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CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

2021 STATUS REPORT
LYMPHOMA WORKING COMMITTEE

Working Committee Leadership	
Co-Chair:	Mohamed Kharfan-Dabaja; Mayo Clinic; kharfandabaja.mohamed@mayo.edu
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INTRODUCTION

a. Minutes and overview plan from 2020 TCT meeting (Attachment 1)

PROPOSALS MOVING FORWARD FOR SCORING (click here to cast your score)

a. PROP 2010-333 Outcomes of chimeric antigen receptor – T cell (CAR-T) therapy for patients with antecedent chronic lymphocytic leukemia (Richters Syndrome) (Farrukh Awan/ Ankit Kansagra/ Praveen Ramakrishnan). (Attachment 2)

b. PROP 2010-297; PROP 2010-49 Efficacy and safety of CD19 directed CAR T-cell therapy for non-hodgkin B-cell lymphomas with secondary central nervous system (CNS) involvement (Hamza Hashmi/ Khaled M. Abouelezz/ Ayman Saad/ Sairah Ahmed). (Attachment 3)

PROPOSALS DROPPED BECAUSE THEY OVERLAP WITH EXISTING STUDIES OR ARE NOT FEASIBLE DUE TO LIMITATIONS OF AVAILABLE PATIENTS OR DATA

a. PROP 2009-15 The impact of salvage therapy on outcomes after autologous stem cell transplant patients with relapsed and refractory Hodgkin lymphoma (Alex Francisco Herrera/ Matthew Mei).

b. PROP 2010-02 Predictors of therapy-related MDS/AML in autologous stem cell transplantation in patients with lymphoma (Dave Raj Gupta/ Amelia A. Langston).

c. PROP 2010-04 Clinical outcomes in ethnic minorities with hodgkin's and non-hodgkin's lymphoma treated with hematopoietic stem cell transplantation in the united states (Elisa K. Quiroz/ James R. Mason).

d. PROP 2010-13 Outcomes following allogeneic hematopoietic stem cell transplantation for large granular lymphocytic leukemia (Nakhle Saba/ Firas Safa/ Tendai Kwaramba/ Hana Safah/ Francisco Socola).

e. PROP 2010-33 Predictors of outcomes after autologous stem cell transplant for primary CNS lymphoma during the last 15 years: The US experience (Pritesh Patel/ Karen Sweiss/ Damiano Rondelli).

f. PROP 2010-34 Haploidentical vs. matched related or unrelated donor in hodgkin lymphoma undergoing allogeneic stem cell transplantation with post-transplant cyclophosphamide-based graft versus host disease prophylaxis (Matthew Genyeh Mei/ Monzr Al Malki/ Reid Merryman).

g. PROP 2010-110 Impact of autologous hematopoietic cell transplantation versus CAR-T cell therapy on outcomes of patients with secondary central nervous system lymphoma (Narendranath Epperla/ Mehdi Hamadani).

h. PROP 2010-120 Outcomes in patients with mantle cell lymphoma receiving chimeric antigen receptor T cell therapy compared to autologous and allogeneic hematopoietic stem cell transplant (Sairah Ahmed/ Mehdi Hamadani/ Michael Wang).

i. PROP 2010-124 Search of optimal conditioning regimen for autologous stem cell transplant (ASCT) for treatment of relapsed and refractory lymphoma – A comparison of BEAM vs. BUCYVP16 using CIBMTR database (Faisal, Muhammad Salman/ Nidhi Sharma/ Yvonne Efebera).

j. PROP 2010-133 Autologous and allogeneic hematopoietic cell transplantation for plasmablastic lymphoma (Pietro R. Di Ciaccio/ Nada Hamad).

k. PROP 2010-144 The impact of lymphodepletion regimen on tisagenlecleucel outcomes in patients with aggressive non-hodgkins lymphoma (Trent Peng Wang/ James Nathan Gerson/ Lazaros John Lekakis).

l. PROP 2010-158 Outcomes for allogeneic versus autologous stem cell transplantation in patients with richter's transformation (Emily C. Ayers).

m. PROP 2010-165 Outcomes of allogeneic HCT after chimeric antigen receptor T-cell therapy for diffuse large B-cell lymphoma (Marie Hu/Joseph Maakaron/ Veronika Bachanova).

n. PROP 2010-166 Impact of targeted- and immune-therapy in the contemporary era to survival outcomes in patients with relapsed/refractory classical hodgkin lymphoma who undergo autologous hematopoietic cell transplantation (Joanna Zurko/ Nirav N. Shah).

o. PROP 2010-167 Outcomes after autologous transplant for peripheral T cell lymphoma: Comparison of patients treated with brentuximab vedotin + CHP versus CHOP or CHOEP (Joanna Zurko/ Nirav N. Shah).

p. PROP P2010-189 Pre-autologous stem cell transplant use of novel agents and outcomes in classical hodgkin lymphoma (Natalie Sophia Grover/ Marcie Riches).

q. PROP 2010-191 Outcomes of haplo hematopoietic stem cell transplant as treatment of MCL with 17p deletion or TP53 mutation, a CIBMTR study (Shatha Farhan).

r. PROP 2010-218 CD19 CAR T cells improve progression-free survival compared to autologous stem cell transplant in patients with diffuse large B Cell lymphoma relapsed/refractory after initial treatment (Ana Alarcon Tomas/ Miguel-Angel Perales).

s. PROP 2010-246 Define clinical outcomes of patient undergoing allogeneic HCT for T- lymphoblastic lymphoma (T-LBL) (Amandeep Salhotra/ Liana Nikolaenko/ Jasmine Zain/ Ryotaro Nakamura).

t. PROP 2010-260 Outcomes of autologous stem cell transplantation for relapsed/ refractory diffuse large B cell lymphoma in the CAR-T cell therapy era (Michael David Jain/ Ariel Perez Perez/ Taiga Nishihori/ Frederick Lundry Locke).

u. 2010-261 Impact of conditioning regimen on autologous stem cell transplantation outcomes for secondary central nervous system lymphoma (Alejandro Marinos/ Samer A. Srour/ Premal Lulla).

v. 2010-277 Outcomes of salvage AHCT in double hit lymphoma (Shivaprasad Manjappa/ Marcos de Lima/ Paolo Caimi/ Leland Metheny).

w. 2010-282 Role of high-dose chemotherapy with autologous hematopoietic cell transplantation in nodular lymphocyte-predominant hodgkin lymphoma (Talal Hilal/ Jose F. Leis).

x. 2010-284 Outcomes of chimeric antigen receptor T cell therapy in immunodeficient patients with aggressive large B-cell lymphoma related to solid organ transplantation (PTLD) or HIV/AIDS (ARL) (Aleksandr Lazaryan/ Frederick Locke).

y. 2010-303 Impact of immune checkpoint inhibitors on outcomes of autologous HCT for classical hodgkin lymphoma (Marie Hu/ Veronika Bachanova).

z. 2010-314 Allogeneic hematopoietic cell transplantation versus CD-19 directed chimeric antigen receptor T-cell therapy for relapsed/refractory mantle cell lymphoma after prior autologous stem cell transplantation and real world data of CAR-T (Sayeef Mirza/ Lohith Gowda/ Chitra Hosing).

aa. 2010-317 A comparative analysis of the timing, conditioning regimens and outcomes in patients with secondary CNS lymphoma (SCNSL) undergoing cellular therapy (Praveen Ramakrishnan Geethakumari/ Ankit Kansagra/ Farrukh Awan).

ab. 2010-318 A comparative analysis of cellular therapy strategies for relapsed/refractory primary mediastinal large B-Cell lymphoma (PMBCL) in the era of novel immunotherapies (Praveen Ramakrishnan Geethakumari/ Ankit Kansagra/ Farrukh Awan).

ac. 2010-324 Determining the optimal conditioning regimen for patients with T-cell non-hodgkin lymphoma undergoing allogeneic hematopoietic cell transplant (Farrukh Awan/ Ankit Kansagra/ Praveen Ramakrishnan Geethakumari).

PROPOSALS NOT ACCEPTED FOR CONSIDERATION AT THIS TIME DUE TO RELATIVE SCIENTIFIC IMPACT COMPARED TO ONGOING STUDIES AND/OR OTHER PROPOSALS

a. PROP 2010-05 Impact of autologous hematopoietic cell transplantation on the outcomes of waldenstrom macroglobulinemia and lymphoplasmacytic lymphoma (Narendranath Epperla).

b. PROP 2010-06 Bendamustine, etoposide, cytarabine, melphalan (BeEAM) vs. carmustine, etoposide, cytarabine, melphalan (BEAM) in relapsed B-cell non-hodgkin lymphoma or Hodgkin lymphoma (Matthew Genyeh Mei/ Alex Francisco Herrera).

c. PROP 2010-07 Outcomes following allogeneic hematopoietic stem cell transplantation for mycosis fungoides and sezary syndrome (Nakhle Saba/ Firas Safa/ Hana Safah/ Erin Boh/ Francisco Socola).

d. PROP 2010-11 Autologous stem cell transplant (ASCT) for the treatment of patients with waldenstrom's macroglobulinemia (WM)/lymphoplasmacytic lymphoma (LPL): A center for international blood and marrow transplant research analysis (Abdullah Mohammad Khan/ Ayman Saad/ Yvonne Efebera).

e. PROP 2010-16 Outcomes of autologous versus allogenic stem cell transplant among patients with relapsed double/triple hit diffuse large B-cell lymphoma (Mayur Narkhede/ Susan Bal/ Luciano Costa).

f. PROP 2010-20 Autologous hematopoietic cell transplantation outcomes in patients with angioimmunoblastic T-cell lymphoma: A center for international blood and marrow transplant research center analysis (Ibrahim Muhsen/ Mahmoud Aljurf/ Mostafa Saleh/ Mehdi Hamadani).

g. PROP 2010-42 Outcomes of autologous and allogeneic hematopoietic cell transplantation for secondary central nervous system lymphoma (Muhammad Husnain/ Hamza Hashmi/ Sairah Ahmed).

h. PROP 2010-56 Outcomes of allogeneic hematopoietic stem cell transplantation in relapsed/refractory aggressive B-cell lymphoma with central nervous system involvement: a CIBMTR analysis (Daria Gaut/ Monica Diane Mead/ Gary Schiller).

i. PROP 2010-65 Comparison of treatment regimens in patients with diffuse large B-cell lymphoma (DLBCL) who relapse after chimeric antigen receptor (CAR) T-cell therapy (Patrick Connor Johnson/ Areej El-Jawahri/ Matthew Frigault).

j. PROP 2010-66 Comparison between autologous and reduced intensity allogeneic stem cell transplantation for different histologic subtypes of chemosensitive relapsed nodal peripheral T cell lymphomas (Lazaros J Lekakis/ Amer Beitinjaneh/ Trent Wang).

k. PROP 2010-69 Evaluating outcomes of allogeneic hematopoietic cell transplantation in cutaneous T-cell lymphoma in the contemporary era (Madiha Iqbal/ Hemant Murthy/ Ernesto Ayala/ Mohamed A. Kharfan-Dabaja).

l. PROP 2010-81 Comparison of stem cell transplant or CAR-T cell therapy in relapsed refractory double hit lymphoma (Dipenkumar Modi/ Joseph Uberti).

m. PROP 2010-89 Effect of time to relapse on survival in classical hodgkin lymphoma patients undergoing autologous hematopoietic cell transplantation (Narendranath Epperla).

n. PROP 2010-91 Outcomes of stem cell transplant in patients failing CD19 directed CAR-T cell therapy for relapsed diffuse large B cell lymphoma (Dipenkumar Modi/ Abhinav Deol/ Mehdi Hamadani).

o. PROP 2010-95 Determination of the optimal conditioning regimen for non-hodgkin lymphoma with Secondary CNS Involvement (Michael Scordo/ Melhem M. Solh/ Craig S. Sauter).

p. PROP 2010-98 Risk of therapy-related myeloid neoplasm (t-MN) following autologous hematopoietic cell transplantation (auto-HCT) for relapsed and refractory aggressive lymphomas: A comparison of platinum-containing salvage regimens (Mariam T. Nawas/ Michael Scordo/ Craig S. Sauter).

q. PROP 2010-125 Trend in survival in lymphoma patients since autologous SCT over the years: In increments in 5 yrs-1990-2019 lymphoma (NHL/HL) (Faisal, Muhammad Salman/ Nidhi Sharma/ Yvonne Efebera).

r. 2010-134 Real world outcomes of patients with brentuximab vedotin maintenance therapy after ASCT in R/R cHL: Is less enough? (Shah Harsh/ Deborah Stephens).

s. PROP 2010-135 Role of novel salvage treatment in relapsed/refractory classical hodgkin lymphoma patients undergoing ASCT (Shah Harsh).

t. PROP 2010-171 Optimal consolidation in nodal, mature T-cell lymphoma patients not achieving a CR after frontline therapies: Auto or allogeneic transplantation? (Nausheen Ahmed/ Siddhartha Ganguly/ Joseph McGuirk).

u. PROP 2010-177 Outcome of relapsed refractory T cell lymphoma after autologous stem cell transplant: retrospective evaluation of the CIBMTR data (Dahlia Sano/ Dipenkumar Modi/ Abhinav Deol).

v. PROP 2010-192 Outcomes of rituximab maintenance post hematopoietic stem cell transplant as treatment of MCL after bendamustine based induction therapy (Shatha Farhan).

w. PROP 2010-224 Outcomes following allogeneic stem cell transplant for mycosis fungoides and sezary syndrome (Daniel O'Leary/ Amrita Goyal/ Murali Janakiram).

x. PROP 2010-226 Comparison of outcomes for patients with angioimmunoblastic T-cell lymphoma treated as initial consolidation therapy with autologous versus allogeneic hematopoietic cell transplantation (Daniel O'Leary/ Murali Janakiram).

y. PROP 2010-236 Evaluating outcomes of hematopoietic cell transplantation in hepatosplenic T Cell lymphoma (Hemant Murthy/ Madiha Iqbal/ Mohamed A. Kharfan-Dabaja).

z. PROP 2010-263 Outcomes with autologous hematopoietic stem cell transplant in peripheral T-cell lymphoma (Aasems Jacob/ Chaitanya Iragavarapu).

aa. PROP 2010-280 Comparison of autologous versus reduced-intensity allogeneic hematopoietic cell transplantation for mature T cell lymphoma in first complete remission (Bhagirathbhai Dholaria/ Bipin Savani).

ab. PROP 2010-281 Allo-HCT versus CAR T therapy in relapsed mantle cell lymphoma (Bhagirathbhai Dholaria/ Bipin Savani).

ac. PROP 2010-285 Effect of different induction chemoimmunotherapies on autologous hematopoietic cell transplantation outcomes in patients with mantle cell lymphoma (Najla El Jurdi/ Claudio Brunstein/ Veronika Bachanova).

ad. PROP 2010-296 Outcome of autologous stem cell transplant (ASCT) after first complete remission (CR1) using intensive therapy in double-hit and double-expressor B-cell lymphoma (Khaled Mohamed Abouelezz).

STUDIES IN PROGRESS

a. **LY18-02** Effect of time to relapse on overall survival in mantle cell lymphoma patients following frontline autologous stem cell transplant. Status: Manuscript Preparation. The manuscript is currently being prepared and the plan is to submit by July 2021.

b. **LY18-03** Transplantation for chronic lymphocytic leukemia undergoing richter's transformation arising in the setting of indolent lymphoma. Status: Manuscript Preparation. An initial manuscript draft will be received by end of December and the plan is to submit by July 2021.

c. **LY19-01a** Post-transplant cyclophosphamide-based haploidentical transplantation versus matched sibling or well matched unrelated donor transplantation for peripheral T-cell lymphoma: A CIBMTR lymphoma working committee and EBMT lymphoma working party analysis. Status: Analysis. The analysis is currently being finalized and the plan is to submit by July 2021.

d **LY19-01b** Reduced-intensity vs. myeloablative conditioning for T-cell NHL patients undergoing allogeneic HCT. Status: Analysis. The analysis is currently being prepared and the plan is to finalize analysis by July 2021.

e. **LY20-01** Comparison of outcomes of diffuse large B-cell lymphoma patients with partial response after salvage therapy who underwent chimeric antigen receptor T versus autologous hematopoietic cell transplantation. Status: Data File Preparation. The data file is currently being prepared and the plan is to finalize the analysis and manuscript by July 2021.

f. **LY20-02** Outcomes of allogeneic transplants in patients with hodgkin lymphoma in the era of checkpoint inhibitors: A joint CIBMTR and EBMT analysis. Status: Protocol Pending. The protocol is currently being finalized and the plan is to complete the data file by July 2021.

PUBLICATIONS, SUBMITTED PAPERS, PRESENTATIONS

a. **LY18-01b** Shah NN, Ahn KW, Litovich C, He Y, Sauter CS, Fenske TS, Hamadani M. Is autologous transplant in relapsed DLBCL patients achieving only a PET+ PR appropriate in the CAR-T cell era? Blood. doi:10.1182/blood.2020007939. Epub 2020 Oct 29.

b. **LY17-02c** Epperla N, Ahn KW, Khanal M, Litovich C, Ahmed S, Ghosh N, Fenske TS, Kharfan-Dabaja MA, Sureda A, Hamadani M. Impact of reduced-intensity conditioning regimens on outcomes in diffuse large B-cell lymphoma undergoing allogeneic transplantation. Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. doi:10.1016/j.bbmt.2020.09.014. Epub 2020 Sep 19.

c. **LY18-01c** Bal S, Costa LJ, Sauter C, Litovich C, Hamadani M. Outcomes of autologous hematopoietic cell transplantation in diffuse large B-cell lymphoma refractory to first line chemoimmunotherapy. Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. doi:10.1016/j.bbmt.2020.09.004. Epub 2020 Sep 16.

d. **LY17-02b** Ghosh N, Ahmed S, Ahn KW, Khanal M, Litovich C, Aljurf M, Bacher VU, Bredeson C, Epperla N, Farhadfar N, Freytes CO, Ganguly S, Haverkos B, Inwards D, Kamble RT, Lazarus HM, Lekakis L, Murthy HS, Nishihori T, Ramakrishnan P, Rizzieri DA, Yared JA, Kharfan-Dabaja MA, Sureda A, Hamadani M. Association of reduced-intensity conditioning regimens with overall survival among patients with non-Hodgkin lymphoma undergoing allogeneic transplant. JAMA Oncology. 2020 Jul 1; 6(7):1011-1018. doi:10.1001/jamaoncol.2020.1278. Epub 2020 Jun 4. PMC7273311.

e. **LY17-02a** Ahmed S, Ghosh N, Ahn KW, Khanal M, Litovich C, Mussetti A, Chhabra S, Cairo M, Mei M, William B, Nathan S, Bejanyan N, Olsson RF, Dahi PB, van der Poel M, Steinberg A, Kanakry J, Cerny J, Farooq U, Seo S, Kharfan-Dabaja MA, Sureda A, Fenske TS, Hamadani M. Impact of type of reduced?intensity conditioning regimen on the outcomes of allogeneic haematopoietic cell transplantation in classical Hodgkin lymphoma. British Journal of Haematology. doi:10.1111/bjh.16664. Epub 2020 Apr 21. PMC7575614.

f. **LY17-02d** Hamadani M, Khanal M, Ahn KW, Litovich C, Chow VA, Eghtedar A, Karmali R, Winter A, Fenske TS, Sauter C, Kharfan-Dabaja MA, Awan FT. Higher total body irradiation dose intensity in fludarabine/TBI-based reduced-intensity conditioning regimen is associated with inferior survival in non-Hodgkin lymphoma patients undergoing allogeneic transplantation. Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2020 Jun 1; 26(6):1099-1105. doi:10.1016/j.bbmt.2020.02.025. Epub 2020 Mar 9. PMC7255948.

g. **LY18-01a** Jagadeesh D, Majhail NS, He Y, Ahn KW, Litovich C, Ahmed S, Aljurf M, Bacher U, Badawy SM, Bejanyan N, Cairo M, Cerny J, Epperla N, Farhadfar N, Freytes CO, Gale RP, Haverkos B, Hossain N, Inwards D, Kamble RT, Kenkre VP, Lazarus HM, Lazaryan A, Lekakis L, Mei M, Murthy HS, Mussetti A, Nathan S, Nishihori T, Olsson RF, Ramakrishnan Geethakumari P, Savani BN, Yared JA, Fenske TS, Kharfan-Dabaja MA, Sureda A, Hamadani M. Outcomes of rituximab?BEAM versus BEAM conditioning regimen in patients with diffuse large B cell lymphoma undergoing autologous transplantation. Cancer. 2020 May 15; 126(10):2279-2287. doi:10.1002/cncr.32752. Epub 2020 Feb 12. PMC7190439.

h. **LY17-02d** Conditioning regimen in allografts for diffuse large B cell lymphoma. *Submitted. Oral presentation at the EBMT 2020 Annual Meeting.*

i. **LY18-01b** Outcomes in B cell non-Hodgkin lymphoma patients who underwent autologous stem cell transplantation following rituximab containing conditioning regimens in partial remission. *Submitted. Oral presentation at the ASCO 2020 Annual Meeting.*

j. **LY19-02** Determining the optimal conditioning regimen for patients with primary central nervous system lymphoma undergoing autologous hematopoietic cell transplantation. *Submitted. Oral presentation at the ASH 2020 Annual Meeting.*

A G E N D A
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
Orlando, FL
Wednesday, February 19, 2020 12:15-2:45 pm

Co-Chair:	**Timothy Fenske, MD, Medical College of Wisconsin, Milwaukee, WI; Telephone: 414-805-4633; E-mail: tfenske@mcw.edu**
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1. Introduction

The CIBMTR Hodgkin and Non-Hodgkin Lymphoma Working Committee was called to order at 12:15 pm on Wednesday, February 19, 2020 by Dr. Mehdi Hamadani. Dr. Tim Fenske introduced the working committee leadership, and highlighted leadership's conflict of interest disclosures per CIBMTR policy. Dr. Fenske also outlined the Working Committee goals, expectations, and limitations and provided an update on the Working Committee productivity including 3 publications, 2 recent submissions, 3 oral presentations at the 2019 American Society of Hematology meeting, and 1 oral presentation at the 2020 EBMT meetings. Dr. Mohamed Kharfan-Dabaja went over the six studies in progress and reviewed the voting guidelines. The guidelines are based on a scale from 1 to 9; 1=high scientific impact, 9=low scientific impact. In addition, Dr. Kharfan-Dabaja presented the future priority of our studies. Dr. Mehdi Hamadani explained the difference between the TED and CRF data collection forms, the study life cycle, and the rules for authorship: 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. Dr. Hamadani emphasized that WC authorship is open to any LYWC Tandem Meetings attendees and encouraged junior faculty, fellows and assistant professors to collaborate actively with the Lymphoma Writing Committee. Dr. Hamadani reviewed the Advisory Committee metrics for the committee, especially highlighting the lack of any manuscripts in preparation for more than one year and no studies in progress for more than 3 years. He also highlighted the committee's highest cited paper in the last five years: Reduced-intensity transplantation for lymphomas using haploidentical related donors vs HLA-matched unrelated donors (Kanate et al, Blood 2016). Dr. Hamadani finished the introduction slides by thanking Dr. Fenske for his work with the committee, as Dr. Fenske's term as Chair is ending. Dr. Fenske welcomed the incoming Chair, Dr. Alex Herrera.

2. Accrual summary

Dr. Mohamed Kharfan-Dabaja presented a slide with the accruals. It was mentioned that the accrual summary was available in the LYWC materials.

3. Presentations, published or submitted papers

Dr. Mohamed Kharfan-Dabaja listed the presentations and publications during 2018, highlighting the great productivity of the LYWC, including the following studies published or presented:

a. **LY17-01b** Allogeneic transplantation in elderly patients ≥65 years with non-Hodgkin lymphoma: a time-trend analysis. (N Shah) *Published in Blood Cancer Journal. Oral presentation at the 2019 EBMT Annual Meeting.*
b. **LY17-02a** Impact of type of reduced-intensity conditioning regimen on the outcomes of allogeneic hematopoietic cell transplantation in classical Hodgkin lymphoma. *Submitted. Presented at ASH Annual Meeting.*
c. **LY17-02b** Evaluating impact of reduced-intensity conditioning regimens on overall survival in non-Hodgkin lymphoma patients undergoing allogeneic transplantation. A CIBMTR registry analysis. *Submitted. Oral presentation at the ASH Annual Meeting.*
d. **LY17-02c** Higher total body irradiation dose-intensity in fludarabine/TBI-based reduced-intensity conditioning regimen is associated with inferior survival in non-Hodgkin lymphoma patients undergoing allogeneic transplantation. *Submitted.*
e. **LY17-02d** Reduced intensity conditioning in allografts for diffused large B-cell lymphoma (Internal) *Oral presentation at the upcoming 2020 EBMT Annual Meeting.*
f. **LY18-01** Outcomes of rituximab-BEAM vs. BEAM conditioning regimen in patients with diffuse large B-cell lymphoma undergoing autologous transplantation. (D Jagadeesh) *Submitted. Oral presentation at the ASH Annual Meeting.*

4. Studies in progress

Dr. Mohamed Kharfan-Dabaja presented the studies in progress and gave an overview of the current standing of each study.

a. **LY17-02d** 2 versus 4 centigray fludarabine/total body irradiation in allografts for non-hodgkin lymphoma (Internal) **Manuscript Preparation**
b. **LY18-01b** Outcomes in b cell non-hodgkin's lymphoma patients who underwent autologous stem cell transplantation following rituximab containing conditioning regimens in partial remission (Internal) **Manuscript Development**
c. **LY18-02** Effect of time to relapse on overall survival in mantle cell lymphoma patients following frontline autologous stem cell transplant (P Riedell/S Smith) **Data file preparation**
d. **LY18-03** Transplantation for CLL undergoing Richter's Transformation arising in the setting of indolent lymphoma (A Herrera) **Data accrual**
e. **LY19-01** Post-transplant cyclophosphamide-based haploidentical transplantation versus matched sibling or well-matched unrelated donor transplantation for peripheral T-cell lymphoma: A CIBMTR Lymphoma working committee and EBMT Lymphoma working party analysis (P Dreger/M Hamadani) **Data file preparation**
f. **LY19-02** Determining the optimal conditioning regimen for patients with primary central nervous system lymphoma undergoing autologous hematopoietic cell transplantation (M Scordo/C Sauter/A Jimenez) **Protocol Development**

5. Introduction to TED (Transplant Essential Data) vs CRF (Comprehensive Report Form)
(M Hamadani)
Dr. Mehdi Hamadani emphasized 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.

6. Future/proposed studies

a. **PROP 1911-51** CAR-T cell Therapy versus Autologous Transplant in Early Rituximab Failure Patients with Diffuse Large B-cell Lymphoma (Shah) *This concept intends to compare overall survival following autologous HCT and CAR-T among patients with frontline Rituximab failure. During discussion, it was mentioned that a limitation of the study will be patients who fail autologous transplants and move on to receive CAR-T, and Dr. Shah agreed that exclusion of patients with prior transplants is important.*

b. **PROP 1911-22** Outcomes of hematopoietic stem cell transplant as treatment of post-transplant lymphoproliferative disorders (Farhan) *This concept intents to study outcomes after autologous HCT for patients with PTLD. Dr. Hamadani explained that PTLD was only added as a distinct histology to CIBMTR forms in 2018, which explains why 70% of the eligible patients were transplanted in 2018. Additionally, it was discussed that looking at pre-HCT treatment would be important, but since there were few CRF-level cases, that data would be limited.*

c. **PROP 1911-88** Outcomes of autologous and allogeneic hematopoietic cell transplantation for Burkitt Lymphoma (Hashmi, Khimani, Nishihori) *This concept intends to study outcomes after HCT for Burkitt Lymphoma. It was mentioned during discussion that it would be important to confirm cases are true Burkitt's, and not Burkitt-like. Dr. Hamadani also emphasized that this would likely be a descriptive analysis, as comparing autologous and allogeneic HCTs is often difficult.*

d. **PROP 1911-93** Evaluating outcomes of Hematopoietic Cell Transplantation in Hepatosplenic T Cell Lymphoma (Murthy, Iqbal, Kharfan-Dabaja) *This concept intends to study the outcomes after allogeneic HCT for patients with hepatosplenic T-cell lymphoma. It was asked why autologous HCTs would not be included in the analysis, and it was explained that the proposal team limited the analysis to autologous on recommendation from committee leadership due to inadequate number of autos. Additionally, it was mentioned that information on splenectomies would be important, and Dr. Hamadani explained that data would be available at the CRF level only.*

e. **PROP 1911-267** Comparison of outcomes of DLBCL patients with partial response after salvage therapy who underwent CAR-T vs. ASCT. (Shadman) *This concept intends to compare CAR-T and autologous HCT as salvage therapy in DLBCL patients with partial response. During the discussion, it was mentioned that this is an important question for the field, and that it is answerable by the CIBMTR. It was suggested that there could be variability in partial response, and that it would be important to adjust for disease characteristics.*

f. **PROP 1910-01/1911-61/1911-185** Outcomes of salvage AHCT in double hit DLBCL (Manjappa, Karmali, Wirk, Caimi, Metheny) *This concept intends to determine the effect of disease status and chemosensitivity of relapsed/refractory DHL on outcomes after autologous HCT. During discussion, it was asked if double expressor lymphoma could be included, which Dr. Hamadani clarified was not captured by the CIBMTR forms and therefore could not.*

g. **PROP 1911-256** Outcome of Patients with Primary Refractory Diffuse large B cell lymphoma (DLBCL) undergoing Autologous Stem Cell Transplantation (AHCT) (Bal, Sauter, Costa) *This concept intends to study the outcomes after autologous HCT for patients with primary refractory DLBCL. There was discussion on the definition of primary refractory.*

h. **PROP 1911-121** Outcomes of autologous stem cell transplantation in patients with follicular lymphoma with early relapse after frontline Bendamustine/Rituximab treatment. (Sheikh, Keating, Kuruvilla) *This concept intends to study the effect of POD24 after frontline Bendamustine/Rituximab on outcomes after autologous HCT. It was mentioned that a collaboration with EBMT could improve the number of patients in the study.*
i. **PROP 1911-42** Outcomes of Allogeneic HCT in patients with Hodgkin Lymphoma in the era of Checkpoint Inhibitors: A joint CIBMTR and EBMT analysis. (Perales, Sureda, Awan, Montoto) *This concept intends to compare the use of checkpoint inhibitors on outcomes after allogeneic HCT for Hodgkin Lymphoma. It was brought up that time from checkpoint inhibitor use to HCT would be an important factor. It was also suggested that a comparison of BM and PBSC might be useful, though there was concern about sample size.*
j. **PROP 1911-204** Trends in Survival post-autologous transplant in Classical Hodgkin Lymphoma. (Shah) *This concept intends to study overall survival following autologous HCT for classical HL. It was mentioned that perhaps looking at drug approval dates as cutoffs might be useful. For example, using Brentuximab's approval date of 2011 as a cutoff.*

Proposed studies; not accepted for consideration at this time

a. **PROP 1909--04** Outcomes of allogeneic stem cell transplantation with different donor types for patients with lymphomas not in remission at the time of transplant.
b. **PROP 1910-02** Optimizing timing of autologous transplantation for transformed follicular lymphoma.
c. **PROP 1911-11** Efficacy of allogeneic transplant in marginal zone lymphoma.
d. **PROP 1911-22** Outcomes of hematopoietic stem cell transplant as treatment of post-transplant lymphoproliferative disorders.
e. **PROP 1911-28** Outcomes of relapsed/refractory lymphoma patients treated with benda-EAM (bendamustine, etoposide, cytarabine, melphalan) versus BEAM (carmustine, etoposide, cytarabine, melphalan) high dose chemotherapy followed by autologous stem cell transplantation.
f. **PROP 1911-32** Impact of pre-transplant induction therapy on outcomes of patient who undergo autologous stem cell transplantation for mantle cell lymphoma in CR1.
g. **PROP 1911-47** Hematopoietic stem cell transplantation for relapsed/refractory marginal zone lymphoma.
h. **PROP 1911-70** Clinical impact of partial remission versus complete remission on outcomes in follicular lymphoma after autologous stem cell transplantation.
i. **PROP 1911-72** Determination of outcomes of upfront consolidative autologous stem cell transplantation in patients with high FLIPI score follicular lymphoma.
j. **PROP 1911-85** Outcomes of allogeneic hematopoietic cell transplantation for mycosis fungoides and Sezary syndrome.
k. **PROP 1911-87** Outcomes of autologous and allogeneic hematopoietic cell transplantation for primary mediastinal large B-Cell lymphoma.
l. **PROP 1911-98** Evaluating the efficacy of high-dose therapy and autologous hematopoietic cell transplantation for primary effusion lymphoma.
m. **PROP 1911-101** Outcomes of patients with mantle cell lymphoma with aberrant TP53 treated with consolidative autologous or allogeneic stem cell transplant.
n. **PROP 1911-126** Outcomes in elderly patients (age ≥ 70) received autologous hematopoietic stem cell transplantation for non-Hodgkin lymphoma.

o. **PROP 1911-136** Matched versus alternative donor allogeneic hematopoietic stem cell transplantation in HTLV-1 associated adult T-cell lymphoma/leukemia in patients of non-Japanese descent.
p. **PROP 1911-151** Outcomes of reduced intensity allografts in classical Hodgkin lymphoma after brentuximab maintenance therapy.
q. **PROP 1911-157** Outcomes of patients ≥ 65 years old undergoing autologous stem cell transplant for mantle cell lymphoma.
r. **PROP 1911-192** Outcomes following allogeneic hematopoietic stem cell transplantation for mycosis fungoides and Sezary syndrome.
s. **PROP 1911-208** Autologous stem cell transplantation for HIV seropositive patients with hematological malignancies.
t. **PROP 1911-222** Utilization and outcomes of autologous and allogeneic HSCT in CNS lymphomas.
u. **PROP 1911-227** Outcomes of patients with HTLV-1 associated adult T cell lymphoma/leukemia: A combined American and European experience.
v. **PROP 1911-229** Effect of mobilization agent on risk of second hematological malignancy in patients with lymphoma who received autologous transplant.
w. **PROP 1911-231** Outcome of autologous and allogeneic hematopoietic cell transplant in marginal zone lymphoma.
x. **PROP 1911-239** High dose therapy and autologous stem cell transplantation in primary central nervous lymphoma in older adults.
y. **PROP 1911-244** Impact of pre- and post-transplantation lymphopenia and 18F-fluorodeoxy glucose–positron emission tomography status on outcomes after autologous hematopoietic cell transplantation for peripheral T-cell lymphoma.
z. **PROP 1911-257** Outcome of autologous hematopoietic stem cell transplant in older patients (age >70 years) with non-Hodgkin's lymphoma.

7. Other Business

After the proposals were presented, the voting process was reiterated, and each participant had the opportunity to rate each new proposal using paper ballots. Without additional comments, the meeting was adjourned at 2:05 pm.

Working Committee Overview Plan for 2020-2021

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to goal 7/1/20	Hours allocated to 6/30/20	Hours allocated 7/1/20-6/30/21	Total Hours allocated
LY17-02a: Allografts following reduced intensity conditioning for hodgkin's lymphoma.	Submitted	Published – May 2020	10	10	10	0	10
LY17-02b: Allografts following reduced intensity conditioning for non-hodgkin disease.	Submitted	Published – May 2020	10	10	10	0	10
LY17-02d: 2 versus 4 centigray fludarabine/total body irradiation in allografts for non-hodgkin lymphoma	Manuscript preparation	Submitted – June 2020 Published – July 2021	20	20	10	10	20
LY18-01a: Outcomes in b cell non-hodgkin's lymphoma patients who underwent autologous stem cell transplantation following rituximab containing conditioning regimens	Submitted	Published – July 2020	10	10	10	0	10
LY18-01b: Outcomes in b cell non-hodgkin's lymphoma patients who underwent autologous stem cell transplantation following rituximab containing conditioning regimens in partial remission	Manuscript preparation	Submitted – July 2020 Published – July 2020	50	60	50	10	60
LY18-02: Effect of time to relapse on overall survival in mantle cell lymphoma patients following frontline autologous stem cell transplant.	Data file preparation	Analysis – June 2020 Manuscript preparation – July 2020 Submitted – July 2021	160	160	90	70	160
LY18-03: Transplantation for CLL undergoing Richter's transformation arising in the setting of indolent lymphoma.	Data file preparation	Analysis – July 2020 Manuscript preparation– September 2020 Submitted – July 2021	220	220	70	150	220

LY19-01: Post-transplant cyclophosphamide-based haploidentical transplantation versus matched sibling or well-matched unrelated donor transplantation for peripheral T-cell lymphoma: a CIBMTR lymphoma working committee and EBMT lymphoma working party analysis.	Protocol development	Submitted – June 2021	160	160	90	70	160
LY19-02: Determining the optimal conditioning regimen for patients with primary central nervous system lymphoma undergoing autologous hematopoietic cell transplantation.	Draft protocol received	Data file preparation – July 2020 Analysis – October Manuscript preparation – July 2021	330	260	100	160	260
LY20-01: Comparison of outcomes of DLBCL patients with partial response after salvage therapy who underwent CAR-T vs. Autologous HCT	Protocol pending	Analysis – May 2021 Manuscript preparation – July 2021	330	260	0	260	260
LY20-02: Outcomes of allogeneic HCT in patients with Hodgkin lymphoma in the era of checkpoint inhibitors: A joint CIBMTR and EBMT analysis	Protocol pending	Protocol development – December 2020 Data file preparation – July 2021	370	100	0	100	100

Oversight Assignments for Working Committee Leadership (March 2019)

Craig Sauter	**LY18-01b** Outcomes in b cell non-hodgkin's lymphoma patients who underwent autologous stem cell transplantation following rituximab containing conditioning regimens
	LY19-02 Determining the optimal conditioning regimen for patients with primary central nervous system lymphoma undergoing autologous hematopoietic cell transplantation.
Mohamed Kharfan-Dabaja	**LY17-02d** 2 versus 4 centigray fludarabine/total body irradiation in allografts for non-hodgkin lymphoma
	LY18-02 Effect of time to relapse on overall survival in mantle cell lymphoma patients following frontline autologous stem cell transplant.
Alex Herrera	**LY18-03** Transplantation for CLL undergoing Richter's transformation arising in the setting of indolent lymphoma.
	LY20-02 Outcomes of allogeneic HCT in patients with Hodgkin lymphoma in the era of checkpoint inhibitors: A joint CIBMTR and EBMT analysis
Mehdi Hamadani	**LY19-01** Post-transplant cyclophosphamide-based haploidentical transplantation versus matched sibling or well-matched unrelated donor transplantation for peripheral T-cell lymphoma: a CIBMTR lymphoma working committee and EBMT lymphoma working party analysis.
	LY20-01 Comparison of outcomes of DLBCL patients with partial response after salvage therapy who underwent CAR-T vs. Autologous HCT

Proposal: 2010-333

Title:
Outcomes of chimeric antigen receptor – T cell (CAR-T) therapy for patients with antecedent chronic lymphocytic leukemia (Richters Syndrome)

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Hypothesis:
Patients with CLL with Richters transformation can be treated efficaciously with CART therapy.

Specific aims:
Assess outcomes in adult patients with CLL undergoing transformation to diffuse large B-cell lymphoma (Richters Syndrome) and undergoing CART therapy.

- **Primary objective:**
  - Overall Survival.
- **Secondary objectives**
  - Progression-free survival (PFS)
  - Cumulative incidence of disease relapse
  - Overall survival (OS)
  - Cumulative incidence of non-relapse mortality (NRM)
  - Cause of death.
- **Additional objectives**
  - To identify factors predictive of outcomes after anti-CD19 CAR-T cell therapy to treat B-cell lymphomas
  - To describe and identify biomarkers predictive of immune-cell effector toxicity (CRS and ICANS)

Scientific rationale:
CART therapy has been a significant recent therapeutic advance in providing an option for patients with chemotherapy refractory lymphoid malignancies. Two products are currently FDA approved with multiple others in development and more approvals expected in the near future. Comparison of all 3 CART options with more substantial available data demonstrate an overall response rate from 50-80% with a complete remission rate of 40-60%. Similarly, 1 year progression free and overall survival ranges around 50-70%. However these results are significantly impacted by study design issues and selection of patients with a more favorable disease biology and disease responsive to salvage therapy.[1,2]
Richters Syndrome (RS) is transformation of CLL into diffuse large B-cell lymphoma and is associated with extremely poor outcomes with currently approved treatments. CART trials have historically excluded patients with RS and data on the utility of this therapeutic option for RS is limited. However, anecdotal reports have demonstrated promising efficacy for this indication. A recent small case series has also shown excellent clinical activity with potentially sustained responses in subset.[3]
Given the increased utility of CART cell therapies, it is expected that a number of suitable patients will undergo this therapy prior for RS. Numerous factors that can impact patient selection outcomes are therefore required to be elucidated, including those specific to CLL patients. Utilizing the CIBMTR

repository offers a unique opportunity to assess these issues and formulate guidance for future clinical efforts.

Patient eligibility population:
This study will include adult patients with diffuse large B-cell NHL with an antecedent history of CLL who received CART therapy between 01/2015 and 12/2019.
Inclusion criteria:

- CART therapy between 2015 and 2019
- Age ≥ 18

Study design:
A retrospective study will be conducted utilizing CIBMTR. Patients will be eligible for inclusion if they are ≥ 18 and who received a CART cell between 01/2015 and 12/2019. The objectives of this analysis are to determine outcomes in patients undergoing CART therapy for RS.
Descriptive tables of patient, disease-, and transplant-related factors will be created. The tables will list median and range for continuous variables and percent of total for categorical variables. Cumulative incidence of ICANS, CRS, relapse/progression, and NRM will be calculated while accounting for competing events. Probabilities of OS will be calculated using the Kaplan-Meier estimator. Multivariate analysis will be performed using Cox proportional hazards models for outcomes for ICANS, CRS, relapse/progression, NRM, PFS, and OS. A stepwise model building approach will then be used to identify the significant risk factors associated with the outcomes. Factors which are significant at a 5% level will be kept in the final model. The potential interactions between main effect and all significant risk factors will be tested. The proportional hazards assumption will be checked for the Cox model. If violated, it will be added as time-dependent covariates.

Data requirements:

- CIBMTR: Utilizing data collected by CIBMTR from pre and post CART, which includes pre-CART essential data form #2400, post-transplant essential data form #2450, chimerism studies form #2451, selective post-transplant selective data form #2455 and 100-day post-HSCT data form #2100. The parameters to be assessed are outlined in table 1 below.

Table 1 Data Requirements:

Type of data	Data point	Specific data
Patient Specific	Patient specific characteristics	• Age at transplant (Date of birth) • Gender • Race • Significant comorbidities • Prior autologous/allogeneic transplant • Prior CART therapy • Remission status (CR1, CR2, etc) • Karnofsky performance status at transplant: ≥ 90 vs. < 90 vs. missing • HCT-CI • HCT-CI/age • CAR-T therapy date (time from diagnosis to ct) • Best response to CART (MACRO RECOVERY)
CART Specific	CART date	CART date
	Preparative regimen used	Dose of conditioning treatment

	Bridging therapy	• Specifics of bridging therapy
	CART characteristic	Specific product
Outcome Measures	Engraftment	• Time to absolute neutrophil count $\geq$500 cells/mm^3 for 3 consecutive laboratory readings • Time to unsupported platelets $\geq$20 x 10^9 cells/L and $\geq$50 x 10^9 cells/L • Donor-recipient chimerism • Graft failure (primary and secondary)
	CRS/ICANS	• Overall CRS/ICANS • Incidence of grade II-IV CRS/ICANS (subset evaluating grade III-IV CRS/ICANS) • Time to CRS/ICANS • CRS/ICANS after day 30 • Incidence of sustained cytopenias > 30 days
	Mortality	• Time to mortality • Day 100, 6 months and 1-year mortality • Treatment related mortality at 6 months and 1 year • Cause of mortality
	Disease relapse	• Incidence of disease relapse • Time to disease relapse

CIBMTR Selection criteria (*to be updated through 2019*)

	Excluded	N
Number of adult patients underwent CART for RS from 2015-2019 in CIBMTR CRF Jan 2020 retrieval		
Consent		
Exclude embargo centers		

References:

1. Locke FL, Ghobadi A, Jacobson CA, et al. Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicentre, phase 1-2 trial. *Lancet Oncol*. 2019;20(1):31-42.
2. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019;380(1):45-56.
3. Kittai AS, Bond DA, William B, et al. Clinical activity of axicabtagene ciloleucel in adult patients with Richter syndrome. Blood Adv. 2020;4(19):4648-4652.

The below selection criteria were applied

Selection criteria	**# excluded**	**N**
Number of patients underwent CART for RS from 2015-2019 in CIBMTR		40
Patients >= 18 yrs old	0	40
Excluding Non-Consent	4	36

Table 1. Characteristics of adult patients underwent CART for RS from 2015-2019 reported to the CIBMTR

Characteristic	1
No. of patients	36
No. of centers	19
Age at infusion, yrs - median (min-max)	69 (41-80)
Age - no. (%)	
40-49	4 (11)
50-59	2 (6)
60-69	14 (39)
>=70	16 (44)
Recipient Sex - no. (%)	
Male	22 (61)
Female	14 (39)
KPS - no. (%)	
90-100	9 (25)
<90	21 (58)
Missing	6 (17)
Recipient race - no. (%)	
Caucasian	31 (86)
African-American	2 (6)
More than one race	2 (6)
Missing	1 (2)
Remission status- no. (%)	
CR	3 (8)
PR	5 (14)
Resistant	25 (69)
Untreated	1 (3)
Unknown	2 (6)
HCT Comorbidity Index - no. (%)	
0	9 (25)
1	5 (14)
2	3 (8)
3+	18 (50)
Missing	1 (3)
Prior HCTs - no. (%)	
No	24 (67)
Yes	12 (33)
Allo	5 (38)

Characteristic	**1**
Auto	7 (62)
Bridging therapy - no. (%)	
No	25 (69)
Yes	11 (31)
Time from diagnosis to CT, median (range) - median (min-max)	12 (2-283)
Time from diagnosis to CT - no. (%)	
<1-year	15 (42)
>/= 1-year	21 (58)
Year of CT - no. (%)	
2018	9 (25)
2019	27 (75)
Follow-up - median (min-max)	12 (3-16)

Combined Proposals: 2010-297; PROP 2010-49

Title:
Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with secondary central nervous system (CNS) involvement

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Sairah Ahmed, MD, SAhmed3@mdanderson.org, UT MD Anderson Cancer Center

Hypothesis:
CD19 directed CAR T-cell therapy is safe and has similar efficacy in aggressive non-Hodgkin B-cell lymphoma lymphomas with secondary CNS involvement.

Specific aims:
- Determine incidence, grade and usage of IL-6 antagonists/corticosteroid/other for management of neurotoxicity for patients with secondary CNS lymphoma undergoing CD19 directed CAR T-cell therapy
- Determine outcomes including overall response rate, complete response rate, relapse rate, progression free survival (PFS), overall survival (OS), non-relapse mortality (NRM) for patients with secondary CNS lymphoma undergoing CD19 directed CAR T-cell therapy

Scientific impact:
Assessment of the safety and efficacy of CD19 directed CAR T-cell therapy in patients with secondary CNS lymphoma using the CIBMTR data would potentially impact the treatment paradigm for patients with secondary CNS lymphoma and may introduce CART cell therapy as an option for long term durable remission in a disease with an otherwise poor prognosis.

Scientific justification:
Chimeric antigen receptor (CAR) T-cell therapy has revolutionized the treatment paradigm for relapsed/refractory B-cell non-Hodgkin lymphoma (NHL). Axicabtagene ciloleucel and Tisagenlecleucel are currently approved CAR T-cell therapy products by the US Food and Drug Administration (FDA), having demonstrated response rates of about 50-80% in B-cell NHL [1,2]. Due to of concerns for CAR T-cell–related neurotoxicity, patients with active central nervous system (CNS) involvement were excluded from both pivotal studies. Hence, per the US Food and Drug Administration label, both CD19 directed CAR T-cell therapies are approved for aggressive B-cell lymphomas with a specific exclusion for primary but not secondary CNS lymphoma. A case report has demonstrated the efficacy of CD19-directed CAR T-cell therapy in a patient with simultaneous CNS and systemic involvement [3]. Frigault et al. [4] reported a cohort of 8 patients treated with Tisagenlecleucel for active secondary CNS lymphoma without excessive neurotoxicity. However, the current studies are limited by the small number of patients and a short follow-up. This is a patient population with limited options for curative treatment after first relapse and an area of necessitating better treatment options. CD19 directed CAR T-cell therapy is a potential treatment option however there is a gap in knowledge in terms of efficacy and toxicity for this indication. This would be an ideal study for the CIBMTR registry to better understand outcomes and potentially guide prospective clinical trials.

Patient eligibility population:

Inclusion criteria:

Adult patients (age ≥18) who received CD19 CAR T-cell therapy for B-cell NHL with secondary CNS involvement

Exclusion criteria:

None

Variables to be described:

Patient related:

- Age at CAR T-cell therapy: continuous and categorical by decade
- Gender: male vs. female
- Race: Caucasian vs. African American vs. Asian/Pacific Islander vs. Hispanic vs. Others vs. missing
- Ethnicity: Hispanic or Latino vs. Non-Hispanic or non-Latino vs. non-resident of the U.S.
- ECOG Performance status / Karnofsky performance score

Underlying neurological disorders (including cerebrovascular ischemia/hemorrhage, autoimmune syndromes with CNS symptoms, psychiatric disorder, Parkinson's disease)

Disease-related:

- Disease histology: B-cell NHL (diffuse large B cell lymphoma, transformed follicular lymphoma, primary mediastinal B cell lymphoma, mantle cell lymphoma vs. others)
- Disease stage at diagnosis: I-II vs. III-IV
- IPI score at diagnosis: 0-3
- Bulky disease (size >10 cm): yes vs. no
- Disease status by FISH (double HIT vs double expressor)
- Site of CNS disease prior to CAR T-cell therapy: supratentorial, spinal cord, leptomeningeal and/or CSF only
- CNS disease at the time of diagnosis: yes vs. no
- CNS disease at the time of relapse: yes vs. no
- Active CNS disease prior to CAR T-cell therapy: yes vs. no
- Prior lines of chemotherapy: 0-1, 2, 3, 4+
- Prior CNS-directed therapy: systemic chemotherapy, intrathecal therapy, cranial/spinal radiation vs. others
- Prior autologous stem cell transplant: yes vs. no
- Prior allogeneic stem cell transplant: yes vs. no
- Disease status prior to CAR T-cell therapy: CR, PR, SD, or PD
- Baseline markers of inflammation (ferritin/CRP) prior to CAR T-cell infusion: continuous and categorical (to be determined)

CAR T-cell therapy related:

- Time from diagnosis to CAR T-cell therapy: continuous and categorical by months/years
- Time from autologous transplant to CAR T-cell therapy
- Use of bridging therapy: yes vs. no
- Type of bridging therapy used: corticosteroid vs. chemotherapy vs. Radiotherapy vs. chemoradiotherapy
- Type of lympho-depleting chemotherapy used: fludarabine/cyclophosphamide vs. others

- CAR T-cell product used: axicabtagene ciloleucel vs. tisagenlecleucel vs. liso-cel vs. bruxa-cel

Data requirements:
None

Sample requirements:
None

Study design:
Outcomes:

- Response: Response rate at the day 30, 6 months and 1 year based on CT-PET, CT, or MRI
- Cytokine release syndrome (CRS) and neurotoxicity: Occurrence of grade 1-5 CRS and neurotoxicity. Lee criteria or modified Lee criteria will be used for the CRS grading. CT CAE v4 or CARTOX grading will be used for grading of neurotoxicity.
    - Use of tocilizumab and corticosteroids will be described on each grade of CRS and neurotoxicity
    - Frequency of seizure and other CNS complications will be described individually
    - Use of seizure prophylaxis will be described
- Overall survival: Time from CAR T-cell infusion to death from any cause. Patients will be censored at the time of last follow up.
- Progression-free survival: Time from CAR-T infusion to death or relapse. Patients will be censored at the time of last follow up.
- CAR T-cell Non-relapse mortality (NRM): Death due to any cause in the first 28 days or death due to conditions other than disease relapse or progression beyond 28 days. Events will be summarized by the cumulative incidence estimate with relapse as a competing risk.
- Relapse: Development of relapse as defined by the CIBMTR. The event will be summarized by the cumulative incidence estimate. NRM will be a competing risk.
    - Relapse will be described based on the location: systemic vs. CNS (or both)
- CNS complications: Development of CNS-related issues post CAR T-cell therapy other than those attributable to CRS/neurotoxicity or CNS relapse will be described. Events of interest includes cerebrovascular accidents (ischemia and/or hemorrhage), seizure beyond 2 months, dementia/memory loss or other reported CNS events
- Causes of death: causes of death will be summarized
- Length of stay (LOS) – assess overall LOS per disease and product

Outcomes of CD19 directed CAR T-cell therapy in aggressive B-cell NHL will be evaluated in this retrospective study. The study will be expected to be descriptive in nature due to anticipated small sample size. Patient-, disease- and CAR T-cell therapy related factors will be described based on categorical and continuous variables. Univariate analysis will be performed on outcomes of interests. OS and PFS probabilities will be estimated by Kaplan-Meier method. Probabilities of CAR T-cell related TRM and disease relapse/progression will be calculated using cumulative incidence curves to accommodate competing risks.

Selection criteria	# excluded	N
Patients who received CD19 CAR T-cell therapy for B-cell NHL with secondary CNS involvement		59
Patients >= 18 yrs old	1	58
Excluding Non-consent	3	55

Non-CIBMTR Data Source:
N/A

References:
1. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. N Engl J Med. 2017;377(26):2531-2544.
2. Schuster SJ, Bishop MR, Tam CS, et al; JULIET Investigators. Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma. N Engl J Med. 2019;380(1):45-56.
3. Abramson JS, McGree B, Noyes S, et al. Anti-CD19 CAR T cells in CNS diffuse large-B-cell lymphoma. N Engl J Med. 2017;377(8):783-784.
4. Frigault MJ, Dietrich J, Martinez-Lage M, et al. Tisagenlecleucel CAR T-cell therapy in secondary CNS lymphoma. Blood. 2019 Sep 12;134(11):860-866. doi: 10.1182/blood.2019001694

Table 1. Characteristics of adult patients (age ≥18) who received CD19 CAR T-cell therapy for B-cell NHL with secondary CNS involvement reported to CIBMTR

Characteristic	CNS involvement at CT	CNS involvement at diagnosis
No. of patients	37	18
No. of centers	16	11
Age at infusion, yrs - median (min-max)	61 (23-83)	63 (34-79)
Age - no. (%)		
20-29	3 (8)	0 (0)
30-39	1 (3)	2 (11)
40-49	4 (11)	3 (17)
50-59	9 (24)	2 (11)
60-69	17 (46)	5 (28)
>=70	3 (8)	6 (33)
Recipient Sex - no. (%)		
Male	21 (57)	12 (67)
Female	16 (43)	6 (33)
Recipient race - no. (%)		
White	26 (71)	18 (100)
African American	3 (8)	0
Asian	3 (8)	0
More than one race	2 (5)	0
Missing	3 (8)	0
KPS - no. (%)		
90-100	11 (30)	7 (39)
<90	24 (65)	8 (44)
Missing	2 (5)	3 (17)
Disease status - no. (%)		
CR	0	2 (11)
PR	12 (32)	4 (22)
Resistant	25 (68)	12 (67)
Disease histology - no. (%)		
DLBCL	32 (87)	18 (100)
Mantle cell lymphoma	2 (5)	0
Other[1]	3 (8)	0
HCT Comorbidity Index - no. (%)		

[1]Other histology:

	N
Burkitt lym/Burkitt cell leukemia	3

Characteristic	CNS involvement at CT	CNS involvement at diagnosis
0	14 (38)	5 (28)
1	10 (27)	0 (0)
2	3 (8)	4 (22)
3+	10 (27)	7 (39)
Missing	0	2 (11)
Prior HCTs - no. (%)		
No	28 (76)	10 (56)
Yes	9 (24)	8 (44)
Allo	0 (0)	1 (13)
Auto	7 (78)	7 (87)
Both allo and auto	1 (11)	0 (0)
Missing	1 (11)	0 (0)
Bridging therapy - no. (%)		
No	26 (70)	14 (78)
Yes	11 (30)	4 (22)
Time from diagnosis to CT, median (range) - median (min-max)	13 (4-113)	14 (4-75)
Time from diagnosis to CT - no. (%)		
<1 year	16 (43)	7 (39)
>=1 year	21 (57)	11 (61)
Year of CT - no. (%)		
2018	6 (16)	5 (28)
2019	21 (57)	6 (33)
2020	10 (27)	7 (39)
Follow-up - median (min-max)	6 (2-26)	12 (3-22)