stem-cell

Field	Response
	transplantation in diffuse large B-cell lymphoma with secondary CNS involvement (MARIETTA): an international, single-arm, phase 2 trial. Lancet Haematol [Internet]. 2021 Feb [cited 2024 Oct 4];8(2):e110–21. Available from: https://linkinghub.elsevier.com/retrieve/pii /S2352302620303665 9. Oh DH, Chua N, Street L, Stewart DA. Treatment of patients with secondary central nervous system lymphoma with high-dose busulfan/thiotepa-based conditioning and autologous stem cell transplant. Leuk Lymphoma [Internet]. 2016 Jan 2 [cited 2024 Oct 4];57(1):28–33. Available from: http://www.tandfonline.com/doi/full/10.3109 /10428194.2015.1026901 10. Maziarz RT, Wang Z, Zhang M, Bolwell BJ, Chen AI, Fenske TS, et al. Autologous haematopoietic cell transplantation for non-H odgkin lymphoma with secondary CNS involvement. Br J Haematol [Internet]. 2013 Sep [cited 2024 Oct 8];162(5):648–56. Available from: https://onlinelibrary.wiley.com/doi/10.1111/bjh.12451 11. Ferreri AJM, Doorduijn JK, Re A, Cabras MG, Smith J, Ilariucci F, et al. MATRix–RICE therapy and autologous haematopoietic stem-cell transplantation in diffuse large B-cell lymphoma with secondary CNS involvement (MARIETTA): an international, single-arm, phase 2 trial. Lancet Haematol [Internet]. 2021 Feb [cited 2024 Oct 4];8(2):e110–21. Available from: https://linkinghub.elsevier.com/retrieve/pii /S2352302620303665 12. Ferreri AJM, Donadoni G, Cabras MG, Patti C, Mian M, Zambello R, et al. High Doses of Antimetabolites Followed By High-Dose Sequential Chemoimmunotherapy and Autologous Stem Cell Transplant in Patients with Systemic B-Cell Lymphoma and Secondary Central Nervous System Involvement: Final Results of a Multicenter Phase II Trial. Blood [Internet]. 2014 Dec 6 [cited 2024 Oct 4];124(21):1724–1724. Available from: https://ashpublications.org/blood/article/124/21/1724 /88454/High-Doses-of-Antimetabolites-Followed-By -HighDose 13. Hashmi H, Epperla N, Ahn K, Allbee-Johnson M, Mercadal S, Lee CJ, et al. Outcomes of Large B-Cell Lymphoma (LBCL) Patients with Secondary Central Nervous System Involvement Following Chimeric Antigen Receptor T-Cell Therapy: A CIBMTR Analysis. Transplant Cell Ther [Internet]. 2024 Feb [cited 2024 Oct 4];30(2):S42. Available from: https://linkinghub.elsevier.com/retrieve/pii /S2666636723018080

Field	Response
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	-

Field	Response
Proposal Number	2410-194-KIDWELL
Proposal Title	Autologous Stem Cell Transplantation For Consolidation Following Frontline Management of Secondary CNS Lymphoma
Key Words	Autologous Stem Cell Transplantation, Secondary CNS Lymphoma
Principal Investigator #1: - First and last name, degree(s)	Adam Kidwell
Principal Investigator #1: - Email address	akidwell@mcw.edu
Principal Investigator #1: - Institution name	Medical College of Wisconsin
Principal Investigator #1: - Academic rank	Fellow Physician
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Nirav N. Shah MD, MSHP
Principal Investigator #2 (If applicable): - Email address:)	nishah@mcw.edu
Principal Investigator #2 (If applicable): - Institution name:	Medical College of Wisconsin
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor of Medicine, Director of the Bone Marrow Transplant and Cellular Therapy Program
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Adam Kidwell
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	None
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-

Field	Response
RESEARCH QUESTION:	What is the role and clinical outcomes regarding autologous stem cell transplantation for consolidation following frontline management of secondary CNS lymphoma
RESEARCH HYPOTHESIS:	Autologous stem cell transplantation as a consolidation following frontline therapy in patients who have a secondary CNS lymphoma can provide significant progression free and overall survival.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	To evaluate clinical outcomes of patients with who receive autologous stem cell transplant as frontline consolidation in the setting of secondary CNS lymphoma. The primary outcome will be to evaluate overall response rates (ORR), Progression free survival (PFS), overall survival (OS), relapse rates and non-relapse mortality among patients who receive autologous stem cell transplant for consolidation following frontline treatment for secondary CNS lymphoma.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Secondary CNS lymphoma, defined as a synchronous diagnosis of diffuse large B-cell lymphoma with CNS dissemination, is a rare diagnosis that generally represent poorer disease outcomes and higher risk of relapse. At this time, there remains relatively limited data regarding secondary CNS lymphoma given the rarity of the disease and lack of conscious amongst experts on both the frontline management of the disease as well as choice of consolidation with the known high risk of disease. Given the possible poor outcomes, we aim to assess in a large registry the outcomes of patients who have undergone autologous stem cell transplant for consolidation of secondary CNS lymphoma in order to best inform ongoing treatment decisions and guide future research.

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.	Diffuse large B-cell lymphoma (DLBCL) is the most common aggressive non-Hodgkin lymphoma (NHL) with an estimated annual incidence of 6 per 100,000 people with an estimated prevalence of between 63,000 and 143,000 cases in the United States1,2. While DLBCL is the most common NHL, it remains rare that at the time of diagnosis patients also have synchronous CNS lymphomatous involvement (known as secondary CNS lymphoma). Currently, it is estimated that secondary CNS lymphoma occurs in around 2-10 percent of all NHL cases annually, most commonly occurring in patients with DLBCL3. This remains a relatively rare entity but does confer much worse general outcomes with limited overall survival4. In the setting of poor clinical outcomes, there has been several studies that have explored treatment options in both the upfront induction as well as consolidation management. On the basis of previous retrospective studies, it was believed that the potential cure was only achievable through autologous transplant. However, given the rare nature of disease there continues to be data limited by relatively small sample size and observational data5,6. The MARIETTA trial was the largest prospective trial focusing on patients with secondary CNS lymphoma7. This was a prospective trial looking at the use of upfront chemotherapy with the matrix chemotherapy regimen followed by autologous stem cell transplant. However, of the 75 patients enrolled only 37 of those patients made it to autotransplant and the majority were patients treated in the relapsed, refractory state, not as a frontline consolidation. While this regimen remained active, the limited numbers of autologous transplant patients continues to limit the generalizability of frontline consolidation stem cell transplant in this disease state. There have been two other large retrospective studies that have recently been completed in this field as well. Khawja et al completed a large retrospective series reviewing patients who had undergone thiotepa based conditioning for autologous bone marrow transplant with secondary CNS lymphoma8. There data shows superior overall and progression free survival in comparison to people who had previously undergone BEAM conditioning. Given this data, it is considered standard of care for CNS lymphoma to undergo thiotepa based conditioning regimens. The largest of the retrospective studies recently published looked at 173 patients with secondary CNS lymphoma who underwent intensive induction therapy3. Again, of this cohort a limited sample size of only 25 patients underwent autologous stem cell transplant, however there was suggestion of

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	significantly improved overall survival from 7.5 months to 61 months in patients who underwent stem cell transplant. At this time, recent research has been limited to single institutions, small sample sizes, and observational studies. Previous work from the CIBMTR surrounding this question was most recently published over a decade ago in 2013 and concluded that CNS involvement should not preclude autologous stem cell transplant, but was limited again by low overall number of patients (n=151) who had secondary CNS involvement9. Of those patients, only 96 total patients were in remission at the time of autologous stem cell transplantation. Results from the study show that patients with active CNS disease at the time of transplant have poor PFS and OS. This is corroborated by other previous studies with estimated 4-year OS of 14 percent3. Of note, an ongoing limitation to the generalizability of this study is that the majority of these patients receive BEAM conditioning regimen, with our most recent understanding showing that a thiotepa based conditioning regimen is preferred in management of CNS lymphomas based on multiple studies in primary CNS lymphoma10. In addition, given ongoing improvement in frontline management of DLBCL as well as evolving treatment algorithms with cellular therapy replacing auto-HCT in many scenarios, the question remains regarding the role of consolidation with autologous stem cell transplant specifically for DLBCL patients with secondary CNS lymphoma at diagnosis. Given that it has been over a decade since the CIBMTR has reviewed data regarding autologous bone marrow transplant in the setting of secondary CNS lymphoma and there is yet to be established guidelines within the current treatment paradigm, we believe this is an unmet need in which a large database review could help to best inform ongoing clinical decisions and guide future research with the goal of normalizing a standardized approach to management.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	• Diagnosis of an aggressive B-cell non-Hodgkin lymphoma with simultaneous diagnosis of CNS involvement • Underwent frontline chemotherapy • Received autologous stem cell transplantation for consolidation of disease in PR or CR to frontline therapy • Patients must be greater than 18 years of age
Does this study include pediatric patients?	No

Field	Response
If this study does not include pediatric patients, please provide justification:	Given that the disease in question in most prevalent in an older age, to make this data most generalizable to the study population, we would plan to focus on adult patients.
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Data will be captured through CIBMTR collection forms
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	N/A
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A

REFERENCES:	1. Wang SS. Epidemiology and etiology of diffuse large B-cell lymphoma. Semin Hematol. Nov 2023;60(5):255-266. doi:10.1053/j.seminhematol.2023.11.004 2.Chihara D, Johnston K, Bolatova T, et al. An Epidemiological Model to Estimate the Prevalence of Diffuse Large B-Cell Lymphoma in the United States. Clin Lymphoma Myeloma Leuk. Dec 2022;22(12):e1092-e1099. doi:10.1016/j.clml.2022.08.008 3. Akin S, Hosing C, Khouri I, et al. Autologous stem cell transplantation for large B-cell lymphoma with secondary central nervous system involvement. Blood Adv. Apr 12 2022;6(7):2267-2274. doi:10.1182/bloodadvances.2021005602 4. Boehme V, Zeynalova S, Kloess M, et al. Incidence and risk factors of central nervous system recurrence in aggressive lymphoma--a survey of 1693 patients treated in protocols of the German High-Grade Non-Hodgkin's Lymphoma Study Group (DSHNHL). Ann Oncol. Jan 2007;18(1):149-157. doi:10.1093/annonc/mdl327 5. Alvarnas JC, Negrin RS, Horning SJ, et al. High-dose therapy with hematopoietic cell transplantation for patients with central nervous system involvement by non-Hodgkin's lymphoma. Biol Blood Marrow Transplant. 2000;6(3A):352-8. doi:10.1016/s1083-8791(00)70060-7 6. Williams CD, Pearce R, Taghipour G, Green ES, Philip T, Goldstone AH. Autologous bone marrow transplantation for patients with non-Hodgkin's lymphoma and CNS involvement: those transplanted with active CNS disease have a poor outcome--a report by the European Bone Marrow Transplant Lymphoma Registry. J Clin Oncol. Nov 1994;12(11):2415-22. doi:10.1200/JCO.1994.12.11.2415 7. Ferreri AJM, Doorduijn JK, Re A, et al. MATRix-RICE therapy and autologous haematopoietic stem-cell transplantation in diffuse large B-cell lymphoma with secondary CNS involvement (MARIETTA): an international, single-arm, phase 2 trial. Lancet Haematol. Feb 2021;8(2):e110-e121. doi:10.1016/S2352-3026(20)30366-5 8. Khwaja J, Kirkwood AA, Isbell LK, et al. International multicenter retrospective analysis of thiotepa-based autologous stem cell transplantation for secondary central nervous system lymphoma. Haematologica. Mar 01 2023;108(3):882-888. doi:10.3324/haematol.2022.281640 9. Maziarz RT, Wang Z, Zhang MJ, et al. Autologous haematopoietic cell transplantation for non-Hodgkin lymphoma with secondary CNS involvement. Br J Haematol. Sep

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	2013;162(5):648-56. doi:10.1111/bjh.12451 10. Scordo M, Wang TP, Ahn KW, et al. Outcomes Associated With Thiotepa-Based Conditioning in Patients With Primary Central Nervous System Lymphoma After Autologous Hematopoietic Cell Transplant. JAMA Oncol. Jul 01 2021;7(7):993-1003. doi:10.1001/jamaoncol.2021.1074
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	N/A

Characteristics of Adult patients (age ≥18) with DLBCL with secondary CNS involvement after 2000

Characteristic	N (%)
Number of patients	89
No. of centers	48
Patient age - median (min-max)	55.2 (20.1-74.9)
Age group - no. (%)	
20-30	6 (6.7)
30-40	13 (14.6)
40-50	13 (14.6)
50-60	26 (29.2)
60-70	26 (29.2)
>=70	5 (5.6)
Sex - no. (%)	
Male	58 (65.2)
Female	31 (34.8)
Race - no. (%)	
White	66 (74.2)
Black or African American	7 (7.9)
Asian	12 (13.5)
American Indian or Alaska Native	1 (1.1)
More than one race	3 (3.4)
Ethnicity - no. (%)	
Hispanic or Latino	8 (9.0)
Non Hispanic or non-Latino	69 (77.5)
Non-resident of the U.S.	6 (6.7)
Not reported	6 (6.7)
HCT-CI - no. (%)	
0	28 (31.5)
1	16 (18.0)
2	16 (18.0)
3+	28 (31.5)
Not reported	1 (1.1)
Karnofsky Score - no. (%)	
<90	45 (50.6)
90-100	39 (43.8)
Not reported	5 (5.6)
Disease status at the time of HCT - no. (%)	
CR	47 (52.8)

Characteristic	**N (%)**
PR	34 (38.2)
Chemoresistant	6 (6.7)
Untreated	1 (1.1)
Unknown	1 (1.1)
Conditioning regimen - no. (%)	
Bu/Cy	4 (4.5)
Bu/Mel	5 (5.6)
CBV	5 (5.6)
BEAM	25 (28.1)
BEAM like	1 (1.1)
Carb/other(s)	1 (1.1)
TBI +/- others	8 (9.0)
Bu/Cy/TT	15 (16.9)
Bcnu/TT	18 (20.2)
Other(s)	7 (7.9)
Extranodal or splenic involvement - no. (%)	
At Diagnosis	52 (58.4)
At last evaluation	25 (28.1)
At both	12 (13.5)
Year of transplant - no. (%)	
2000-2004	7 (7.9)
2005-2009	20 (22.5)
2010-2014	13 (14.6)
2015-2019	36 (40.4)
2020-2024	13 (14.6)
Follow-up of survivors - median (range)	65.2 (3.3-191.6)