A G E N D A
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
Orlando, FL
Wednesday, February 15, 2023, 1:00 p.m. – 3:00 p.m. (EST)

Co-Chair:	**Alex Herrera, MD, City of Hope National Medical Center, Duarte, CA; Telephone: 626-256-4673; E-mail: aherrera@coh.org**
Co-Chair:	**Craig Sauter, MD, Cleveland Clinic Foundation, Cleveland, OH; Telephone: 212-639-3460; E-mail: sauterc@ccf.org**
Outgoing Co-Chair:	**Mohamed Kharfan-Dabaja, MD, MBA, Mayo Clinic, Jacksonville, FL; Telephone: 904-953-2000; E-mail: kharfandabaja.mohamed@mayo.edu**
Incoming Co-Chair:	**Mazyar Shadman, MD, MPH, Fred Hutchinson Cancer Center, WA; Telephone: 206-667-5467; E-mail: mshadman@fredhutch.org**
Scientific Director:	**Mehdi Hamadani, MD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0700; E-mail: mhamadani@mcw.edu**
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Statistician:	**Manmeet Kaur, MPH, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-736-3467; E-mail: mkaur@mcw.edu**

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1. **Introduction**
   a. **Minutes and Overview Plan from February 2022 meeting** (Attachment 1)

2. **Accrual Summary** (Attachment 2)

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

   a. **LY18-01e** Munshi PN, Chen Y, Ahn KW, Awan FT, Cashen A, Shouse G, Shadman M, Shaughnessy P, Zurko J, Locke FL, Goodman AM, Bisneto JCV, Sauter C, Kharfan-Dabaja MA, Meyers G, Jaglowski S, Herrera A, Hamadani M. Outcomes of autologous hematopoietic cell transplantation in older patients with diffuse large B-cell lymphoma. ***Transplantation and Cellular Therapy. 2022 Aug 1; 28(8):487.e1-487.e7. doi:10.1016/j.jtct.2022.05.029. Epub 2022 May 21. PMCID:PMC9375438. Presentation: EBMT 2022.***

   b. **LY19-01c** Furqan F, Ahn KW, Chen Y, Kaur M, Abutalib SA, Ahmed N, Ahmed S, Kharfan-Dabaja MA, Friedberg J, Gregory T, Hill L, Sterling C, Barta SK, Shadman M, Perales M-A, Zain J, Herrera AF, Sauter C, Hamadani M. Allogeneic haematopoietic cell transplant in patients with relapsed/refractory anaplastic large cell lymphoma. ***British Journal of Haematology. 2023 Jan 1; 200(1):54-63. doi:10.1111/bjh.18467. Epub 2022 Sep 19. PMCID:PMC9772096. Presentation: EBMT 2022.***

4. **Studies in Progress** (Attachment 3)

a. **LY20-02** Outcomes of Allogeneic HCT in patients with Hodgkin Lymphoma in the era of Checkpoint Inhibitors: A joint CIBMTR and EBMT analysis. (Miguel-Angel Perales/Ana Maria Sureda) **Manuscript Preparation.**
b. **LY22-01** Comparing CAR vs. Auto-HCT in Aggressive B-cell lymphomas: Addressing questions unanswered by randomized trials (Mazyar Shadman/Mehdi Hamadani/Trent Wang/ Antonio Martin Jimenez Jimenez/Zurko Joanna) **Data File Preparation.**
c. **LY22-02** CAR-T Outcomes in Rare Lymphoma Subtypes: A Basket Protocol (Hamza Hashmi/Naren Epperla/Sairah Ahmad/Santiago Mercadal/Catherine Lee/Priyanka Pophali/Joshua Fein/Roni Shouval/Mazyar Shadman/Swetha Kambhampati/Kalyan Nadiminti/Alex Herrera/Mehdi Hamadani/Jordan Gauthier) **Protocol Development.**

5. Future/Proposed Studies

a. **PROP 2210-189/2210-253/2210-271** Outcomes of allogeneic hematopoietic cell transplantation (allo-HCT) for large B-cell lymphoma (LBCL) progressing after chimeric antigen receptor T-cell therapy (CAR T) (Xia Bi/Usama Gergis/Dipenkumar Modi/Baldeep Wirk)(Attachment 4)
b. **Prop 2210-284/2210-58** Outcomes Following CD19 Directed Chimeric Antigen Receptor (CAR) T-Cell Therapy for Relapsed Refractory Follicular Lymphoma: Real-World Data from the Center for International Blood and Marrow Transplant Research (CIBMTR)(Rajan Mohty/Aleksandr Lazaryan/Swetha Kambhampati/Alex Herrera)(Attachment 5)
c. **PROP 2210-87/2205-04** Allogeneic hematopoietic stem cell transplantation for advanced mycosis fungoides and Sezary syndrome: an analysis of CIBMTR data and consensus guidelines for patient selection and treatment protocol (Amrita Goyal/Firas Safa/Nakhle Saba/Francine Foss)(Attachment 6)
d. **PROP 2210-147** Evaluating outcomes of novel therapies post CD19 CAR T in Diffuse Large B-cell Lymphoma (Swetha Kambhampati/Alex Herrera) (Attachment 7)
e. **PROP 2210-198** Efficacy of hematopoietic stem cell transplantation in patients with plasmablastic lymphoma (Adeel/Masood/Sairah Ahmad)(Attachment 8)
f. **PROP 2210-235** Secondary malignant neoplasms after CD-19 CAR-T cell therapy in Large B cell lymphoma (Sushanth Gouni/Sairah Ahmad)(Attachment 9)

Proposed Studies; not accepted for consideration at this time

a. PROP 2205-03 Impact of peri-transplant radiation therapy in relapsed or refractory Hodgkin Lymphoma undergoing autologous stem cell transplantation
b. PROP 2210-18 Comparison of clinical outcomes of patients with large B-cell lymphomas who relapse or progress after anti-CD19 CART during 2nd line of therapy versus 3rd line of therapy
c. PROP 2210-56 Real-world outcomes of second line CD19 CAR T for primary refractory/early relapse diffuse large B-cell lymphoma
d. PROP 2210-59 Outcomes of autologous stem cell transplantation after CD19 CAR T in patients with relapsed refractory DLBCL
e. PROP 2210-65 The impact of TP53 genomic alterations in large B-cell lymphoma treated with CD19-CAR-T
f. PROP 2210-78 Outcomes and Utilization Trends of Autologous Hematopoietic Cell Transplantation for Classical Hodgkin Lymphoma
g. PROP 2210-82 The Impact of Bridging Therapy on the Safety and Efficacy of CAR T-cells for Large B-cell Lymphoma
h. PROP 2210-86 Outcomes of Hematopoietic Cell Transplant Strategies in Patients with CLL and Hodgkin Lymphoma variant Richter's Syndrome

i. PROP 2210-88 Optimal Transplant Strategy for Patients with Non-Hodgkin Lymphoma Who Relapse After 2nd-line CAR T cell therapy
j. PROP 2210-94 EFS6, EFS12 and EFS24 as predictors of long-term outcomes in patients with diffuse large B-cell lymphoma treated with chimeric antigen T cell receptor therapy
k. PROP 2210-100 Outcomes of CAR T therapy in LBCL patients with CNS involvement
l. PROP 2210-109 Outcomes of Hematopoietic Stem Cell Transplantation (HSCT) in Rare T Cell Lymphoma (TCL) Subtypes – Hepatosplenic TCL (HSTCL) and Enteropathy Associated TCL (EATL)
m. PROP 2210-111 Outcomes of Mantle Cell Lymphoma Patients Undergoing Autologous Stem Cell Transplant Based on Initial Induction Regimen
n. PROP 2210-115 Stratified comparison of CD19-directed CAR-T cell products in lymphoma patients who receive and do not receive bridging therapy
o. PROP 2210-140 Allogeneic Transplant for PTCL in Partial Remission or Less
p. PROP 2210-145 Outcomes of Salvage AHCT in Double Hit DLBCL
q. PROP 2210-153 Outcomes of Mantle Cell Lymphoma (MCL) Beyond First Relapse with Chimeric Antigen Receptor (CAR) T-Cell Therapy compared to Autologous and Allogenic Stem Cell Transplant
r. PROP 2210-168 Outcomes of patients with aggressive B-cell lymphomas after CD19 CAR T-cells that required bridging therapy prior to infusion
s. PROP 2210-171 CAR-T outcomes after prior CD19-directed therapy in large B-cell lymphoma
t. PROP 2210-174 A Comparison of HLA-matched Allogeneic versus CART for Diffuse Large B Cell Lymphoma
u. PROP 2210-177 Comparative outcomes of patients with B cell lymphomas treated with Lisocabtagene maraleucel (liso-cel) compared to Axicabtagene ciloleucel (axi-cel) and Tisagenlecleucel (tisa-cel)
v. PROP 2210-192 Autologous transplant following second line CAR T- cell therapy failure for Large B-cell lymphoma
w. PROP 2210-197 Comparative safety and efficacy of CD19-CAR T cell therapy for patients with transformed follicular lymphomas
x. PROP 2210-200 Compare outcomes of high-risk Mantle cell with Cellular therapy vs autologous vs allogeneic stem cell transplant.
y. PROP 2210-229 Outcomes of Relapsed-refractory Post-Transplant Lymphoproliferative Disorder after Cellular Therapies
z. PROP 2210-242 Outcomes of Mantle Cell Lymphoma (MCL) Beyond First Relapse with Chimeric Antigen Receptor (CAR) T-Cell Therapy compared to Autologous and Allogenic Stem Cell Transplant
aa. PROP 2210-260 Comparison of Autologous Stem Cell Transplant and CAR T-Cell Therapy for Relapsed Follicular Lymphoma
bb. PROP 2210-266 Allogeneic hematopoietic cell transplantation versus chimeric antigen receptor T-cell therapy for relapsed refractory mantle cell lymphoma.
cc. PROP 2210-278 Impact of immune checkpoint inhibitors on outcomes of autologous HCT for classical Hodgkin lymphoma
dd. PROP 2210-291 Impact of CAR-T and allogeneic transplant in Relapsed Mantle Cell Lymphoma: A Contemporary CIBMTR analysis

6. Ongoing study presentation

LY22-01a: Comparing CAR vs Auto-HCT in Aggressive B-cell lymphomas: Addressing questions unanswered by randomized trials (Mazyar Shadman/Mehdi Hamadani)

A G E N D A
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
Salt Lake City, UT
Saturday, April 23, 2022, 12:15-2:45 pm

Co-Chair:	**Alex Herrera, MD, City of Hope National Medical Center, Telephone: 626-256-4673; E-mail: aherrera@coh.org**
Co-Chair:	**Mohamed Kharfan-Dabaja, MD, MBA, Mayo Clinic, Jacksonville, FL; Telephone: 904-953-2000; E-mail: kharfandabaja.mohamed@mayo.edu**
Co-Chair:	**Craig Sauter, MD, Memorial Sloan Kettering Cancer Center, New York, NY; Telephone: 212-639-3460; E-mail: sauterc@mskcc.org**
Scientific Director:	**Mehdi Hamadani, MD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0700; E-mail: mhamadani@mcw.edu**
Statistical Director:	**Kwang Woo Ahn, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-456-7387; E-mail: kwooahn@mcw.edu**
Statistician:	**Manmeet Kaur, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-736-3467; E-mail: mkaur@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 Saturday, April 23, 2022 by Dr. Mehdi Hamadani. Dr. Craig Sauter introduced the working committee leadership, and highlighted leadership's conflict of interest disclosures per CIBMTR policy. Dr. Sauter emphasized the process of becoming a Working Committee member. Then outlined the Working Committee goals, expectations, limitations, and the voting guidelines. The guidelines are based on a scale from 1 to 9; 1=high scientific impact, 9=low scientific impact. In addition, emphasized the rules of 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. Then encouraged junior faculty, fellows, and assistant professors to collaborate actively with the Lymphoma Writing Committee. Dr. Sauter also detailed the LYWC study life cycle. Then Dr. Hamadani provided an update on the Working Committee productivity including 11 publications, 2 recent submissions, 1 presentation at the 2021 American Society of Clinical Oncology meeting, and 3 presentations at the 2022 EBMT meetings. Dr. Hamadani went over the three studies in progress and detailed the goals for these studies. Then indicated the availability of publicly available dataset for secondary analyses and explained the difference between the TED and CRF data collection forms. Dr. Hamadani finished the introduction slides by inviting the members to attend the Collaborative Study Proposal Session.

2. Accrual summary

Dr. Hamadani referenced the accrual tables with a slide, but it was not formally presented due to full agenda. The full accrual summary was available online as part of the LYWC materials.

3. Presentations, published or submitted papers

Dr. Mohamed Kharfan-Dabaja listed the presentations and publications during 2021, highlighting the great productivity of the LYWC, including the following studies published or presented:

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

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

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

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

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

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

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

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

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

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

4. Studies in progress

Dr. Mehdi Hamadani presented the studies in progress and gave an overview of the current standing of each study.

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

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

5. 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.

6. Future/proposed studies

Dr. Kharfan-Dabaja presented the first five proposed concepts. Dr. Herrera emphasized that first proposal is presenting its concept virtually and explained that Dr. Kharfan-Dabaja will be moderating the virtual component of the meeting. Finally encourage the virtual attendants to submit their questions on the chat.

a. **PROP 2109-07** Outcomes with autologous hematopoietic stem cell transplant in peripheral T-cell lymphoma (Aasems Jacob; Chaitanya Iragavarapu) (Attachment 4)

Dr. Aasems Jacob presented the concept virtually. The proposed study wants to look the outcomes with autologous hematopoietic stem cell transplant in peripheral T-cell lymphoma in cases with autologous hematopoietic transplant (ASCT) in mature T-cell non-Hodgkin lymphoma between 2010-2021. It will determine the factors determining outcome like age, comorbidities, different induction regimens, first CR vs. second or subsequent CR, type of peripheral T-cell lymphoma. A total of 2461 cases met the selection criteria for this study.

The proposal was opened for questions from the audience. A question was raised on the purpose of analyzing patients with auto-HCT consolidation in CR1 and why not allo-HCT and auto-HCT in CR1. In the past, 2 studies looked on allo-HCT and auto-HCT in CR1 but found cohorts as heterogenous. Another member from the audience asked on availability of how many

patients got novel agents to achieve the CR. Out of 3000, only 300 cases are on CRF track. Out of the 300 cases, we can know how many got BV and front line. A concern was raised as for those there is no comparison group for patients who got BV. Patients who got treated with BV-CHP and never got an auto-HCT is another limitation.

b. **PROP 2109-08** Bendamustine, etoposide, cytarabine, melphalan (BeEAM) vs. carmustine, etoposide, cytarabine, melphalan (BEAM) in relapsed B-cell lymphoma (Matthew Mei; Alex Herrera) (Attachment 5)
Dr. Alex Herrera presented the proposal on behalf of the study group. The proposed study hypothesizes that patients with relapsed B-cell lymphoma who undergo autologous stem cell transplant (ASCT) with bendamustine, etoposide, cytarabine, and melphalan (BeEAM) conditioning have superior progression-free survival (PFS) compared to patients who undergo ASCT with carmustine, etoposide, cytarabine, and melphalan (BEAM).
The study aims to estimate and compare the outcomes of patients with lymphoma who undergo ASCT with BeEAM vs. BEAM. For the purposes of the statistical analysis, the patients will be stratified by histology (Hodgkin lymphoma and non-Hodgkin lymphoma). A total of 3277 of adult patients who underwent ASCT for B cell lymphoma between 2017 – 2021 met the study selection criteria, only 69 cases received BeEAM compared to 3208 BEAM.
The proposal was opened for questions from the audience. A member of the audience asked about limitations on sample size. Another member from the audience commented that longer accrual time is needed to make fair comparison. A member asked the leadership about the possibility of combining this study with the EBMT data to overcome small samples size limitations. Lastly, a comment was raised on the available data on toxicities. Information is limited due to small number of CRF cases.

c. **PROP 2110-11** Chimeric Antigen Receptor T-cell Therapy versus Autologous Hemopoietic Cell Transplantation for Relapsed Myc-Rearranged DLBCL in Partial or Complete Remission (Joanna Zurko; Mehdi Hamadani) (Attachment 6)
Dr. Joanna Zurko presented the concept to the audience. This study hypothesizes that in patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) with myc-rearrangement or high grade b-cell lymphoma with myc and bcl2 and/or bcl6 rearrangements (double hit lymphoma [DHL]/triple hit lymphoma [THL]) who achieve a complete response (CR) or partial response (PR) with salvage therapy, anti-CD19 chimeric antigen receptor T-cell therapy may lead to equivalent or improved outcomes compared to autologous hematopoietic cell transplantation (auto-HCT). A total of 395 R/R DLBCL with myc rearrangement or high-grade b-cell lymphoma with myc and bcl2 and/or bcl6 rearrangements received auto-HCT (n=272) from 2015 to 2021 or CAR T-cell therapy (n=123) from 2017 to 2021 met the criteria for this study.
The floor was open for questions. A member of the audience had a question concerning a possible overlap with a study from Cellular immunotherapy committee looking at aggressive biology of double-hit and triple-hit lymphomas. Leadership clarified that it is not an overlap with the study mentioned as it will not be a comparison of CAR-T and auto-HCT. Another member commented on insurance approval on dependance of disease status, the numbers are reverse in 2 groups: We will need to stratify to address this. A possible fix for this could be excluding patients who got 1 line of therapy because these are probably double hits who got transplanted in CR1. A question was raised on possible overlap groups in CAR-T group are ones who has prior failed auto-HCT. There would be no overlapping as patients receiving prior auto or CAR-T will be excluded. Comments on disease status were and timing differences from HCT to CAR-T treatment were raised. An additional comment was made pointing out a possible bias stating

that all partial remission (PRs) patients are not same because good PRs are treated with auto and bad PRs with CAR-T. Possible solution would be controlling this based on number of largest lymph nodes that is present at time of CAR-T or cell therapy administration but there is no good or bad (PR) patients.

d. **PROP 2110-131** Autologous Hematopoietic Stem Cell Transplantation for Intravascular Large B-cell Lymphoma (IVLBCL): a CIBMTR registry analysis (Praveen Ramakrishnan Geethakumari; Farrukh T. Awan) (Attachment 7)
Dr. Praveen Geethakumari presented the proposal to the audience. This study hypothesizes that consolidative high dose chemotherapy and autologous stem cell transplantation (SCT) for patients with intravascular large B-cell lymphoma (IVLBCL) improves overall (OS) and progression-free (PFS) survival, compared to chemoimmunotherapy alone. A total of 38 of patients with intravascular large B-cell lymphoma received auto-HCT during 2000-2020, only 9 cases have CRF level data.
The proposal was open for questions from the audience. First question from the audience asked about availability of data regarding the number of lines of therapy, CR1 or subsequent responses. Data is available for CRF patients. A member commented on the importance of this proposal since this disease is usually under-reported or under-diagnosed and we need to learn more about it, but challenge will be number of cases. Lastly, a member suggested could be collaborative multi-center retrospective review to obtain more details about these cases.

e. **PROP 2110-190** Impact of pre-leukapheresis bendamustine-containing therapies on outcomes of CD19 CAR T-cell therapy for large B-cell lymphoma (Jordan Gauthier) (Attachment 8)
Dr. Jordan Gauthier presented the concept virtually. This study hypothesizes that bendamustine-containing regimens administered prior to leukapheresis are associated with worse outcomes after CD19 CAR T-cell therapy for R/R LBCL compared to alternative regimens. The main objective of the study is to evaluate the complete response rate (at time of best response). Secondaries objectives: look to evaluate the overall response rate (at time of best response), duration of response after CD19 CAR T-cell therapy, - Progression-free and overall survival after CD19 CAR T-cell therapy and estimate the CRS incidence and ICANS incidence and their severity. A total of 2989 adult patients with large B-cell lymphoma received CD19 CAR T-cell therapy during 2017-2021. 766 patients received a bridging therapy before the infusion.
The floor was open for questions. A member of the audience asked if we could delineate if Bendamustine was given before or after apheresis during bridging. Leadership assured it is possible to determine. Another asked if could query sites to add pre-leukapheresis CBC, it was shown to be important in recent publications. A member suggested to adjust for Bendamustine, or any chemotherapy use that could be lymphodepleting. Data is limited for this purpose, but it was suggested by the committee leadership that this is a good study to collaborate with industry and collection of this manufacturing. Another member asked how many have both Bendamustine and Pola or Bendamustine alone? Leadership confirmed that this can be figured out from the forms. Lastly, a member suggested addition of other subtypes ie. Indolent, Mantle cell lymphoma. Concerns of introducing too many diseases, will need more variables to adjust.

Dr. Alex Herrera presented the last five concepts.

f. **PROP 2110-223** Risk of therapy-related myeloid neoplasm (t-MN) following autologous hematopoietic cell transplantation (auto-HCT) for relapsed and refractory diffuse large B-cell lymphoma (DLBCL): A comparison of platinum-containing salvage regimens (Mariam Nawas; Michael Scordo) (Attachment 9)

Dr. Mariam Nawas presented the proposal on behalf of the study group. The study hypothesizes that t-MN rates after auto-HCT with BCNU, etoposide, Ara-C, and melphalan (BEAM) conditioning in patients with relapsed or refractory DLBCL are higher in patients who received ifosfamide/carboplatin/etoposide (ICE) salvage therapy compared to other platinum-containing salvage regimens. The study aims to compare the incidences of t-MN after auto-HCT with BEAM conditioning in patients receiving platinum-based salvage regimens for relapsed or refractory DLBCL. Also compare the differences in non-relapse mortality (NRM) and causes of death. A total of 1262 adult patients with R/R DLBCL received auto-HCT with CRF level information met the study criteria.

The proposal was open for questions from the audience. A member from the audience asked about on hypothesis on why a particular part in regimen would be more likely to cause myeloneoplasia. There is a dataset where they investigated solid tumors and different platinum-based chemotherapy and only carboplatin platinum-based therapy was associated with clonal hematopoiesis. Even more broadly in solid tumors, carbo platinum therapy is more closely associated with t-MN. A concern was raised on the data categorized as unknown for TED cases and suggested using CRF only cases. A member commented that some of regimens given for lymphoid malignancies can be associated with secondary malignancies especially lenalidomide and ask on how you will be looking onto those cases? It was suggested to look into cases with 2 lines of therapy and investigate patients. Another member presented a concern about the downside for removing patients having more lines of therapy and restricting to more homogenous population. Lastly, a question was raised on whether this study will exclude patients who transformed from a low grade. The study will be excluding these patients.

g. **PROP 2110-16/ 2110-83/2110-117/2110-57** Impact of Prior Therapies on Outcomes in Relapsed/Refractory Mantle Cell Lymphoma Patients treated with Brexucabtagene autoleucel. (Mazyar Shadman; Mehdi Hamadani; Nausheen Ahmed; Swetha Kambhampati; Alex Herrera; Natalie Grover) (Attachment 10)

Dr. Mayzar Shadman presented the proposal to the audience. This study hypothesizes that CD-19 CAR-T efficacy is independent of the number and type of prior therapies, including BTK exposure. The study aims to compare outcomes (ORR, CR, OS, PFS, and relapse rate) in patients who received CAR-T therapy after prior BTK inhibitor vs. no prior. Also compare outcomes in patients who received CAR-T therapy after 1 vs.2 vs. 3-4 vs. >4 lines of prior therapy; a prior autologous stem cell transplant (ASCT) vs. no prior transplant. Lastly to compare outcomes of relapse within 24 months of finishing induction (POD24) treatment vs. others. A total of 260 patients met the criteria for the study.

The floor was opened for questions. A member on the audience asked why CD-19 CAR-T efficacy is independent of prior therapy? The presenter mentioned that to be dependent on prior therapy, we may be using data for current BTK-inhibitors and CAR-T, and inhibitors are given concurrently during treatment and even after CAR-T. A concern was raised with BTK-inhibitors data collected at CIBMTR. The concern is that data is not captured for all the new BTK-inhibitors and sometimes they are not captured in the data collection. Another concern raised was that there is only 350 cases in total for mantle cell-lymphoma and if restricted to BTK-inhibitors it will reduce to 20% of the cohort. A member commented that BTK-inhibitors are a broadly used term but there are only 3 that are approved currently, so there could be data which might be used as to study different impact of each. This was well received but data is available but very limited. Lastly a member asked if this study could look at the comparison of first-generation vs second-generation BTK-inhibitors. The leadership expressed that numbers would need to be assessed first.

h. **PROP 2110-98/ 2110-181/2110-22/2110-85/2110-116** CART Outcomes in rare subtypes of aggressive B-cell lym (Priyanka Pophali; Shwetha Kambhampati; Joshua Fein; Narendranath Epperla; Mazyar Shadman; Jordan Gauthier; Kalyan Nadiminti; Roni Shouval; Mehdi Hamadani; Alex Herrera) (Attachment 11)
Dr. Priyanka Pophali presented the proposal on behalf of the groups. The study hypothesize that CART-related outcomes differ among the rare subtypes of aggressive B-cell lymphomas (THRLBCL, PMBCL, HGBCL, transformed iNHL, Richter transformation of CLL). The primary aim of the study is to compare overall survival of relapsed/refractory rare subtypes of aggressive B-cell lymphomas (THRLBCL, PMBCL, HGBCL, transformed iNHL, Richter transformation of CLL) treated with CAR. The secondary outcomes aim to compare NRM, PFS, relapse/progression, response rates, rates of CRS and ICAND, engraftment and cause of death. A total of 1242 patients who underwent CAT-T therapy for rare subtypes between 2017 – 2021, majority of patients being HGBCL.
The proposal was open for input. A member of the audience asked about a possible overlap with a previous study was performed 2 years back looking over some of the same diseases mentioned in the proposal. Leadership clarified that study referenced, is still ongoing. This study is different since it is looking over effective factors for duration of response and include some of the diseases from this proposal. There is some overlap in patients but the analysis among sub-groups is different in both studies.

i. **PROP 2109-26/2110-94/2110-275** Impact of CD19 directed CAR T-cell therapy on outcomes for primary and secondary central nervous system B-cell lymphomas (Narendranath Epperla; Santiago Mercadal; Hamza Hashmi; Catherine Joy Lee; Mehdi Hamadani; Sairah Ahmed) (Attachment 12)
Dr. Ahmed Sairah presented the proposal on behalf of the group. The study hypothesizes that CAR-T cell therapy is safe and efficacious in patients with primary CNSL (PCNSL) and secondary CNSL (SCNSL). The primary aim of the study is to evaluate overall in patients with primary CNSL (PCNSL) and secondary CNSL (SCNSL). The secondary outcomes aim to compare NRM, PFS, relapse/progression, response rates, rates of CRS and ICANS, engraftment and cause of death. A total of 143 adult patients who underwent CAT-T therapy for SCNSL between 2017 – 2021 met the criteria of the study.
The proposal was opened for input from the audience. A member asked if due to low number of PCNSL patients and considering retrospective references, will there by consideration for submitting those cases? Question was well received, as it will give information about these cases. A member asked how many patients have prior-auto or allo as one of inclusion criteria? There are 96 cases with no prior HCT, 2 cases with prior allo-HCT, 41 cases with prior auto-HCT, and 4 with no reported data. Two-thirds of data have no prior HCT. A comment was made on the availability of Breyanzi treated cases. There is only 1 patient right now for Breyanzi but by the time of analysis, there could be more addition of cases for Breyanzi leading to increase in total population. Lastly a member asked which product for CAR-T is used most among these patients? Majority of these are Yescarta (56%).

j. **PROP 2110-82/2110-90** Outcome of patients with large cell lymphoma receiving ASCT vs. CAR-T therapy while in complete remission. (Mehdi Hamadani; Mazyar Shadman; Antonio Jimenez; Trent Wang) (Attachment 13)

The study hypothesizes that patients with large cell lymphoma who are in complete remission (CR) after salvage therapy, ASCT provides superior clinical outcomes. The primary aim of the study is to OS, PFS and relapse rate and NRM in patients who received ASCT vs. CAR-T therapy while in a CR. The secondary objective is to compare cause of death. A total of 218 patients with large cell lymphoma receiving ASCT vs. 111 CAR-T therapies while in complete remission met the criteria of this study.

The proposal was opened for questions. First question asked if this proposal could be merged with previous proposal presented, which is looking at CR vs PR, auto vs CAR-T in MYC? The leadership considered that there is no major overlap as other proposal is focusing in MYC and this will be a different population. Another member asked, how do we account for patients in this analysis who were refractory to first line of therapy and come into CR after platinum-based second line of therapy as this CR would be different from true CR? Time from diagnosis to treatment could be used as a proxy in the analysis in combination with other variables as well. Another suggestion made was to look stable disease, progression, and R-CHOP regimens as done in Dr. Susan Ball's study.

Proposed studies; not accepted for consideration at this time

Dr. Hamadani thanked all the investigators who submitted their concepts but where not accepted from presentation.

a. **PROP 2109-10** Characteristics and Outcomes of Adolescents and Young Adults with Relapsed/Refractory Non-Hodgkin Lymphoma Undergoing First Autologous Hematopoietic Stem Cell Transplant.
b. **PROP 2109-21** Outcomes of Autologous vs Allogeneic Stem Transplant after first line or second line therapy for patients with Double Hit and Triple Hit DLBCL.
c. **PROP 2110-15** Impact of early versus late relapse pre–Chimeric Antigen Receptor (CAR) T-Cell therapy on clinical outcomes of CAR-T cell therapy for Diffuse Large B-Cell Lymphoma (DLBCL)
d. **PROP 2110-17** Effect of Time to Relapse on Overall Survival in Diffuse large B cell lymphoma (DLBCL) patients following CD19-Chimeric antigen receptor T cell (CART) therapy.
e. **PROP 2110-127** Outcomes of Salvage Autologous Transplant in Double Hit DLBCL.
f. **PROP 2110-133** Outcomes of relapsed/refractory post-transplant lymphoproliferative disorders-diffuse large B cell lymphoma (PTLD-DLBCL) treated with hematopoietic stem cell transplant (HSCT) or chimeric antigen T cell (CART) therapy.
g. **PROP 2110-134** Search of optimal conditioning regimen for autologous stem cell transplant (ASCT) for treatment of relapsed and refractory lymphoma – A comparison of BEAM vs. BUCYVP16 using CIBMTR database.
h. **PROP 2110-136** Outcomes of relapsed/refractory post-transplant lymphoproliferative disorders-diffuse large B cell lymphoma (PTLD-DLBCL) treated with hematopoietic stem cell transplant (HSCT) or chimeric antigen T cell (CART) therapy.
i. **PROP 2110-144** Outcomes of Autologous Stem Cell Transplantation for Early Versus Late Relapsing Nodular Lymphocyte-Predominant Hodgkin Lymphoma.
j. **PROP 2110-152** Outcomes of HIV+ Lymphoma treated with Chimeric Antigen Receptor T-Cell Therapy.
k. **PROP 2110-156** Evaluating outcomes of Hematopoietic Cell Transplantation in Hepatosplenic T Cell Lymphoma.
l. **PROP 2110-159** Trend in survival in Lymphoma (NHL/HL) Patients post-autologous SCT.
m. **PROP 2110-161** Efficacy and Safety of CAR T-cells in patients with Relapsed/Refractory Post-Transplant Lymphoproliferative Disease.

n. **PROP 2110-166** Outcome of allogeneic hematopoietic stem cell transplant for refractory cutaneous T-cell lymphoma.
o. **PROP 2110-171** Outcomes of CAR T-cell therapy for Diffuse Large B cell Lymphoma patients with HIV or viral hepatitis.
p. **PROP 2110-172** Hematopoietic Stem Cell Transplantation for Mature T- and NK-cell Malignancies in Children, Adolescents, and Young Adults.
q. **PROP 2110-187** Autologous stem cell transplantation for diffuse large B cell lymphoma: impact of CD19 CAR T-cell therapy approvals on patient characteristics and outcomes.
r. **PROP 2110-197** Real world practice pattern and clinical outcomes of subsequent therapy after CAR-T treatment in patients with lymphoma.
s. **PROP 2110-209** Autologous Hematopoietic Stem Cell Transplantation for Intravascular Large B-Cell Lymphoma (IVLBCL): A CIBMTR Registry Analysis.
t. **PROP 2110-219** Outcomes of Large B-cell lymphoma Progressing following CAR T-cell therapy.
u. **PROP 2110-225** Clinical outcomes of chimeric antigen receptor T cell therapy after allogeneic stem cell transplant in patients with relapsed/refractory aggressive B-cell lymphoma.
v. **PROP 2110-232** Clinical outcomes of allogeneic and autologous stem cell transplant after anti-CD19 chimeric antigen receptor T cell therapy in patients with relapsed/refractory aggressive B-cell lymphoma.
w. **PROP 2110-264** Clinical Impact of first-line therapy after CAR T cell failure.
x. **PROP 2110-269** Does access to CAR improves outcomes in DLBCL? The Phase 3 trial that will not be done.
y. **PROP 2110-270** Impact of Tumor Biology on Outcomes in Chimeric Antigen Receptor T-cell Therapies and Autologous Stem Cell Transplant in Diffuse Large B-cell Lymphoma.
z. **PROP 2110-277** Analysis of the outcomes of autologous stem cell transplant in peripheral T-cell lymphomas treated with brentuximab vedotin.
aa. **PROP 2110-286** Pre CAR-T Splenic and Extra nodal Disease to predict Relapse pattern post-CAR-T Therapy for Relapsed/Refractory Lymphoma.
bb. **PROP 2110-290** CAR-T versus allogeneic transplant in Mantle Cell Lymphoma: A Real world CIBMTR analysis.
cc. **PROP 2110-291** Comparison between outcomes of CAR-T cell therapy versus allo-HCT in R/R Mantle cell lymphoma.
dd. **PROP 2110-296** Efficacy and Safety of Allogeneic transplant after CAR T-cell therapy in patients with Relapsed/Refractory Diffuse Large B-cell Lymphoma.
ee. **PROP 2110-36** Outcomes of autologous and allogeneic hematopoietic cell transplantation for secondary central nervous system lymphoma.
ff. **PROP 2110-46** Outcomes of allo-HCT for patients with lymphoid B cell malignancies who received treatment with bispecific antibodies.
gg. **PROP 2110-47** Autologous versus Allogeneic Stem Cell Transplantation for B cell lymphomas patients who failed anti-CD19 CART as first or second-line of therapy.
hh. **PROP 2110-56** Impact of Bridging Therapy on Outcomes of Diffuse Large B-cell Lymphoma Patients Undergoing Chimeric Antigen Receptor T-cell Therapy.
ii. **PROP 2110-73** Outcomes of Allogeneic Hematopoietic Stem Cell Transplantation in Relapsed/Refractory Aggressive B-Cell Lymphoma with Central Nervous System Involvement: a CIBMTR Analysis.
jj. **PROP 2110-96** Effect of time to relapse on survival in classical Hodgkin lymphoma patients undergoing autologous hematopoietic cell transplantation.
kk. **PROP 2110-302** Toxicities and outcomes after Chimeric Antigen Receptor (CAR) T-Cell therapy in Mantle cell Lymphoma (MCL).

ll. **PROP 2110-316** Allo-HCT versus CAR T therapy in relapsed mantle cell lymphoma.

mm. **PROP 2110-327** Outcomes of autologous HCT for diffuse large B-cell lymphoma by cell of origin and disease status.

7. Other Business

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 until May 2. Without additional comments, the meeting was adjourned at 2:05 pm.

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2022						
	HLA-Identical Sibling		Alternative Donor		Autologous	
	TED only	Research	TED only	Research	TED only	Research
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Anaplastic large cell	328	59	466	174	2004	204
PIF	43 (13)	9 (15)	55 (12)	25 (14)	198 (10)	16 (8)
CR1	47 (14)	10 (17)	68 (15)	26 (15)	861 (43)	83 (41)
Rel 1	33 (10)	9 (15)	34 (7)	11 (6)	174 (9)	24 (12)
CR2	93 (28)	17 (29)	145 (31)	48 (28)	469 (23)	50 (25)
Other/Unknown	112 (34)	14 (24)	164 (35)	64 (37)	302 (15)	31 (15)
Burkitt/small non-cleaved	176	57	112	105	584	143
PIF	23 (13)	8 (14)	10 (9)	19 (18)	63 (11)	25 (17)
CR1	35 (20)	14 (25)	21 (19)	17 (16)	199 (34)	55 (38)
Rel 1	26 (15)	7 (12)	11 (10)	16 (15)	50 (9)	14 (10)
CR2	43 (24)	21 (37)	42 (38)	36 (34)	149 (26)	38 (27)
Other/Unknown	49 (28)	7 (12)	28 (25)	17 (16)	123 (21)	11 (8)
Diffuse large cell/immunoblastic	1855	345	1958	895	21818	2634
PIF	332 (18)	83 (24)	332 (17)	221 (25)	2659 (12)	341 (13)
CR1	191 (10)	54 (16)	250 (13)	100 (11)	3935 (18)	497 (19)
Rel 1	285 (15)	47 (14)	202 (10)	94 (11)	3720 (17)	479 (18)
CR2	257 (14)	33 (10)	341 (17)	119 (13)	6293 (29)	763 (29)
Other/Unknown	790 (43)	128 (37)	833 (43)	361 (40)	5211 (24)	554 (21)
Follicular	1492	535	1326	733	5173	925
PIF	167 (11)	73 (14)	135 (10)	114 (16)	521 (10)	74 (8)
CR1	108 (7)	39 (7)	95 (7)	43 (6)	599 (12)	114 (12)
Rel 1	202 (14)	107 (20)	151 (11)	108 (15)	916 (18)	170 (18)
CR2	188 (13)	77 (14)	178 (13)	85 (12)	1317 (25)	219 (24)
Other/Unknown	827 (55)	239 (45)	767 (58)	383 (52)	1820 (35)	348 (38)
Lymphoblastic	172	49	125	106	266	35
PIF	18 (10)	7 (14)	8 (6)	12 (11)	14 (5)	1 (3)
CR1	50 (29)	11 (22)	21 (17)	18 (17)	118 (44)	19 (54)
Rel 1	28 (16)	8 (16)	10 (8)	16 (15)	23 (9)	1 (3)
CR2	32 (19)	12 (24)	35 (28)	34 (32)	32 (12)	6 (17)
Other/Unknown	44 (26)	11 (22)	51 (41)	26 (25)	79 (30)	8 (23)

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2022						
Mantle	950	210	1151	490	9199	973
PIF	127 (13)	39 (19)	109 (9)	76 (16)	793 (9)	84 (9)
CR1	185 (19)	40 (19)	199 (17)	81 (17)	6394 (70)	667 (69)
Rel 1	145 (15)	36 (17)	165 (14)	86 (18)	253 (3)	32 (3)
CR2	185 (19)	33 (16)	340 (30)	107 (22)	466 (5)	60 (6)
Other/Unknown	308 (32)	62 (30)	338 (29)	140 (29)	1293 (14)	130 (13)
Marginal	95	27	106	39	392	43
PIF	13 (14)	8 (30)	16 (15)	9 (23)	41 (10)	9 (21)
CR1	9 (9)	3 (11)	17 (16)	5 (13)	69 (18)	4 (9)
Rel 1	10 (11)	1 (4)	13 (12)	6 (15)	52 (13)	3 (7)
CR2	13 (14)	3 (11)	9 (8)	4 (10)	81 (21)	10 (23)
Other/Unknown	50 (53)	12 (44)	51 (48)	15 (38)	149 (38)	17 (40)
NK T cell	275	53	375	122	802	82
PIF	41 (15)	7 (13)	72 (19)	22 (18)	103 (13)	14 (17)
CR1	73 (27)	14 (26)	115 (31)	46 (38)	352 (44)	37 (45)
Rel 1	25 (9)	6 (11)	22 (6)	8 (7)	57 (7)	5 (6)
CR2	53 (19)	5 (9)	77 (21)	28 (23)	127 (16)	13 (16)
Other/Unknown	83 (30)	21 (40)	89 (24)	18 (15)	163 (20)	13 (16)
T cell	993	245	1465	597	3930	442
PIF	236 (24)	78 (32)	354 (24)	208 (35)	447 (11)	53 (12)
CR1	195 (20)	49 (20)	314 (21)	115 (19)	2256 (57)	232 (52)
Rel 1	117 (12)	24 (10)	154 (11)	63 (11)	273 (7)	44 (10)
CR2	149 (15)	32 (13)	272 (19)	70 (12)	401 (10)	52 (12)
Other/Unknown	296 (30)	62 (25)	371 (25)	141 (24)	553 (14)	61 (14)
NHL not specified	180	24	102	120	857	44
PIF	15 (8)	4 (17)	7 (7)	31 (26)	92 (11)	8 (18)
CR1	13 (7)	0 (0)	5 (5)	13 (11)	107 (12)	11 (25)
Rel 1	28 (16)	2 (8)	7 (7)	18 (15)	63 (7)	5 (11)
CR2	15 (8)	2 (8)	18 (18)	19 (16)	111 (13)	5 (11)
Other/Unknown	109 (61)	16 (67)	65 (64)	39 (33)	484 (56)	15 (34)
Other	728	192	1081	388	8942	957
PIF	152 (21)	52 (27)	260 (24)	94 (24)	1481 (17)	163 (17)
CR1	146 (20)	33 (17)	259 (24)	100 (26)	2874 (32)	336 (35)
Rel 1	69 (9)	18 (9)	90 (8)	34 (9)	1075 (12)	96 (10)
CR2	98 (13)	15 (8)	192 (18)	51 (13)	2461 (28)	219 (23)

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2022						
Other/Unknown	263 (36)	74 (39)	280 (26)	109 (28)	1051 (12)	143 (15)
Hodgkin	1396	339	1690	1124	19540	2372
PIF	210 (15)	55 (16)	219 (13)	178 (16)	2695 (14)	429 (18)
CR1	75 (5)	24 (7)	119 (7)	91 (8)	2454 (13)	307 (13)
Rel 1	165 (12)	54 (16)	186 (11)	136 (12)	3559 (18)	445 (19)
CR2	151 (11)	51 (15)	229 (14)	156 (14)	6172 (32)	709 (30)
Other/Unknown	795 (57)	155 (46)	937 (55)	563 (50)	4660 (24)	482 (20)
Graft type	8640	2135	9957	4893	73507	8854
BM	873 (10)	189 (9)	1672 (17)	1037 (21)	711 (1)	74 (1)
PB	7704 (89)	1938 (91)	7697 (77)	3198 (65)	72049 (98)	8721 (98)
Other/Unknown	63 (1)	8 (0)	588 (6)	658 (13)	747 (1)	59 (1)

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

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
Number of patients	5158	1619	1116
Source of data			
CRF	2571 (50)	610 (38)	449 (40)
TED	2587 (50)	1009 (62)	667 (60)
Number of centers	204	156	211
Disease at transplant			
Non-Hodgkin lymphoma	4211 (82)	1361 (84)	904 (81)
Hodgkin lymphoma	947 (18)	258 (16)	212 (19)
NHL Disease status at transplant			
CR1	598 (14)	262 (19)	125 (14)
CR2	781 (19)	259 (19)	145 (16)
CR3+	365 (9)	114 (8)	80 (9)
PR	448 (11)	112 (8)	95 (11)
Advanced	1928 (46)	588 (43)	424 (47)
Missing	71 (2)	18 (1)	32 (4)
Recipient age at transplant			
0-9 years	58 (1)	11 (1)	17 (2)
10-17 years	153 (3)	37 (2)	31 (3)

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
18-29 years	704 (14)	186 (11)	145 (13)
30-39 years	726 (14)	219 (14)	158 (14)
40-49 years	975 (19)	280 (17)	230 (21)
50-59 years	1408 (27)	429 (26)	276 (25)
60-69 years	1039 (20)	393 (24)	240 (22)
70+ years	95 (2)	64 (4)	19 (2)
Median (Range)	50 (2-79)	52 (3-78)	49 (2-77)
Recipient race/ethnicity			
White, Non-Hispanic	4423 (86)	1341 (83)	827 (74)
Black or African American, Non-Hispanic	239 (5)	77 (5)	50 (4)
Asian, Non-Hispanic	89 (2)	43 (3)	36 (3)
Native Hawaiian or Pacific Islander, Non-Hispanic	4 (<1)	2 (<1)	0
American Indian or Alaska Native, Non-Hispanic	5 (<1)	8 (<1)	2 (<1)
Hispanic	281 (5)	101 (6)	60 (5)
Missing	117 (2)	47 (3)	141 (13)
Recipient sex			
Male	3235 (63)	1055 (65)	722 (65)
Female	1923 (37)	564 (35)	394 (35)
Karnofsky score			
10-80	1765 (34)	601 (37)	375 (34)
90-100	3133 (61)	934 (58)	690 (62)
Missing	260 (5)	84 (5)	51 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	4 (<1)	6 (<1)	0
4/6	10 (<1)	9 (1)	5 (<1)
5/6	615 (12)	153 (11)	123 (12)
6/6	4378 (87)	1223 (88)	912 (88)
Unknown	151 (N/A)	228 (N/A)	76 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	46 (1)	12 (1)	3 (<1)
6/8	123 (3)	15 (1)	19 (2)
7/8	959 (20)	186 (16)	177 (22)
8/8	3680 (77)	945 (82)	610 (75)
Unknown	350 (N/A)	461 (N/A)	307 (N/A)
HLA-DPB1 Match			
Double allele mismatch	807 (28)	99 (21)	82 (25)
Single allele mismatch	1626 (57)	239 (51)	185 (55)
Full allele matched	442 (15)	134 (28)	67 (20)
Unknown	2283 (N/A)	1147 (N/A)	782 (N/A)
High resolution release score			
No	2538 (49)	1615 (>99)	1090 (98)
Yes	2620 (51)	4 (<1)	26 (2)

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
KIR typing available			
No	4376 (85)	1617 (>99)	1114 (>99)
Yes	782 (15)	2 (<1)	2 (<1)
Graft type			
Marrow	1055 (20)	279 (17)	234 (21)
PBSC	4101 (80)	1321 (82)	880 (79)
PBSC+UCB	2 (<1)	19 (1)	1 (<1)
Others	0	0	1 (<1)
Conditioning regimen			
Myeloablative	2024 (39)	522 (32)	362 (32)
RIC/Nonmyeloablative	3094 (60)	1085 (67)	741 (66)
TBD	40 (1)	12 (1)	13 (1)
Donor age at donation			
To Be Determined/NA	107 (2)	314 (19)	50 (4)
0-9 years	1 (<1)	0	0
18-29 years	2407 (47)	692 (43)	486 (44)
30-39 years	1455 (28)	354 (22)	315 (28)
40-49 years	929 (18)	199 (12)	199 (18)
50+ years	259 (5)	60 (4)	66 (6)
Median (Range)	31 (0-69)	29 (18-68)	31 (18-61)
Donor/Recipient CMV serostatus			
+/+	1087 (21)	318 (20)	221 (20)
+/-	564 (11)	188 (12)	143 (13)
-/+	1473 (29)	351 (22)	279 (25)
-/-	1714 (33)	435 (27)	337 (30)
CB - recipient +	2 (<1)	13 (1)	1 (<1)
CB - recipient -	0	6 (<1)	0
Missing	318 (6)	308 (19)	135 (12)
GvHD Prophylaxis			
No GVHD prophylaxis	18 (<1)	5 (<1)	4 (<1)
Ex vivo T-cell depletion	55 (1)	10 (1)	14 (1)
CD34 selection	53 (1)	14 (1)	5 (<1)
Post-CY + other(s)	258 (5)	190 (12)	89 (8)
Post-CY alone	5 (<1)	5 (<1)	6 (1)
Tacrolimus + MMF +- others	839 (16)	219 (14)	163 (15)
Tacrolimus + MTX +- others (except MMF)	2251 (44)	732 (45)	366 (33)
Tacrolimus + others (except MTX, MMF)	316 (6)	126 (8)	80 (7)
Tacrolimus alone	170 (3)	54 (3)	23 (2)
CSA + MMF +- others (except Tacrolimus)	548 (11)	112 (7)	119 (11)
CSA + MTX +- others (except Tacrolimus, MMF)	412 (8)	96 (6)	154 (14)
CSA + others (except Tacrolimus, MTX, MMF)	74 (1)	18 (1)	25 (2)
CSA alone	52 (1)	8 (<1)	36 (3)

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
Other GVHD prophylaxis	78 (2)	21 (1)	16 (1)
Missing	29 (1)	9 (1)	16 (1)
Donor/Recipient sex match			
Male-Male	2308 (45)	674 (42)	480 (43)
Male-Female	1187 (23)	308 (19)	211 (19)
Female-Male	871 (17)	287 (18)	216 (19)
Female-Female	693 (13)	192 (12)	164 (15)
CB - recipient M	0	10 (1)	0
CB - recipient F	2 (<1)	9 (1)	1 (<1)
Missing	97 (2)	139 (9)	44 (4)
Year of transplant			
1986-1990	3 (<1)	1 (<1)	1 (<1)
1991-1995	47 (1)	12 (1)	15 (1)
1996-2000	255 (5)	62 (4)	54 (5)
2001-2005	820 (16)	156 (10)	202 (18)
2006-2010	1433 (28)	257 (16)	228 (20)
2011-2015	1633 (32)	433 (27)	298 (27)
2016-2020	790 (15)	499 (31)	241 (22)
2021-2022	177 (3)	199 (12)	77 (7)
Follow-up among survivors, Months			
N Eval	2033	785	490
Median (Range)	73 (0-315)	37 (0-291)	44 (0-296)

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

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
Number of patients	506	125	170
Source of data			
CRF	387 (76)	88 (70)	94 (55)
TED	119 (24)	37 (30)	76 (45)
Number of centers	90	39	66
Disease at transplant			
NHL	403 (80)	98 (78)	134 (79)
Hodgkins Lymphoma	103 (20)	27 (22)	36 (21)
NHL Disease status at transplant			
CR1	63 (16)	9 (9)	25 (19)
CR2	75 (19)	22 (22)	35 (26)
CR3+	45 (11)	11 (11)	12 (9)
PR	68 (17)	12 (12)	16 (12)
Advanced	149 (37)	43 (44)	42 (32)
Missing	0	1 (1)	3 (2)
Recipient age at transplant			
0-9 years	23 (5)	5 (4)	3 (2)
10-17 years	27 (5)	3 (2)	12 (7)
18-29 years	76 (15)	17 (14)	25 (15)
30-39 years	90 (18)	18 (14)	31 (18)
40-49 years	91 (18)	35 (28)	32 (19)
50-59 years	121 (24)	20 (16)	40 (24)
60-69 years	73 (14)	25 (20)	25 (15)
70+ years	5 (1)	2 (2)	2 (1)
Median (Range)	45 (1-73)	46 (5-78)	44 (7-73)
Recipient race/ethnicity			
White, Non-Hispanic	289 (57)	78 (62)	87 (51)
Black or African American, Non-Hispanic	95 (19)	25 (20)	25 (15)
Asian, Non-Hispanic	35 (7)	7 (6)	10 (6)
Native Hawaiian or Pacific Islander, Non-Hispanic	1 (<1)	0	1 (1)
American Indian or Alaska Native, Non-Hispanic	6 (1)	0	0
Hispanic	67 (13)	13 (10)	22 (13)
Missing	13 (3)	2 (2)	25 (15)
Recipient sex			
Male	297 (59)	74 (59)	95 (56)
Female	209 (41)	51 (41)	75 (44)
Karnofsky score			

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
10-80	146 (29)	36 (29)	38 (22)
90-100	337 (67)	82 (66)	125 (74)
Missing	23 (5)	7 (6)	7 (4)
HLA-A B DRB1 groups - low resolution			
<=3/6	17 (3)	6 (6)	2 (1)
4/6	241 (49)	50 (50)	85 (54)
5/6	198 (41)	37 (37)	62 (40)
6/6	32 (7)	8 (8)	7 (4)
Unknown	18 (N/A)	24 (N/A)	14 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	266 (63)	54 (71)	91 (71)
6/8	104 (25)	11 (14)	26 (20)
7/8	36 (9)	9 (12)	8 (6)
8/8	14 (3)	2 (3)	4 (3)
Unknown	86 (N/A)	49 (N/A)	41 (N/A)
HLA-DPB1 Match			
Double allele mismatch	57 (42)	5 (50)	12 (43)
Single allele mismatch	74 (54)	5 (50)	16 (57)
Full allele matched	6 (4)	0	0
Unknown	369 (N/A)	115 (N/A)	142 (N/A)
High resolution release score			
No	422 (83)	122 (98)	169 (99)
Yes	84 (17)	3 (2)	1 (1)
KIR typing available			
No	429 (85)	125 (100)	169 (99)
Yes	77 (15)	0	1 (1)
Graft type			
UCB	460 (91)	106 (85)	162 (95)
PBSC+UCB	44 (9)	19 (15)	6 (4)
Others	2 (<1)	0	2 (1)
Number of cord units			
1	398 (79)	0	112 (66)
2	108 (21)	0	58 (34)
Unknown	0 (N/A)	125 (N/A)	0 (N/A)
Conditioning regimen			
Myeloablative	207 (41)	50 (40)	58 (34)
RIC/Nonmyeloablative	299 (59)	74 (59)	110 (65)
TBD	0	1 (1)	2 (1)
Donor age at donation			
To Be Determined/NA	366 (72)	37 (30)	132 (78)
0-9 years	100 (20)	69 (55)	33 (19)
10-17 years	4 (1)	4 (3)	3 (2)
18-29 years	11 (2)	4 (3)	0

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
30-39 years	8 (2)	2 (2)	1 (1)
40-49 years	7 (1)	4 (3)	1 (1)
50+ years	10 (2)	5 (4)	0
Median (Range)	5 (0-68)	5 (0-68)	4 (1-43)
Donor/Recipient CMV serostatus			
CB - recipient +	318 (63)	75 (60)	101 (59)
CB - recipient -	182 (36)	44 (35)	64 (38)
CB - recipient CMV unknown	6 (1)	6 (5)	5 (3)
GvHD Prophylaxis			
No GVHD prophylaxis	2 (<1)	0	1 (1)
Ex vivo T-cell depletion	3 (1)	1 (1)	1 (1)
CD34 selection	29 (6)	6 (5)	1 (1)
Post-CY + other(s)	0	1 (1)	1 (1)
Tacrolimus + MMF +- others	185 (37)	40 (32)	50 (29)
Tacrolimus + MTX +- others (except MMF)	14 (3)	5 (4)	2 (1)
Tacrolimus + others (except MTX, MMF)	32 (6)	7 (6)	8 (5)
Tacrolimus alone	26 (5)	10 (8)	5 (3)
CSA + MMF +- others (except Tacrolimus)	177 (35)	50 (40)	83 (49)
CSA + MTX +- others (except Tacrolimus, MMF)	3 (1)	1 (1)	2 (1)
CSA + others (except Tacrolimus, MTX, MMF)	12 (2)	1 (1)	7 (4)
CSA alone	1 (<1)	0	1 (1)
Other GVHD prophylaxis	17 (3)	2 (2)	5 (3)
Missing	5 (1)	1 (1)	3 (2)
Donor/Recipient sex match			
CB - recipient M	297 (59)	74 (59)	95 (56)
CB - recipient F	209 (41)	51 (41)	75 (44)
Year of transplant			
1996-2000	1 (<1)	0	0
2001-2005	6 (1)	7 (6)	3 (2)
2006-2010	157 (31)	34 (27)	49 (29)
2011-2015	260 (51)	52 (42)	68 (40)
2016-2020	77 (15)	23 (18)	46 (27)
2021-2022	5 (1)	9 (7)	4 (2)
Follow-up among survivors, Months			
N Eval	224	47	64
Median (Range)	72 (0-166)	65 (0-194)	49 (0-144)

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

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
Number of patients	1140	208	99
Source of data			
CRF	351 (31)	49 (24)	31 (31)
TED	789 (69)	159 (76)	68 (69)
Number of centers	70	37	22
Disease at transplant			
NHL	936 (82)	168 (81)	76 (77)
Hodgkins Lymphoma	204 (18)	40 (19)	23 (23)
NHL Disease status at transplant			
CR1	174 (19)	39 (23)	16 (21)
CR2	176 (19)	34 (20)	10 (13)
CR3+	100 (11)	18 (11)	4 (5)
PR	68 (7)	13 (8)	7 (9)
Advanced	409 (44)	63 (38)	39 (51)
Missing	5 (1)	0	0
Recipient age at transplant			
0-9 years	11 (1)	4 (2)	0
10-17 years	40 (4)	10 (5)	1 (1)
18-29 years	141 (12)	34 (16)	8 (8)
30-39 years	122 (11)	29 (14)	17 (17)
40-49 years	187 (16)	28 (13)	21 (21)
50-59 years	329 (29)	54 (26)	30 (30)
60-69 years	290 (25)	41 (20)	21 (21)
70+ years	20 (2)	8 (4)	1 (1)
Median (Range)	52 (3-76)	50 (2-75)	51 (12-72)
Recipient race/ethnicity			
White, Non-Hispanic	739 (65)	117 (56)	62 (63)
Black or African American, Non-Hispanic	133 (12)	31 (15)	15 (15)
Asian, Non-Hispanic	51 (4)	15 (7)	2 (2)
Native Hawaiian or Pacific Islander, Non-Hispanic	4 (<1)	1 (<1)	0
American Indian or Alaska Native, Non-Hispanic	5 (<1)	0	0
Hispanic	162 (14)	27 (13)	16 (16)
Missing	46 (4)	17 (8)	4 (4)
Recipient sex			
Male	729 (64)	135 (65)	61 (62)
Female	411 (36)	73 (35)	38 (38)
Karnofsky score			

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
10-80	384 (34)	72 (35)	26 (26)
90-100	707 (62)	124 (60)	64 (65)
Missing	49 (4)	12 (6)	9 (9)
HLA-A B DRB1 groups - low resolution			
<=3/6	194 (23)	53 (38)	15 (22)
4/6	65 (8)	12 (9)	4 (6)
5/6	19 (2)	1 (1)	4 (6)
6/6	573 (67)	73 (53)	46 (67)
Unknown	289 (N/A)	69 (N/A)	30 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	240 (31)	59 (46)	17 (27)
6/8	13 (2)	4 (3)	3 (5)
7/8	14 (2)	1 (1)	2 (3)
8/8	510 (66)	64 (50)	40 (65)
Unknown	363 (N/A)	80 (N/A)	37 (N/A)
HLA-DPB1 Match			
Single allele mismatch	59 (26)	1 (50)	0
Full allele matched	168 (74)	1 (50)	4 (100)
Unknown	913 (N/A)	206 (N/A)	95 (N/A)
High resolution release score			
No	804 (71)	208 (100)	95 (96)
Yes	336 (29)	0	4 (4)
Graft type			
Marrow	154 (14)	34 (16)	18 (18)
PBSC	985 (86)	173 (83)	81 (82)
BM+PBSC	0	1 (<1)	0
Others	1 (<1)	0	0
Conditioning regimen			
Myeloablative	416 (36)	68 (33)	27 (27)
RIC/Nonmyeloablative	720 (63)	136 (65)	71 (72)
TBD	4 (<1)	4 (2)	1 (1)
Donor age at donation			
To Be Determined/NA	4 (<1)	0	2 (2)
0-9 years	17 (1)	2 (1)	0
10-17 years	49 (4)	10 (5)	2 (2)
18-29 years	179 (16)	42 (20)	14 (14)
30-39 years	168 (15)	37 (18)	20 (20)
40-49 years	214 (19)	43 (21)	16 (16)
50+ years	509 (45)	74 (36)	45 (45)
Median (Range)	48 (0-81)	42 (0-71)	48 (0-74)
Donor/Recipient CMV serostatus			
+/+	458 (40)	95 (46)	31 (31)
+/-	147 (13)	20 (10)	10 (10)

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Variable	N (%)	N (%)	N (%)
- /+	214 (19)	37 (18)	26 (26)
-/-	296 (26)	47 (23)	22 (22)
Missing	25 (2)	9 (4)	10 (10)
GvHD Prophylaxis			
No GVHD prophylaxis	10 (1)	3 (1)	3 (3)
Ex vivo T-cell depletion	9 (1)	2 (1)	0
CD34 selection	3 (<1)	0	0
Post-CY + other(s)	355 (31)	80 (38)	31 (31)
Post-CY alone	9 (1)	1 (<1)	0
Tacrolimus + MMF +- others	108 (9)	13 (6)	4 (4)
Tacrolimus + MTX +- others (except MMF)	440 (39)	58 (28)	43 (43)
Tacrolimus + others (except MTX, MMF)	104 (9)	40 (19)	13 (13)
Tacrolimus alone	10 (1)	0	0
CSA + MMF +- others (except Tacrolimus)	9 (1)	4 (2)	0
CSA + MTX +- others (except Tacrolimus, MMF)	22 (2)	0	1 (1)
CSA + others (except Tacrolimus, MTX, MMF)	14 (1)	4 (2)	1 (1)
CSA alone	3 (<1)	0	0
Other GVHD prophylaxis	23 (2)	1 (<1)	2 (2)
Missing	21 (2)	2 (1)	1 (1)
Donor/Recipient sex match			
Male-Male	432 (38)	77 (37)	41 (41)
Male-Female	209 (18)	32 (15)	17 (17)
Female-Male	292 (26)	57 (27)	19 (19)
Female-Female	200 (18)	41 (20)	19 (19)
Missing	7 (1)	1 (<1)	3 (3)
Year of transplant			
2006-2010	118 (10)	15 (7)	15 (15)
2011-2015	487 (43)	66 (32)	35 (35)
2016-2020	435 (38)	84 (40)	42 (42)
2021-2022	100 (9)	43 (21)	7 (7)
Follow-up among survivors, Months			
N Eval	688	127	67
Median (Range)	48 (0-148)	36 (0-123)	60 (0-145)

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TO: Lymphoma Working Committee Members

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

RE: Studies in Progress Summary

LY20-02 Outcomes of Allogeneic HCT in patients with Hodgkin Lymphoma in the era of Checkpoint Inhibitors: A joint CIBMTR and EBMT analysis. (Miguel-Angel Perales/Ana Maria Sureda).
This study is in collaboration with EBMT. The PIs are currently working on the manuscript preparation. The goal of this study is to have manuscript published by June 2023.

LY22-01 Comparing CAR vs. Auto-HCT in Aggressive B-cell lymphomas: Addressing questions unanswered by randomized trials (Mazyar Shadman/Mehdi Hamadani/Trent Wang/ Antonio Martin Jimenez Jimenez/Zurko Joanna)**.**
This study consists of 3 different parts and is in data file preparation phase for all parts currently. The goal for this study is to have manuscripts published in 2023 for all parts.

LY22-02 CAR-T Outcomes in Rare Lymphoma Subtypes: A Basket Protocol (Hamza Hashmi/Naren Epperla/Sairah Ahmad/Santiago Mercadal/Catherine Lee/Priyanka Pophali/Joshua Fein/Roni Shouval/Mazyar Shadman/Swetha Kambhampati/Kalyan Nadiminti/Alex Herrera/Mehdi Hamadani/Jordan Gauthier)
This study is currently in protocol development phase.

I. Study Title

Outcomes of allogeneic hematopoietic cell transplantation (allo-HCT) for large B-cell lymphoma (LBCL) progressing after chimeric antigen receptor T-cell therapy (CAR T)

II. Key Words

Diffuse large B-cell lymphoma; DLBCL; LBCL; CAR T; allogeneic hematopoietic cell transplant; allo-HCT

III. Principal Investigator Information

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Underrepresented/minority: yes

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IV. Proposed Working Committee

Lymphoma Working Committee

V. Research Question

What are the outcomes of allo-HCT for (relapsed/refractory) R/R LBCL progressing after CAR T-cell therapy?

VI. Research Hypothesis

Allo-HCT can provide long-term disease control and remains a viable option in selected patients with R/R LBCL after anti-CD19 CAR T-cell therapy.

VII. Specific Objectives/Outcomes to be Investigated

Primary objectives

1. Overall survival (OS) at 1-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 1-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. Rate of neutrophil and platelet engraftment
   a. Time to neutrophils (ANC) > 0.5 x10^9/L sustained for three consecutive days within 28- and 100- days post-transplant.
   b. Time to achieve a platelet count of (a) >20 x 10^9/L independent of platelet transfusions for 3 consecutive days, and (b) >50 x 10^9 /L independent of platelet transfusions for 3 consecutive days within 28- and 100- days post-transplant.
2. Cumulative incidence of non-relapse mortality (NRM)
   a. Cumulative incidence of NRM at day 100 and 1 year. NRM is defined as death without preceding disease relapse/progression. Relapse and progression are competing events.
3. Cumulative incidence of disease relapse or progression
   a. Cumulative incidence of disease relapse/progression at 1 year with NRM as competing event.
4. Cumulative incidence and severity of acute graft-versus-host disease (GVHD) and chronic GVHD
   a. Cumulative incidence of grade II-IV acute GVHD per consensus criteria at day +100 and +180, with death as competing risk.
   b. Overall incidence of acute GVHD.
   c. One-year cumulative incidence of limited and extensive chronic GVHD, with death as competing risk.
5. GVHD-free relapse-free (GRFS) survival at 1-year
6. Intensity of conditioning regimen on transplant outcomes
   a. Myeloablative vs reduced intensity vs non-myeloablative
7. Primary causes of death: descriptive only
   a. Rate of infection-related deaths
   b. Other causes of death such as treatment-related toxicity

VIII. 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 significantly improved the outcomes of patients with R/R LBCL. However, the majority of patients who receive CAR T-cell therapy eventually progress. The outcomes of allo-SCT for LBCL patients progressing after CAR T-cell therapy are unknown, and the incidence and severity of posttransplant toxicities are of particular

concern. Using the CIBMTR database, our study aims to evaluate outcomes of allo-SCT for LBCL relapsing after anti-CD19 CAR T-cell therapy. The results of this study will provide robust evidence on the safety and efficacy of allo-SCT following CAR-T failure in relapsed LBCL.

IX. 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 CAR T-cell therapy (CART) has emerged as a promising treatment option for patients with multiply relapsed and refractory large B-Cell lymphoma (LBCL) (1-3). In addition, it is approved for primary refractory or early relapsed (within 12 months of initial therapy) LBCL. CAR T-cell therapy has been shown to improve event-free survival (EFS) and overall relapse rate (ORR) in comparison with autologous stem cell transplant (autoSCT) in the second-line setting. (3-5). Anti-CD19 CAR T-cell therapy offers a durable complete remission in 30 to 40% of B-cell non-Hodgkin lymphoma (1, 2, 3). However, a significant number of patients does not respond to CAR T-cell therapy or remains at risk of relapse or disease progression after CAR T-cell therapy (4, 5). Outcomes of these patients are poor with a median overall survival (OS) of less than 6 months (6, 7). Allo-HCT remains a viable treatment option for transplant eligible patients and may provide durable disease remission through graft-versus-lymphoma effect. The 3-year OS and progression-free survival (PFS) after allo-HCT in patients with relapsed or refractory LBCL in the pre-CAR-T era were reported at 40-60% and 30-50%, respectively (8-10). Even patients who are chemotherapy resistant before allo-HCT can achieve a PFS of 20% at 2 years.

  However, the literature on transplant outcomes after CAR T-cell therapy is limited due to small sample size, and the factors associated with improved outcomes in this population are unknown (11, 12). Additionally, it is uncertain if patients experience higher rates of posttransplant toxicity including opportunistic infections as well as acute and chronic GVHD. The results from our analysis will provide valuable information on transplant outcomes in patients who relapse after CAR T-cell therapy as well as identify factors associated with increased toxicity.

X. Participant Selection Criteria

- State inclusion and exclusion criteria.

  Inclusion criteria: Adult patients ≥18 years old with relapsed or refractory LBCL (including those with transformed DLBCL, high-grade B-cell lymphoma, double hit lymphoma, primary mediastinal large B cell lymphoma) treated with CD19-directed CAR T-cell therapy (axi-cel, tisa-cel, liso-cel) between 2010 and 2022 and subsequently received an allo-HCT for disease progression; patients treated with investigational CAR T-cell therapy are included if it targeted the CD19 antigen.

Exclusion criteria: Patients who were in a durable CR following CAR T-cell therapy who then received an allo-HCT as a consolidation or for indications other than relapsed/refractory disease were excluded. Patients with primary central nervous system (CNS) lymphoma are excluded.

XI. Data Requirements

- After reviewing data available on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses.
- Data collection forms are available at: http://www.cibmtr.org/DataManagement/DataCollectionForms/Pages/index.aspx

Patient related:

1. Age at HCT: continuous to find the appropriate cutoff point for the survival model
2. Gender: male vs. female
3. Karnofsky performance score: ≥90 vs. <90% and continuous.
4. Sorror Co-morbidity index: 0 vs. 1-2 vs. 3
5. Race: Caucasian, African American, Asian pacific islander
6. Ethnicity: Hispanic vs. non-Hispanic

Disease related:

1. Disease subtype: de novo DLBCL; transformed DLBCL; primary mediastinal large B-cell lymphoma; high grade B cell lymphoma, NOS
2. Cell of origin: GCB vs. non-GCB vs unknown
3. Double/triple hit DLBCL: yes vs no vs unknown
4. Disease stage at diagnosis: I/II vs. III/IV
5. Primary refractory disease: Yes vs No
6. Elevated LDH at HCT: yes vs no
7. Bulky disease at HCT: yes vs no
8. Bulky disease at diagnosis: yes vs no
9. Bone marrow involvement at HCT: yes vs no vs unknown
10. Bone marrow involvement at diagnosis: yes vs no vs unknown
11. Extranodal involvement at HCT: yes vs no
12. Revised International Prognostic Index: 0 vs. 1-2 vs. 3-5
13. Time from diagnosis to CAR T-cell therapy: <1year vs. ≥1 year and continuous
14. Type of CAR T-cell therapy: axi-cel vs tisa-cel vs liso-cel
15. Time from CAR T cell therapy to HCT
16. Time from CAR T-cell therapy to relapse
17. Best response to CAR T-cell therapy: CR, PR, stable disease, progression
18. Number of prior chemotherapy regimens received: <2 vs. >=2 lines of therapy between CART and allo-HCT

19. Prior radiotherapy: yes vs no
20. Disease status at HCT: CR vs. PR vs. chemoresistant vs. untreated/unknown
21. Prior autologous HCT: yes vs no

Transplant related:

1. TBI in conditioning regimen: Yes vs. No
2. Conditioning: MAC versus RIC versus NMA
3. Graft type: bone marrow vs peripheral blood
4. Donor type: matched related vs related haploidentical vs matched unrelated vs mismatched
5. Year of HCT: Continuous
6. GVHD prophylaxis: calcineurin inhibitors + MTX +/- others VS. calcineurin inhibitor + MMF +/-others VS. PTCY + tacrolimus + MMF
7. Donor/Recipient gender F/F vs. M/M vs. F/M vs. M/F
8. Donor/Recipient CMV status -/+ vs. others
9. ATG/alemtuzumab use: Yes vs No

XII. Patient-Reported Outcome (PRO) Requirements

- If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROs.
- For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Committees/wc/LateEffects/Pages/default.aspx
- NA

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

- If the study requires biologic samples from the CIBMTR Repository, the proposal should also include a detailed description of the proposed testing methodology and sample requirements and a summary of the investigator's previous experience with the proposed assay systems.
- NA

XIV. Non-CIBMTR Data Source, *if applicable*

- A description of the external data source to which the CIBMTR data will be linked.
- The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

- NA

XV. References

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Table 1. Baseline characteristics of the adult patients who received allo-HCT post CAR-T for LBCL

Characteristic	**N (%)**
No. of patients	58
No. of centers	33
TED or CRF track – no. (%)	
TED	52 (90)
CRF	6 (10)
Age – median (min-max)	54 (20-73)
Age group – no. (%)	
18-40	15 (26)
41-60	28 (48)
>60	15 (26)
Sex of recipient – no. (%)	
Male	37 (64)
Female	21 (36)
Karnofsky score prior to HCT – no. (%)	
90-100%	33 (57)
< 90%	21 (36)
Not reported	4 (7)
HCT-CI – no. (%)	
0	16 (28)
1	7 (12)
2	12 (21)
3+	23 (40)
Race – no. (%)	
White	48 (83)
Black or African American	2 (3)
Asian	1 (2)
Not reported	7 (12)
Disease status prior to transplantation – no. (%)	
CR	27 (47)
PR	17 (29)
Resistant	10 (17)
Untreated	2 (3)
Unknown	2 (3)
Graft type – no. (%)	
Bone marrow	4 (7)
Peripheral blood stem cells	54 (93)
Donor type – no. (%)	

Characteristic	**N (%)**
HLA-identical sibling (may include non-monozygotic twin)	22 (38)
HLA-mismatched relative	16 (28)
HLA-matched unrelated	15 (26)
HLA-mis. Matched unrelated	5 (9)
Conditioning regiment intensity – no. (%)	
No drugs reported	1 (2)
MAC	12 (21)
RIC	35 (60)
NMA	9 (16)
TBD	1 (2)
Total number lines of therapy – no. (%)	
1 line	3 (5)
2 lines	5 (9)
3+ lines	50 (86)
Time from diagnosis to transplant(months) – no. (%)	
<6-month	1 (2)
6-month-12-month	6 (10)
>=12-month	51 (88)
Year of transplant – no. (%)	
2019	12 (21)
2020	40 (69)
2021	6 (10)
Follow-up among survivors, months – median (range)	12 (0-13)

Note: Data is incomplete from 2020-2022 due to database transitioning.

CIBMTR proposal

Study title

Outcomes Following CD19 Directed Chimeric Antigen Receptor (CAR) T-Cell Therapy for Relapsed Refractory Follicular Lymphoma: Real-World Data from the Center for International Blood and Marrow Transplant Research (CIBMTR)

Keywords

CD19 directed CAR T-cell, Outcomes, Toxicity, Follicular Lymphoma, CRS, ICANS

1st PI Information:

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Current ongoing work with CIBMTR: DLI post-haploidentical stem cell transplantation. The manuscript is written and is currently under review by the committee

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PI Name: Swetha Kambhampati (Junior Investigator), Alex Herrera (Senior Investigator)
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Institution name: City of Hope
Academic rank: Assistant Professor (Dr. Kambhampati), Associate Professor (Dr. Herrera)
Junior Investigator status: Assistant Professor at City of Hope
Current ongoing work with CIBMTR: PI of study evaluating outcomes of CAR T for transformed DLBCL, Dr. Herrera is Co-chair of Lymphoma Working Group

PROPOSED WORKING GROUP

Lymphoma Group

RESEARCH QUESTION

What are the safety, efficacy and predictors of outcomes (efficacy and toxicity) following anti-CD19 CAR T cell therapy for relapsed/refractory (R/R) follicular lymphoma (FL) and what is the significance and prognostic role of toxicity- and progression-free survival in FL?

RESEARCH HYPOTHESIS

We hypothesize that real-world outcomes of CD19 CAR T cell therapy as standard of care for relapsed and refractory (R/R) follicular lymphoma (FL) are similar to those reported in the ZUMA-5 and ELARA clinical trials. Additionally, we hypothesize that predictors of toxicity following anti-CD19 CAR T cell therapy for FL might be different from other types of B cell lymphoma, notably high-grade lymphoma.

We aim to identify real-world safety and efficacy of CD19 CAR T cell therapy for relapsed refractory FL and to identify predictors of safety and efficacy among patients reported to CIBMTR. We would also like to characterize a novel toxicity-free, progression-free survival (TPFS) endpoint in CAR T cell receipients with FL and explore its significance in predicting subsequent survival.

SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED

Primary Aim:

- To evaluate progression-free survival (PFS) of CD19 CAR T cell recipients with R/R FL

Secondary Aim:

- To evaluate the response rates (ORR, CR, PR), survival outcomes (OS; overall survival, and TPFS; toxicity-free, progression-free survival), and duration of response (DOR) of patients with follicular lymphoma treatment with anti-CD19 CAR T-cell therapy.
- To evaluate survival outcomes of SOC CAR T in R/R FL stratified by type of CAR T (axi-cel and tisa-cel)
- To evaluate toxicities (both any grade and high grade) including cytopenias, time to hematologic recovery, cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome, and infections stratified by type of CAR T (axi-cel and tisa-cel)
- To establish adjusted predictors of survival outcomes, ORR, response and toxicity after anti-CD19 CAR T-cell therapy for follicular lymphoma (ie. demographics, POD24 status, prior treatment, bispecific antibody therapy, lenalidomide, and bendamustine, timing of treatment prior to CAR T [< 1 year or > 1 year] etc)

SCIENTIFIC IMPACT:

Follicular lymphoma (FL) is the second most common lymphoma diagnosed in the western hemisphere.[1, 2] It accounts for approximately one-third of all non-Hodgkin lymphomas and over two-thirds of the indolent ones.[3, 4] The disease is characterized by a heterogeneous clinical course, with some patients having a very indolent clinical presentation without requiring treatment for a relatively long time and others having a more aggressive presentation requiring more immediate treatment for disease control. For patients requiring first-line treatment, anti-CD20 monoclonal antibody alone or in combination with chemo- or radiation therapy are the most commonly used.[5-9] Standard treatments for patients with relapsed/refractory (R/R) FL include conventional therapy using phosphoinositide-3 kinase inhibitors (PI3Ki), *EZH2* inhibitors, autologous (auto-) hematopoietic cell transplantation (HCT) HCT or allo-HCT (allogeneic HCT).[10-13] Patients failing two or more lines of therapy are nowadays offered chimeric antigen receptor T-cell (CAR T) therapy. Two products are currently approved by the United States Food and Drug Administration (FDA), namely axicabtagene ciloleucel (axi-cel) and tisagenlecleucel, based on results of ZUMA-5 (March 2021) and ELARA (May 2022) studies, respectively. [14, 15]

The ZUMA-5 is a single-arm phase 2 trial including 148 patients with R/R indolent non-Hodgkin lymphoma (NHL), FL (n=124) and marginal zone lymphoma (MZL) (n=24) treated with axi-cel.[14] The primary endpoint was overall response rate (ORR). Patients with FL had bulky disease (52%), stage IV (49%), were heavily pretreated with more than 3 lines of therapy (63%), had a

progression of disease within 24 months of receiving frontline chemoimmunotherapy (POD24) (55%), and had received and failed previous autologous stem cell transplant (auto-HCT) (24%). Bridging therapy was given to 4% of all patients (4/124 patients with follicular lymphoma). The median time from leukapheresis to CAR T product delivery was 17 days. The median follow-up for FL patients was 24.4 months. The ORR following axi-cel for patients with FL was high at 94%, with 79% of the patients achieving complete remission (CR). High response rates translated into durable responses with a duration of response (DOR) in FL patients of 38.6 months, and 57% of eligible patients were in ongoing response at data cut-off. The estimated median progression free survival (PFS) and overall survival (OS) were 39.6 months and not reached for patients with FL, respectively. Long-term PFS rates were consistent among key subgroups, namely high-tumor burden, ≥4 lines of prior therapy. In terms of toxicity, the cytokine release syndrome (CRS) and neurologic events (NE) rates were relatively high (for FL, CRS=78% and NE=56%). Higher grade≥3 CRS and NE were 6% and 15%, respectively. The most common grade≥3 NE was encephalopathy (8%). In terms of cytopenias, 24%, 10%, 4% had grade>3 anemia, neutropenia and decrease in white blood cells (WBC), respectively.[14]

The ELARA is single arm, phase 2 trial included 97 patients with R/R FL treated with tisa-cel.[15] The primary endpoint was CR rate. The median age was 57 years. Median prior lines of therapy were 4 lines, with 27.8% of the patients being refractory to >4 lines of treatment. Patients with bulky disease comprised 63.9% of the entire study population; also 85.6% had stage III-IV disease, 62.9% had POD24, and 36.1% had received and failed a previous auto-HCT. Bridging therapy was administered to 45% of the patients consisting mainly of chemotherapeutic regimens. Median time from enrollment to infusion was 46 days. At a median follow-up of 9.9 months, the CR rate was 75.3% (95% confidence interval [CI] 64.7-84, p<0.0001), and the ORR was 91.8% (95% CI 83.9-96.6). The 1-year PFS for all patients and patients achieving CR were 67% and 85.5%, respectively. The 1-year PFS was lower in patient with POD24 (60.8% vs 77.9%), high baseline total metabolic tumor volume (TMTV) >510 cm^3 (54.5% vs 68.5%), and ≥5 lines of therapy (59.6% vs 69.7%). Median OS was not reached. The 9-month DOR was 86.5%. In terms of side effects, CRS occurred in 48.5% of the patients, which were all grade 1-2, and 34% of the patients required at least one dose of tocilizumab. Neurologic events were observed in 37.1% of the patients, with only 3.1% being grade≥3. Pertaining to hematologic toxicity, 32% had grade≥3 neutropenia, 13.4% had grade≥3 anemia, and 12.4% had grade≥3 decrease in white blood cell count (WBC). By 12-month, 92.3%, 100% and 100% recovered their WBC, hemoglobin, and neutrophils, respectively.[15]

As shown in these studies, anti-CD19 CAR T cell therapy for patients with FL is associated with higher ORR (axi-cel 94% and tisa-cel 91.8%) and CR rates (axi-cel 79% and tisa-cel 75.3%) compared to conventional therapies (CR rate 12% with copansilib [PI3Ki] and 13% with EZH2 inhibitors).[10, 11, 14, 15] Yet, it is associated with toxicity, namely cytopenias, CRS, and ICANS.

Since clinical trials often have stringent eligibility criteria, the trial outcomes reported may not be reflective of real-world practice. It is therefore important to understand the safety, efficacy and predictors of outcomes of standard of care (SOC) CD19 CAR T in R/R FL patients in real-world clinical practice. To our knowledge there are no current published data addressing this issue. We

thus propose a retrospective study using the CIBMTR database to delineate the characteristics and outcomes of patients treated with commercially available axi-cel or tisa-cel CAR T and to evaluate their safety and efficacy in the real-world setting including the product comparison according to the newly defined composite outcome of TPFS.

SCIENTIFIC JUSTIFICATION

Both axi-cel and tisa-cel have demosntrated excellent efficacy based on results of ZUMA-5 and ELARA trials showing ORR/CR rate of 94%/79% and 91.8%/75.3%, respectively.[14, 15] Severe CRS/NE were observed in 6%/15% and 0/3.1% in ZUMA-5 and ELARA trials respectively.[14, 15] While limited data on indirect comparison between axi-cel and tisa-cel point at similar efficacy but higher toxicity with axi-cel, no study to date has compared both products in the RW setting or evaluated the predictors of toxicities in patients with FL receiving CAR T cell therapy. Hence, selection of tisa-cel vs axi-cel as the preferred therapy in the RW setting has been largely based on physician discretion and/or familiarity with a specific product. In a "Matched adjusted indirect comparison of tisa-cel and axi-cel", similar ORR, CR rates, and PFS (Hazard Ratio [HR]=1.13, p=0.70), with tisa-cel associated with a better safety profile compared to axi-cel (severe CRS/NE, 0.08%/0.97% vs 6.45%/15.32).[16] While such comparison has inherent biases, it suggests that using either of those CAR T products could possibly lead to similar outcomes.

Identifying factors associated with increased toxicity associated with these products would help clinician with treatment decision pertaining to product choice and would guide future studies on combinatorial approaches to mitigate toxicities. We also aim to capture these toxicities and efficacy by composite end point. Such novel endpoint may allow for leveled and more comprehensive comparison between CAR T cell constructs and their major outcomes. Our proposed toxicity-free and progression-free survival (TPFS) composite endpoint is defined as absence of severe CRS, ICANS, progression and nonrelapse mortality within 6 months after CAR T cell infusion. Since each of these TPFS components is clinically meaningful, TPFS may represent an ideal recovery outcome after CAR T cell therapy (at 6 months) and also a measure of initial success without progression, major morbidity and mortality.

We propose to use CIBMTR database to evaluate real-world safety and efficacy of standard of care CD19 CAR T for patients with R/R FL. Through this large retrospective analysis, we hope to not only describe response and toxicity outcomes of CD19 CAR T in R/R FL but also to better understand real-world differences between axi-cel and tisa-cel in terms of prognostic factors associated with toxicities and efficacy as reflected by toxicity-free and progression-free survival (TPFS). This novel endpoint may allow for leveled and more comprehensive comparison between CAR T cell constructs and their major outcomes at 6 mos following CART infusion. Our proposed toxicity-free and progression-free survival (TPFS) composite endpoint is defined as absence of severe CRS or ICANS, disease progression and nonrelapse mortality within 6 months after CAR T cell infusion. Since each of these TPFS components is clinically meaningful, TPFS may represent an ideal recovery outcome after CAR T cell therapy (at 6 months) and also a measure of initial success without progression, major morbidity and mortality.

SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)
N/A

PARTICIPANT SELECTION CRITERIA:

Inclusion criteria:
Adult patients (age ≥ 18) treated with any commercially available anti-CD19 CAR T-cell therapy for relapsed refractory follicular lymphoma.

Exclusion criteria:
Patients who received CAR T as part of a clinical trial.

Variables:
The following variable will be analyzed

Patient- and Disease-related:

- Age at time of CAR-T: continuous and categorical by decade (< 60, **≥** 60, median age)
- Gender: male vs. female
- Race: Caucasian vs. African American vs. Asian/Pacific Islander vs. Hispanic vs. Others
- Performance status at the time of CAR T-cell infusion
- Autoimmune Disease requiring systemic therapy within 2 years (Yes, No)
- FL histologic category (Grade 1, Grade 2, Grade 3A)
- Stage (I, II, III, IV)
- BM involved prior to CAR T (Yes/No)
- Extranodal disease
- Disease status prior to CAR T (primary refractory, refractory, relapsed)
- FLIPI scoreprior to CAR T (1-5)
- Bulky Disease by GELF criteria (Yes, No)
- POD24 (Yes/No)
- Number of prior lines of therapy (**≥** 3 prior lines of therapy, median # of prior lines [range])
- Prior treatments: PIK3A (Yes/No), anti-CD20 monoclonal antibody (Yes/No), alkylating agent (ie. Bendamustin; Yes/No), lenalidomide (Yes/No), checkpoint inhibitor therapy (Yes, No), Radiation therapy (Yes, No),
- Prior Auto SCT (Yes, No), Date
- Prior Allo SCT (Yes, No), Date
- Renal insufficiency GFR < 60 (Yes, No)

CAR-T related:

- Specific product
- Lymphodepleting agent used
- Time from cell diagnosis to CAR T cell therapy
- Number of cells infused
- Bridging therapy (Yes/No)
- Type of bridging therapy (chemotherapy, XRT, steroids, targeted therapy)
- Time from leukapheresis to CAR T cell infusion
- Date of best reponse
- Time to best reponse

- Date of post-CAR-T progression/relapse
- Date of last reponse
- Date of death
- Cause of death
- Date of last contact
- CRS (yes vs. no), maximum grade, time of onset and duration
- ICANS (yes vs. no), maximum grade, time of onset and duration
- Tocilizumab administered (Y/N)
- Steroids administered (Y/N)
- Anakinra administered (Y/N)
- Median time of hospital stay
- ICU stay (Yes/No; median time of ICU stay)
- Infection (<180 days post CAR T-cell, maximum grade)
- Baseline and days 30, 90, 180 cytopenia present (Y/N)
- Need for G-CSF beyond day 14
- Renal insufficiency GFR < 60 (Yes, No)

Outcomes:

- Responses: overall response rate, complete response rates, PR as defined by Lugano 2014
- Overall survival (OS): Time from CAR T-cell to death due to any cause. Patients will be censored at the time of last follow up.
- Progression free survival (PFS): Time from CAR T-cell to death or relapse. Patients will be censored at the time of last follow up.
- Duration of response (DOR): Time from first response after CAR T to progression. Patients will be censored at the time of last follow-up
- Relapse/ Progression: Progressive or recurrent disease as defined by the Lugano 2014 be counted as an event. Those who survive without recurrence or progression to be censored at the date of last follow-up.
- Toxicities: incidence of CRS, ICANS, infections, and cytopenias
- Toxicity-free, progression-free survival (TPFS): Time from CAR T-cell to 6 months post CAR T cell therapy.

DATA REQUIREMENTS

Data will be captured via relevant CIBMTR data collection forms.

SAMPLE REQUIREMENTS:

No biological samples required for this proposed study.

PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS

N/A

CONFLICTS OF INTEREST:

R.M. and S.K. do not have any competing conflict of interest.

- A.L: Sanofi/Kadmon

- Alex Herrera:

Bristol Myers Squibb – research funding, consultancy
Genentech – research funding, consultancy
Merck – research funding, consultancy
Seattle Genetics - research funding, consultancy
KiTE Pharma - research funding
Gilead Sciences – research funding
AstraZeneca – research funding, consultancy
Karyopharm – consultancy
ADC Therapeutics – research funding, consultancy
Takeda – consultancy
Tubulis - consultancy
Regeneron - consultancy
Genmab - consultancy
Pfizer - consultancy
Caribou - consultancy
Adicet Bio - consultancy
Abbvie - consultancy

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Table1. Baseline characteristics of adult patients who received CAR-T for Follicular lymphoma

Characteristic	**N (%)**
No. of patients	333
No. of centers	82
Age at CAR-T - median (min-max)	62 (29-87)
Age at CAR-T cell infusion - no. (%)	
18-29	1 (0)
30-39	7 (2)
40-49	38 (11)
50-59	97 (29)
60-69	132 (40)
>=70	58 (17)
Gender - no. (%)	
Male	199 (60)
Female	134 (40)
Performance score prior to CT - no. (%)	
90-100	167 (50)
80	105 (32)
<80	44 (13)
Not reported	17 (5)
HCT-CI - no. (%)	
0	109 (33)
1	86 (26)
2	48 (14)
3+	87 (26)
TBD, unclear lineage of prior hematologic malignancies	2 (1)
Not reported	1 (0)
Recipient race - no. (%)	
White	283 (85)
African American	18 (5)
Asian	11 (3)
Natice American	2 (1)
Unknown	13 (4)
Not reported	6 (2)
Recipient ethnicity - no. (%)	
Hispanic or Latino	39 (12)
Non-Hispanic or non-Latino	278 (83)
N/A - Not a resident of the U.S.	5 (2)
Unknown	11 (3)

Characteristic	**N (%)**
Disease status prior to CT - no. (%)	
CR	15 (5)
PR	57 (17)
resistant	210 (63)
untreated	30 (9)
unknown	21 (6)
Product - no. (%)	
Kymriah	2 (1)
Yescarta	330 (99)
Tecartus	1 (0)
Bridging therapy - no. (%)	
No	243 (73)
Yes	32 (10)
Not reported	58 (17)
Time from diagnosis to CT - no. (%)	
1-12 months	29 (9)
>12 months	304 (91)
Year of CT - no. (%)	
2018	10 (3)
2019	8 (2)
2020	6 (2)
2021	158 (47)
2022	151 (45)
Follow-up among survivors - median (range)	7 (0-51)

Study Title

Allogeneic hematopoietic stem cell transplantation for advanced mycosis fungoides and Sezary syndrome: an analysis of CIBMTR data and consensus guidelines for patient selection and treatment protocol

Key Words

Cutaneous T-cell lymphoma; mycosis fungoides; Sezary syndrome; allogeneic; hematopoietic stem cell transplantation

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Proposed Working Committee

Lymphoma Working Committee

Research Question

We seek to perform a comprehensive analysis of allogeneic-HSCT performed for patients with advanced mycosis fungoides (MF) and Sezary syndrome (SS) in the United States from 2000-2020.

Hypothesis: We hypothesize that allo-HSCT is an effective treatment for a subset of patients with MF and SS; advances in the field of BMT including in donor selection, GVHD prophylaxis, and supportive care over the last decade have resulted in improved outcomes of allo-HSCT for MF/SS compared to previous data.

With the assistance of the CIBMTR Lymphoma Working Group and the United States Cutaneous Lymphoma Consortium (USCLC), we plan to use this analysis to build consensus guidelines for patient selection and transplant protocols.

Specific Aims

Aim 1: Assess survival outcomes in patient with MF/SS undergoing allo-HSCT.
These outcomes include overall survival (OS), relapse/progression free survival (PFS), non-relapse mortality (NRM), and rates of acute and chronic GVHD.

Aim 2: Analyze risk factors impacting outcomes of allo-HSCT for MF/SS.
We will analyze the impact of the following variables:

(1) The time interval between diagnosis of CTCL and first allo-HSCT
(2) The degree of disease control at the time of transplant
(3) The role of the conditioning regimen, particularly total body irradiation and lymphocyte depletion
(4) Donor type, including cord blood and haploidentical donors
(5) Reduced intensity conditioning versus myeloablative protocols
(6) The use of post-transplant cyclophosphamide for GVHD prophylaxis
(7) Donor lymphocyte infusion and cellular therapy for relapse

Scientific Impact

Analysis of CIBMTR data on allo-HSCT for CTCL from 2000-2020 would offer invaluable insight into the patient characteristics and transplant-related factors that may impact treatment outcomes. At this time there are no consensus guidelines on the selection of patients who would most benefit from transplant, and transplant protocols and conditioning regimens differ significantly from institution to institution. This work will allow us to generate data that would significantly advance clinical care of patients with these rare, aggressive lymphomas.

Scientific Justification

Mycosis fungoides (MF) and Sezary syndrome (SS) are rare forms of cutaneous T-cell lymphoma (CTCL). Although mycosis fungoides (MF) is generally indolent, a subset of patients, including those with folliculotropic disease, large cell transformation (LCT), extensive blood involvement, or visceral involvement may experience rapid disease progression with treatment-refractory disease and significant resulting morbidity and mortality.[1] Although long-term remission may rarely occur in MF patients treated with combinations of cytotoxic chemotherapy, targeted therapies, radiation, photopheresis, and other modalities, progressive disease typically proves to be refractory to multiple lines of treatment. Sezary syndrome is an aggressive systemic lymphoma that is frequently refractory to numerous lines of therapy and associated with high risk of death due to immune compromise and opportunistic infection. Allo-HSCT is the only available potentially curative therapeutic option for patients with SS and for patients with aggressive MF.[1] Allo-HSCT for the treatment of MF and SS has become more widely available over the last decade, but outcomes remain poor due to high rates of relapse and graft-versus-host disease.[2–5] Despite many years of use of allo-HSCT for MF/SS, data guiding patient selection and treatment protocols have been limited.

Although analyses of data from the CIBMTR from 2000-2009[3] and from the European Society for Blood and Marrow Transplantation (ESBMT) from 1997-2011[2] have been published, this data fails to adequately address some of the

most fundamental and pressing questions about allo-HSCT for advanced CTCL. These data do not reflect the impact of recent changes in the field, such as the increased utilization of cord blood, haplo-identical donors, post-transplant cyclophosphamide, or the impact of prior treatment with new targeted therapies such as mogamalizumab.

The most recent analysis of CIBMTR data for CTCL was published in 2014 and included data on patients transplanted from 2000-2009.[3] In this study, the majority of patients were transplanted during the last 5 years of the study period, indicating an uptrend in the use of allogeneic HCT for advanced MF. The overall survival at one year was around 50%, with a PFS of 31% at one year and 17% at five years. NRM was 20% at one year with no significant differences between the type of conditioning regimen used whether myeloablative conditioning (MAC) or reduced intensity conditioning (RIC).[1] Retrospective studies from the European Society for Blood and Marrow Transplantation[2] and the French Society of Bone Marrow Transplantation,[4] showed comparable results to the CIBMTR report with one-year OS and PFS rates of 65-66% and 39-42%, respectively.[2,4] Although the ESBMT analysis showed that total body irradiation (TBI)-based conditioning regimens were used in 40% of patients, the impact of TBI on outcomes was not analyzed in detail.[3] The only reported prospective study treated 47 MF patients with allogeneic HCT between years 2001 and 2013. The four-year OS and PFS rates were 51% and 26%, respectively. Although this study was more capable of evaluating patients' outcomes based on the type of conditioning regimen and disease status prior to transplant, the number of patients included was relatively small.[18]

Since the publication of these studies, there have been significant shifts in the field of HSCT, including a expanded pools of donor selection, use of post-transplant cyclophosphamide (PTCY), and the use of reduced intensity conditioning protocols.[6,7] There is a paucity of data on the relationship between disease control at the time of transplant (specifically the presence of residual cutaneous disease) and rates of disease relapse for MF and SS.[4,5] Data suggest that patients in CR at the time of transplant have lower rates of relapse. This would have significant implications for selection of conditioning methods prior to transplant including TBI and lymphocyte depletion.[4,8,10] The impact of post-transplant cyclophosphamide on rates of GVHD has not been studied extensively in CTCL.[6,7]

Finally, we seek to determine if time elapsed between diagnosis of MF and transplant impacts survival. There is evidence that patients transplanted before 46 months have significantly better survival,[10] which if corroborated would have significant impact on treatment protocols and encourage earlier moves to transplant in patients with aggressive disease.

Thus, there is a tremendous need for a comprehensive analysis of CIBMTR data of patients with MF treated with allogeneic HCT in order to determine the safety, efficacy, and best timing of allogeneic HCT as well as prognostic factors that impact overall outcomes of this line of therapy.

Study Design

This is a retrospective proposal to study the role of allogenic HCT in patients with a diagnosis of MF using data available at CIBMTR. We plan to collect both transplant essential data (TED) and CRF data. Outcomes to be analyzed include overall response rate (ORR), rate of complete response (CR), OS, PFS and NRM. PFS and OS will be estimated using the Kaplan-Meier method, with the variance estimated by Greenwood's formula. Log-rank test will be used for comparison of Kaplan-Meier curves. Multivariable regression analysis will be performed using Cox proportional hazards model for OS and PFS and competing risks regression mode.

Specific Objectives/Outcomes

Primary endpoints:

- Mortality at 30 days, 100 days
- Non-relapse mortality at 1 year, 3 years, 5 years
- Progression/relapse at 1 year, 3 years, 5 years
- Progression free survival 1 year, 3 years, 5 years
- Overall survival 1 year, 3 years, 5 years

Secondary endpoints:

- Neutrophil engraftment at 28 days, 100 days
- Platelet engraftment at 28 days, 100 days
- Acute GVHD (II-IV)
- Chronic GVHD at 180 days, 1 year, 2 years

Participant Selection Criteria

Inclusion criteria:

- Patients with any stage MF who underwent allo-HSCT between 2000-2020
- Patients with any stage SS who underwent allo-HSCT between 2000-2020

Exclusion criteria:

- Transplant performed outside of 2000-2020

Data Requirements

Patient related:

- Age
- Gender: male vs. female
- Race: Caucasian vs American Indian vs. Asian vs. African American vs. Hispanic vs. Native Hawaiian/Pacific Islander
- Karnofsky performance score

Disease related:

- Diagnosis: Mycosis fungoides vs. Sezary syndrome vs other
- Disease stage: I vs. II vs. III. vs IV
- Disease status at transplant: Primary induction failure (never in complete remission), vs. first CR vs. first relapse vs. ≥ second relapse
- Interval from diagnosis to transplant: <12 months, 12-36 months, >36 months
- LDH > upper limit at diagnosis: yes vs. no.
- Extranodal or splenic involvement sites prior to conditioning: Yes vs. no
- Use of Mogamulizumab prior to transplant: Yes or No
    a. Time interval between completion of mogamalizumab treatment and transplant: ≥6 months vs. <6 months

Transplant related:

- Year of transplant
- Graft type: Peripheral blood vs. bone marrow vs. umbilical cord blood
- Donor type: HLA identical sibling vs. well-matched related vs. partially-matched related vs. mismatched unrelated vs. HLA-matched other relative vs. HLA-mismatched other relative

- Type of conditioning regimen: Myeloablative vs. Reduced intensity/Non-myeloablative
- Total body irradiation: yes vs. no.
- GVHD prophylaxis: in vivo T-cell depletion, cyclosporine, alemtuzumab, methotrexate, tacrolimus, other
- Acute Graft-versus-Host disease: Yes or No (Skin GVHD)
- Chronic GVHD: Yes vs. no (Skin GVHD)
- Immunosuppression therapy (IST): Yes or No
- Subsequent donor lymphocyte infusion: Yes or No
- Subsequent repeat allo-HSCT: Yes or no
- Subsequent CAR-T: Yes or no

Sample Requirements

Not applicable

Non-CIBMTR Data Source

Not applicable

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XVI. Conflicts of Interest

Dr. Goyal reports no conflicts of interest.
Dr. Safa reports no conflicts of interest.
Dr. Nakhle Saba reports the following conflicts of interest:

- Advisory Board and Speaker Bureau, Ibrutinib, Pharmacyclics and Jansen, more than $5,000 annually.
- Advisory Board, Mogamulizumab, Kyowa Hakko Kirin, less than $5,000 annually.

Dr. Foss has served as a consultant for Kyowa and Mallinkrodt.

Characteristics of adult patients who underwent allo-HCT for mycosis fungoides and sezary syndrome from 2001 to 2019

Characteristic	Mycosis fungoides	Sezary syndrome	Total
No. of patients	349	150	499
No. of centers	112	63	131
Is recipient on Ted or on CRF? - no. (%)			
TED	199 (57)	105 (70)	304 (61)
CRF	150 (43)	45 (30)	195 (39)
Age at transplant - no. (%)			
Median (min-max)	51 (19-74)	58 (20-74)	53 (19-74)
18-39	84 (24)	11 (7)	95 (19)
40-49	74 (21)	32 (21)	106 (21)
50-59	116 (33)	51 (34)	167 (33)
>=60	75 (21)	56 (37)	131 (26)
Gender of recipient - no. (%)			
Male	198 (57)	86 (57)	284 (57)
Female	151 (43)	64 (43)	215 (43)
Karnofsky score prior to HCT - no. (%)			
90-100%	183 (52)	84 (56)	267 (54)
< 90%	145 (42)	60 (40)	205 (41)
Not reported	21 (6)	6 (4)	27 (5)
Race - no. (%)			
White	203 (58)	114 (76)	317 (64)
Black or African American	85 (24)	15 (10)	100 (20)
Asian	8 (2)	1 (1)	9 (2)
Native Hawaiian or other Pacific Islander	2 (1)	1 (1)	3 (1)
American Indian or Alaska Native	3 (1)	0 (0)	3 (1)
More than one race	6 (2)	1 (1)	7 (1)
Not reported	42 (12)	18 (12)	60 (12)
Ethnicity - no. (%)			
Hispanic or Latino	35 (10)	10 (7)	45 (9)
Not Hispanic or Latino	260 (74)	110 (73)	370 (74)
NA, non-resident of USA	50 (14)	26 (17)	76 (15)
Not reported	4 (1)	4 (3)	8 (2)
CCN region - no. (%)			
US	278 (80)	109 (73)	387 (78)
Canada	11 (3)	5 (3)	16 (3)
Europe	37 (11)	25 (17)	62 (12)

Characteristic	Mycosis fungoides	Sezary syndrome	Total
Asia	3 (1)	1 (1)	4 (1)
Australia/New Zealand	12 (3)	4 (3)	16 (3)
Mideast/Africa	0 (0)	1 (1)	1 (0)
Central/South America	8 (2)	5 (3)	13 (3)
Donor - no. (%)			
HLA-identical sibling (may include non-monozygotic twin)	113 (32)	49 (33)	162 (32)
Unrelated donor	174 (50)	79 (53)	253 (51)
HLA-matched other relative	6 (2)	2 (1)	8 (2)
HLA-mismatched relativer	37 (11)	18 (12)	55 (11)
HLA-matched unrelated	12 (3)	1 (1)	13 (3)
HLA-mis. matched unrelated	5 (1)	1 (1)	6 (1)
Not reported	2 (1)	0 (0)	2 (0)
Graft source - no. (%)			
Bone marrow	37 (11)	11 (7)	48 (10)
Peripheral blood	289 (83)	134 (89)	423 (85)
Umbilical cord blood	23 (7)	5 (3)	28 (6)
Disease status prior to HCT (NHL/HD) - no. (%)			
CR	73 (21)	26 (17)	99 (20)
PR	171 (49)	81 (54)	252 (51)
Chemoresistant	88 (25)	36 (24)	124 (25)
Untreated	3 (1)	1 (1)	4 (1)
Unknown	14 (4)	6 (4)	20 (4)
Conditioning regimen intensity - no. (%)			
MAC	60 (17)	23 (15)	83 (17)
RIC/NMA	243 (70)	109 (73)	352 (70)
Not reported	46 (13)	18 (12)	64 (13)
TBI usage as part of conditioning regimen - no. (%)			
Yes	113 (32)	47 (31)	160 (32)
No	236 (68)	103 (69)	339 (68)
Time from diagnosis to transplant, months - median (min-max)	41 (5-386)	22 (4-189)	33 (4-386)
Transplant year - no. (%)			
2001	2 (1)	0 (0)	2 (0)
2003	3 (1)	0 (0)	3 (1)
2004	2 (1)	0 (0)	2 (0)
2005	4 (1)	0 (0)	4 (1)
2006	7 (2)	0 (0)	7 (1)
2007	6 (2)	0 (0)	6 (1)
2008	15 (4)	8 (5)	23 (5)

Characteristic	Mycosis fungoides	Sezary syndrome	Total
2009	21 (6)	9 (6)	30 (6)
2010	26 (7)	14 (9)	40 (8)
2011	25 (7)	5 (3)	30 (6)
2012	29 (8)	15 (10)	44 (9)
2013	35 (10)	19 (13)	54 (11)
2014	34 (10)	14 (9)	48 (10)
2015	28 (8)	6 (4)	34 (7)
2016	29 (8)	12 (8)	41 (8)
2017	23 (7)	13 (9)	36 (7)
2018	24 (7)	15 (10)	39 (8)
2019	36 (10)	20 (13)	56 (11)
Follow-up among survivors - median (range)	72 (2-170)	62 (3-148)	69 (2-170)

Response Summary:

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

Q1. Study Title

Evaluating outcomes of novel therapies post CD19 CAR T in Diffuse Large B-cell Lymphoma

Q2. Key Words

post CD19 CAR T, DLBCL, novel therapies

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Swetha Kambhampati
Email address:	skambhampati@coh.org
Institution name:	City of Hope
Academic rank:	Assistant Professor

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

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

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

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

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Swetha Kambhampati

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

N/A

LETTER OF COMMITMENT:

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

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

Dr. Kambhampati is the PI of study evaluating outcomes of CAR T for transformed DLBCL, Dr. Herrera is Co-chair of Lymphoma Working Group

Q13. PROPOSED WORKING COMMITTEE:

- Lymphoma

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

- No

Q15. RESEARCH QUESTION:

What is the safety and efficacy of treatments and particularly novel agents (loncastuximab tesirine, polatuzumab vedotin-bendamustine-rituximab, tafasitamab-lenalidomide, selinexor) post CD19 CAR T

Q16. RESEARCH HYPOTHESIS:

We hypothesize that novel therapies including immunotherapies and targeted therapies will be safe efficacious post CD19 CAR T.

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

Suggested word limit of 200 words:

Primary objective:
-evaluate overall response rate of novel therapies (targeted therapy, immunotherapy, chemotherapy, transplant, or radiation) post CD19 CAR T
Secondary objectives:
-evaluate complete response rate and duration of response of novel therapies post CD19 CAR T
-evaluate progression free survival and overall survival of novel therapies post CD19 CAR T
-evaluate incidence and severity of adverse events of novel therapies post CD19 CAR T
-evaluate for predictive markers of response to novel therapies at time of first relapse post CD19 CAR T including time to relapse post CD19 CAR T, presence of CD19/CD20 at time of relapse post CD19 CAR T, stage of disease, LDH, and IPI at time of relapse post CD19 CAR T, prior lines of therapy, and CD19 CAR T administered in second-line or third-line setting

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

As CAR T therapy is now being moved to the second line setting in high risk DLBCL patients (primary refractory/early relapse), how to treat patients who relapse post CD19 CAR T is an emerging important question. This study aims to assess the safety and efficacy of treatments post CD19 CAR T in the era of novel targeted therapies.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Diffuse large B-cell lymphoma (DLBCL) is the most common aggressive form of non-hogkin lymphoma (NHL). Second-line treatments for relapsed refractory (R/R) DLBCL include high dose chemotherapy and autologous stem cell transplantation (auto-SCT). However more than half of the patients relapse after auto-SCT1 and more than 60% of DLBCL patients are transplant-ineligible thus presenting a therapeutic challenge.2 CD19-directed CAR T cell therapy has recently transformed the landscape of DLBCL with initial approval of three products (axicabtagene ciloleucel (axi-cel), tisagenlecleucel (tisa-cel), and lisocabtagene maraleucel (lisa-cel)) in the third-line setting based on pivotal ZUMA-1,3 BELINDA,4 and TRANSCEND5 trials respectively. More recently, axi-cel and tisa-cel have also received approval for primary refractory/early relapse DLBCL patients based on ZUMA-76 and TRANSFORM7 studies respectively. Although these therapies have shown efficacy with durable complete responses (CRs), their use may be limited for the general population with R/R DLBCL due to the toxicity profile which requires carefully selected participants and treatment in only certified centers with specially trained staff. In addition, the waiting period associated with CAR T manufacturing may not be feasible in some participants with rapidly progressing disease. Despite the above-mentioned improvement in the therapeutic approaches in R/R DLBCL, clinical outcome of majority of patients with R/R DLBCL treated with third line CD19 CAR T, remains poor given the at best up to 40% 5-year PFS.8 There is a significant unmet need in patients with R/R DLBCL particularly in patients who relapse post CD19 CAR T where traditional therapies have had ORR of 29% and outcomes are dismal.9

Several other novel therapeutic agents have been recently approved for R/R DLBCL.10 Loncastuximab tesirine (lonca), an antibody drug conjugate (ADC) targeting CD19, has demonstrated efficacy with an ORR of 48.3%, CR rate of 24.1%, and median duration of response of 10.3 months based on the phase II LOTIS trial.11 Most common treatment-related adverse events (TrAEs) include cytopenias, transaminitis, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain. Serious adverse events (AEs) occurred in 28% of patients, with those occurring in ≥ 2% being febrile neutropenia, pneumonia, edema, pleural effusion, and sepsis.11 Polatuzumab vedotin (Pola), an ADC targeting CD79b, in combination with bendamustine-rituximab (BR) has also been approved for R/R DLBCL in transplant-ineligible patients with a CR rate of 40% and median PFS of 9.5 months and median OS of 12.4 months at median follow-up of 22.3 months. Main TrAEs with this combination include cytopenias and low-grade, transient peripheral neuropathy.12 Tafasitamab, a monoclonal antibody targeting CD19, in combination with lenalidomide has also demonstrated CR rate of 43% in transplant-ineligible patients with most common toxicity being cytopenias. However, it is important to note that serious AEs did occur in 51% of patients with those occurring in ≥ 2% being pneumonia, febrile neutropenia, pulmonary embolism, bronchitis, atrial fibrillation, and congestive heart failure.13 Selinexor, a selective inhibitor of XPO-1 nuclear export, was also approved in R/R DLBCL based on ORR of 28% with the most common grade 3-4 AEs being cytopenias, fatigue, hyponatremia and nausea and most common serious AEs being pyrexia, pneumonia, and sepsis.14 Other targeted therapy options include bruton tyrosine kinase inhibitors (BTKi) such as ibrutinib, an inhibitor of B-cell receptor signaling, that shows particular activity in non-GCB DLBCL with ORR 37%, but is associated with cytopenias, bleeding, GI side effects, and atrial fibrillation.15 Lenalidomide, an immunomodulatory agent, monotherapy or in combination with rituximab is also well-tolerated with minimal cardiac toxicities and with efficacy in R/R DLBCL.16,17 Venetoclax is an oral selective inhibitor of BCL-2, an anti-apoptotic molecule overexpressed in DLBCL,18 that has demonstrated single agent activity19 and response in combination with other targeted agents such as ibrutinib and lenalidomide.20 PD1 blockade with pembrolizumab after CD19-directed CAR T-cell therapy also appears safe and may achieve clinical responses in some patients with B-cell lymphomas refractory to or relapsed after CAR T-cell therapy by reverse T-cell exhaustion after CAR T-cell therapy. While all of these treatment options have demonstrated efficacy in R/R DLBCL, none of these therapies are curative at this time.

There are several ongoing clinical trials evaluating the role of novel therapies. Bispecific T-cell engagers are a new class of immunotherapy which enhances the patients' immune cells to attack tumors by retargeting T-cells (engaged by CD3) to tumor cells (engaged by CD20). There are four bispecific antibodies that are currently being investigated in DLBCL, including mosunetuzumab,21 glofitamab,22 epcoritamab,23 and odronextamab.24 Each of these agents has demonstrated promising early data including in heavily pre-treated patients who have progressed after CAR T cell therapy. Bispecific agents are anticipated FDA approval in DLBCL.

There have been prior studies demonstrating that targeted therapy and immunotherapy have safety and efficacy post CD19 CAR T.25,26 However, to our knowledge there has been no recent large study evaluating the real-world outcomes of novel targeted or immunotherapy agents in DLBCL (ie loncastuximab tesirine, polatuzumab-bendamustine-rituximab, selinexor, tafasitamab-lenalidomide, bispecifics) for first relapse post CD19 CAR T either in the third-line or second-line setting. This is an important question given that post-CAR T relapses are an unmet need. We will also evaluate risk factors that may predict response to novel therapies post CD19 CAR T.

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

N/A

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

Inclusion criteria:
Aged atleast 18 years
Relapsed or refractory DLBCL, high grade B cell lymphoma, primary mediastinal B cell lymphoma, transformed DLBCL from any indolent lymphoma (including Richter's syndrome), or FL grade 3B by pathological assessment
Relapsed after CD19 autologous CAR T cell therapy and received atleast one subsequent therapy

Q21. Does this study include pediatric patients?

- No

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

CD19 CAR T is approved in adult relapsed refractory DLBCL patients

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

Baseline characteristics at time of first relapse post CD19 CAR T:
-No of patients
-Age < 60, ≥ 60, median age
-Sex (female)
-race and ethnicity
-ECOG PS 0,1,2,3,4
-Stage of Disease I or II, III or IV
-IPI Score
-LDH
-CD19 and CD20 status positive by flow cytometry, positive by IHC
-bulky disease
-extranodal disease
-prior therapies: ≥ 3 prior lines of therapy, median # of prior lines (range)
-primary refractory disease to initial chemoimmunotherapy
-primary refractory to most recent CD19 CAR T therapy
Treatment:
-time from initial diagnosis to CD19 CAR T treatment
-treatment with Axi-cel, Tiso-cel, or Liso-cel for CD19 CAR T
-second-line vs third-line CAR T
-bridging therapy received and name
-time from CAR T infusion to first relapse post CD19 CAR T
-time from CAR T administration to first novel therapy initiated post CAR T relapse
-name of novel therapy given for relapse post CD19 CAR T
-date of starting and stopping novel therapy post CD19 CAR T
Safety of first novel therapy post CD19 CAR T:
-any grade adverse events
-any ≥ grade 3 adverse events
-hospitalizations or ICU stays
-death attributed to adverse events
Survival (PFS and OS) outcomes to first novel therapy post CD19 CAR T:
-date of progression
-date of last response
-date of death
-date of last contact
Response to first novel therapy post CD19 CAR T:
-overall response rate and best response rate as CR and PR
-time to best response
-duration of response
-time to next treatment

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

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

N/A

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

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

N/A

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

N/A

Q26. REFERENCES:

1. Gisselbrecht C, Glass B, Mounier N, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. J Clin Oncol. 2010;28(27):4184-4190.
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Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

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

Q27a. If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.

-Swetha Kambhampati: None
-Alex Herrera:
Bristol Myers Squibb – research funding, consultancy
Genentech – research funding, consultancy
Merck – research funding, consultancy
Seattle Genetics - research funding, consultancy
KiTE Pharma - research funding
Gilead Sciences – research funding
AstraZeneca – research funding, consultancy
Karyopharm – consultancy
ADC Therapeutics – research funding, consultancy
Takeda – consultancy
Tubulis - consultancy
Regeneron - consultancy
Genmab - consultancy
Pfizer - consultancy
Caribou - consultancy
Adicet Bio - consultancy
Abbvie - consultancy

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

Embedded Data:

N/A

Table 1. Baseline characteristics of the adult patients who received novel agents ((loncastuximab tesirine, polatuzumab vedotin-bendamustine-rituximab, tafasitamab-lenalidomide, selinexor) for DLBCL, high grade B-cell lymphoma, primary mediastinal lymphoma, and FL grade 3B

Characteristic	**N (%)**
No. of patients	520
No. of centers	95
Age at CAR-T cell infusion - median (min-max)	63 (21-86)
Age at CAR-T cell infusion - no. (%)	
18-29	13 (3)
30-39	28 (5)
40-49	60 (12)
50-59	113 (22)
60-69	182 (35)
>=70	124 (24)
Gender - no. (%)	
Male	330 (63)
Female	190 (37)
Performance score prior to CT - no. (%)	
90-100	225 (43)
80	164 (32)
<80	85 (16)
Not reported	46 (9)
HCT-CI - no. (%)	
0	153 (29)
1	84 (16)
2	79 (15)
3+	198 (38)
TBD, unclear lineage of prior hematologic malignancies	2 (0)
Not reported	4 (1)
Recipient race - no. (%)	
White	425 (82)
African American	34 (7)
Asian	20 (4)
Pacific Islander	3 (1)
Natice American	1 (0)
More than one race	7 (1)
Unknown	14 (3)
Not reported	16 (3)
Recipient ethnicity - no. (%)	
Hispanic or Latino	49 (9)

Characteristic	N (%)
Non-Hispanic or non-Latino	441 (85)
N/A - Not a resident of the U.S.	16 (3)
Unknown	14 (3)
Disease status prior to CT - no. (%)	
CR	13 (3)
PR	111 (21)
resistant	346 (67)
untreated	29 (6)
unknown	21 (4)
Product - no. (%)	
Kymriah	141 (27)
Yescarta	305 (59)
Breyanzi	23 (4)
Other	51 (10)
Bridging therapy - no. (%)	
No	331 (64)
Yes	149 (29)
Not reported	40 (8)
Time from diagnosis to CT - no. (%)	
1-12 months	240 (46)
>12 months	280 (54)
Year of CT - no. (%)	
2017	1 (0)
2018	39 (8)
2019	121 (23)
2020	181 (35)
2021	138 (27)
2022	40 (8)
Follow-up among survivors - median (range)	24 (3-48)

Response Summary:

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

Q1. Study Title

Efficacy of hematopoietic stem cell transplantation in patients with plasmablastic lymphoma.

Q2. Key Words

Plasmablastic lymphoma; Autologous stem cell transplant; Allogeneic stem cell transplant

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Adeel Masood, MD
Email address:	amasood2@mdanderson.org
Institution name:	MD Anderson Cancer Center, Houston TX
Academic rank:	Clinical research fellow

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

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Sairah Ahmed, MD
Email address:	sahmed3@mdanderson.org
Institution name:	MD Anderson Cancer Center, Houston TX
Academic rank:	Associate Professor, Department of Lymphoma/Myeloma, Director CART Program MD Anderson Cancer Center

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

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Sairah Ahmed, MD

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

N/A

LETTER OF COMMITMENT:

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

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

Principal Investigator #3:
Krina Patel, MD
E-mail: KPatel1@mdanderson.org
Institution: MD Anderson Cancer Center, Houston TX

Q13. PROPOSED WORKING COMMITTEE:

- Lymphoma

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

- No

Q15. RESEARCH QUESTION:

Outcomes of patients treated with plasmablastic lymphoma with autologous transplant compared to allogeneic transplant.

Q16. RESEARCH HYPOTHESIS:

Hematopoietic stem cell transplantation is an effective option for patients with plasmablastic lymphoma.

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

Suggested word limit of 200 words:

1. Primary: Compare survival between patients who receive autologous SCT in CR1 vs others
2. Compare the survival of patients who receive autoSCT vs alloSCT beyond 1st relapse
3. Secondary:

a. To identify the patient, disease and treatment-related factors that are predictive of relapse, NRM, PFS, and OS across types of transplant and conditioning (RIC vs MAC)

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

This is a rare disease without evidence-based data to guide treatment decisions, this analysis would allow clinicians to lean on solid retrospective registry data to assist in discussing toxicity versus benefits with patients.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

PBL is predominantly a disease of immunocompromised associated with human immunodeficiency virus (HIV), elderly population, or immunosuppressed state related to solid organ transplantation. The PBL cells have a plasmacytic immunophenotype. Since these cells lack CD20 expression, there is no role of anti-CD20 monoclonal antibodies that have revolutionized the treatment of other lymphomas and leukemias. PBL is not only an aggressive disease associated with early relapse and resistance to chemotherapy, but it is also difficult to diagnose due to overlapping diagnostic features with multiple myeloma and lymphomas (1).

Currently, there is no standard of care treatment regimen for PBL. The use of highly active antiretroviral therapy (HAART) in combination with chemotherapy for HIV-positive PBL shows some promise with median overall survival (OS) of 15 months (3-year OS of 25%). In patients with HIV-negative disease, current treatment regimens are associated with median OS of nine months (3-year OS of 10% only). While the outcomes remain dismal with median OS of 3-4 months in untreated patients (1,2).

The role of autoSCT is controversial and one of the earliest single-center experiences from Moffit Cancer Center by Liu et al. 2011 reported nine patients with HIV-negative PBL wherein extra-nodal disease was present in 89% (n=8/9) patients, most common oral-facial and lymph node involvement (55.6% and 44.4%, respectively). Four patients received autoSCT after achieving complete response (CR). Half patients in the autoSCT group received CHOP regimens, while the rest received hyperCVAD. All five patients in the non-transplant group received CHOP regimens. The sample size in this study was too small for inferential statistics but the median survival at the last follow-up was 30.9 months (Range: 13.3-46.7 months) in the autoSCT group compared to 15.5 months (Range: 6.8-73.4 months) in the non-transplant group. The median disease-free survival was almost 16 months in patients receiving autoSCT (Range: 2-38.5 months) (3).

The largest multicenter retrospective study on autoSCT in PBL was reported by Cattaneo et al. 2015 from EBMT (European Society of Blood and Marrow Transplantation). They reported 24 patients (75% males) with a median age of 43 years (Range: 16-63 years). Fifty percent of the patients were in first CR at the time of autoSCT, while 17% were in first partial remission (PR). HIV status was only available for eight patients, of which seven were positive. Almost 30% patients (n=7) relapsed at two years post autoSCT (95% confidence interval (CI); 8%-57%). All relapses occurred within four months of auto SCT, indicating long remission if disease free beyond four months of auto SCT. After a median follow-up of 30 months (Range: 3-132 months), 2-year OS was 53% (95% CI; 28%-73%). This study was significant for the low incidence of relapse and mortality if patients received autoSCT during CR (4).

One Italian single-center experience reported outcomes for 17 newly diagnosed HIV associated PBL, of which five received HDC followed by autoSCT. Three patients received auto SCT as first-line consolidation therapy after the CHOP regimen; all patients achieved a CR. While two patients received autoSCT as second-line treatment after relapse, achieving a second CR. This study was significant for better prognosis associated with a CD4 count of 200 or higher in these patients (5).

Similarly, another multicenter EBMT report published in 2019 by Hubel et al. reported outcomes of autoSCT in lymphomas associated with HIV. PBL was present in 6.8% (n=8/118) of patients in this report. The PFS and OS at two years were reported to be 52% and 70% in PBL patients receiving autoSCT. This study also reported favorable outcomes with a CD4 count of 150 or above in general with HIV-associated lymphomas (6).

The experience with HDC followed by autoSCT in the relapsed setting is rather limited, although there is some suggestion that persistent complete remission can be achieved in chemotherapy-sensitive disease (4). The use of alloSCT in HIV-positive PBL showed limited efficacy. For example, 26.5% of patients (n=314/1185) included in an early EBMT registry matched study on alloSCT in lymphoma comprised of PBL. More than 80% patients had a stage III or IV disease and 12% had CNS involvement. Almost 74% patients were in CR at the time of alloSCT. The 4-year OS was reported 42% while median PFS was reported 7.6 months in patients with PBL in this study. Acute graft vs. host disease was associated with decreased OS but improved relapse rate (HR=0.50, 95%CI;0.39-0.91). Now with the availability of reduced intensity conditioning, alloSCT needs reevaluation in these patients (2,7).

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

N/A

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

Inclusion Criteria:

1. Adult patients (age ≥18) with a diagnosis of PBL from inception.
2. Patients who received hematopoietic stem cell transplant (autologous or allogeneic).
3. Prior response/timing of stem cell transplant (at CR1 vs. other)

Q21. Does this study include pediatric patients?

- No

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

No pediatric population.

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

Main effect:
- Response to SCT
Patient-related:
- Age at SCT (continuous variable)
- Gender: male or female
- Karnofsky performance status at auto SCT: < 80% vs. ≥ 80%
- HCT Co-morbidity index at transplant 0, 1, 2, and > 3
- Additional markers
o LDH,
o baseline inflammatory markers (IL-6, IL-2, serum ferritin, interferon gamma, C reactive protein)
o thrombocytopenia
o neutropenia
o lymphopenia
o anemia
Disease-related:
- Immune status (Deficient vs. competent)
- Immunodeficient (HIV vs. organ transplant vs. others)
- HIV status (positive vs. negative)
- EBV status (positive vs. negative)
- Prior HCT (yes vs. no)
- Stage at diagnosis
- CNS involvement at diagnosis
- Newly diagnosed vs. refractory/relapsed disease
- Number of prior therapies (≤2 vs. ≥3)
- Disease status at the time of SCT: chemo-sensitive vs. non-responsive/refractory
- Extranodal involvement (yes vs. no)
- Bone marrow involvement (yes vs. no)
- Prior CR (yes vs. no)
- Length of prior CR1 (<= 12 vs. >12 months)
Donor-related:
• Donor-recipient gender match: male-male vs. male-female vs. female-male vs. female-female
• Donor-recipient CMV status: +/+ vs. +/- vs. -/+ vs. -/-
Transplant:
- Time from diagnosis to transplantation (continuous variable in months)
- Year of transplant
- Type of transplant (autologous vs. allogeneic)
- Conditioning regimen (myeloablative vs. reduced intensity)
- GVHD prophylaxis in case of alloSCT (tacrolimus/CSA vs. others)
- Graft source (PB vs. BM)
- Donor type (matched related vs. matched unrelated vs. haploidentical vs. cord blood)
- Chemosensitive vs chemorefractory at time of transplant
- Use of ATG/campath/post cytoxan

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

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

NA

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

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

NA

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

NA

Q26. REFERENCES:

1. Castillo JJ, Bibas M, Miranda RN. The biology and treatment of plasmablastic lymphoma. Blood. 2015;125(15):2323-2330. doi:10.1182/blood-2014-10-567479
2. Al-Malki MM, Castillo JJ, Sloan JM, Re A. Hematopoietic cell transplantation for plasmablastic lymphoma: a review. Biol Blood Marrow Transplant. 2014;20(12):1877-1884. doi:10.1016/j.bbmt.2014.06.009
3. Liu JJ, Zhang L, Ayala E, et al. Human immunodeficiency virus (HIV)-negative plasmablastic lymphoma: a single institutional experience and literature review. Leuk Res. 2011;35(12):1571-1577. doi:10.1016/j.leukres.2011.06.023
4. Cattaneo C, Finel H, McQuaker G, Vandenberghe E, Rossi G, Dreger P. Autologous hematopoietic stem cell transplantation for plasmablastic lymphoma: the European Society for Blood and Marrow Transplantation experience. Biol Blood Marrow Transplant. 2015;21(6):1146-1147. doi:10.1016/j.bbmt.2015.03.008
5. Cattaneo C, Re A, Ungari M, et al. Plasmablastic lymphoma among human immunodeficiency virus-positive patients: results of a single center's experience. Leuk Lymphoma. 2015;56(1):267-269. doi:10.3109/10428194.2014.911867
6. Hübel K, Re A, Boumendil A, et al. Autologous stem cell transplantation for HIV-associated lymphoma in the antiretroviral and rituximab era: a retrospective study by the EBMT Lymphoma Working Party. Bone Marrow Transplant. 2019;54(10):1625-1631. doi:10.1038/s41409-019-0480-x
7. Peniket AJ, Ruiz de Elvira MC, Taghipour G, et al. An EBMT registry matched study of allogeneic stem cell transplants for lymphoma: allogeneic transplantation is associated with a lower relapse rate but a higher procedure-related mortality rate than autologous transplantation. Bone Marrow Transplant. 2003;31(8):667-678. doi:10.1038/sj.bmt.1703891

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

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

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

Q27a. If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.

N/A

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

Embedded Data:

N/A

Table 1. Baseline characteristics of adult patients who received HCT for plasmablastic lymphoma

Characteristic	allo	auto	Total
No. of patients	16	117	133
No. of centers	15	77	83
Is recipient on Ted or on CRF? - no. (%)			
TED	15 (94)	110 (94)	125 (94)
CRF	1 (6)	7 (6)	8 (6)
Age at transplant - no. (%)			
Median (min-max)	55 (28-74)	54 (20-76)	54 (20-76)
18-39	5 (31)	24 (21)	29 (22)
40-49	2 (13)	21 (18)	23 (17)
50-59	6 (38)	31 (26)	37 (28)
>=60	3 (19)	41 (35)	44 (33)
Gender of recipient - no. (%)			
Male	10 (63)	92 (79)	102 (77)
Female	6 (38)	25 (21)	31 (23)
Karnofsky score prior to HCT - no. (%)			
90-100%	9 (56)	60 (51)	69 (52)
< 90%	7 (44)	54 (46)	61 (46)
Not reported	0 (0)	3 (3)	3 (2)
Race - no. (%)			
White	12 (75)	77 (66)	89 (67)
Black or African American	2 (13)	11 (9)	13 (10)
Asian	2 (13)	6 (5)	8 (6)
Not reported	0 (0)	23 (20)	23 (17)
Ethnicity - no. (%)			
Hispanic or Latino	4 (25)	28 (24)	32 (24)
Not Hispanic or Latino	9 (56)	63 (54)	72 (54)
NA, non-resident of USA	3 (19)	24 (21)	27 (20)
Not reported	0 (0)	2 (2)	2 (2)
CCN region - no. (%)			
US	13 (81)	89 (76)	102 (77)
Canada	1 (6)	12 (10)	13 (10)
Asia	0 (0)	1 (1)	1 (1)
Australia/New Zealand	1 (6)	1 (1)	2 (2)
Mideast/Africa	1 (6)	1 (1)	2 (2)
Central/South America	0 (0)	13 (11)	13 (10)
Donor - no. (%)			
HLA-identical sibling	4 (25)	0 (0)	4 (3)

Characteristic	allo	auto	Total
Matched Unrelated Donor (MUD)	1 (6)	0 (0)	1 (1)
HLA-mismatched relative	5 (31)	0 (0)	5 (4)
HLA matched unrelated	4 (25)	0 (0)	4 (3)
HLA mismatched unrelated	2 (13)	0 (0)	2 (2)
Not reported	0 (0)	117 (100)	117 (88)
Graft source - no. (%)			
Peripheral blood	16 (100)	117 (100)	133 (100)
Disease status prior to HCT (NHL/HD) - no. (%)			
CR	8 (50)	68 (58)	76 (57)
PR	4 (25)	43 (37)	47 (35)
Chemoresistant	4 (25)	5 (4)	9 (7)
Unknown	0 (0)	1 (1)	1 (1)
Time from diagnosis to transplant, months - median (min-max)	20 (6-90)	9 (3-104)	10 (3-104)
Transplant year - no. (%)			
2018	0 (0)	26 (22)	26 (20)
2019	4 (25)	25 (21)	29 (22)
2020	3 (19)	22 (19)	25 (19)
2021	7 (44)	24 (21)	31 (23)
2022	2 (13)	20 (17)	22 (17)
Follow-up among survivors - median (range)	12 (3-13)	14 (1-49)	13 (1-49)

Response Summary:

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

Q1. Study Title

Secondary malignant neoplasms after CD-19 CAR-T cell therapy in Large B cell lymphoma

Q2. Key Words

Secondary malignant neoplasm, secondary malignancies, CAR-T, Non-Hodgkin Lymphoma, Large B cell lymphoma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Sushanth Gouni, MD
Email address:	sgouni@mdanderson.org
Institution name:	MD Anderson Cancer Center
Academic rank:	Fellow

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

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Sairah Ahmed, MD
Email address:	sahmed3@mdanderson.org
Institution name:	MD Anderson Cancer Center
Academic rank:	Associate Professor

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

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Sairah Ahmed, MD

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

N/A

LETTER OF COMMITMENT:

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

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

- Dr Ahmed – chair for CICWC, 2 ongoing proposals pending

Q13. PROPOSED WORKING COMMITTEE:

- Lymphoma

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

- No

Q15. RESEARCH QUESTION:

What is the frequency of secondary malignant neoplasms, particularly subsequent myeloid neoplasms after CAR-T cell therapy in Large B cell lymphoma?

Q16. RESEARCH HYPOTHESIS:

Both patient and disease-related factors impact the development of secondary neoplasms (SN), particularly subsequent malignant myeloid neoplasms (SMN) in patients who receive commercial chimeric antigen receptor (CAR) T-cell therapy, Axicabtagene ciloleucel (Yescarta®, Axi-cel), Tisagenlecleucel (Kymriah, Tisa-Cel), or Lisocabtagene maraleucel (Breyanzi, Lisa-Cel) in large B cell lymphoma (LBCL). We hypothesize that the analysis of these factors can help predict patients who may later develop SN and SMNs.

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

Suggested word limit of 200 words:

- Primary: Clinical and laboratory characteristics of Large B-cell lymphoma patients who developed therapy related SN and SMN following CAR-T cell therapy
- Secondary: Characteristics and outcomes of patients who develop SN and SMN following CAR-T cell therapy

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

A systematic study of SN, particularly SMN after receipt of CAR-T cell therapy has not been performed to date. As more patients receive CAR-T due to expanding FDA approvals, data on SN and SMN incidence, risk-factors and surveillance are going to be an essential component of long-term survivorship outcomes.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

CAR-T cell therapy has represented a paradigm shift in the treatment landscape for patients with relapsed/refractory (R/R) Non-Hodgkin lymphomas. CD-19 directed CAR-T cell therapies have well described acute toxicities including cytokine release syndrome (CRS) and Immune effector cell-associated neurotoxicity syndrome (ICANS), but long term-adverse events are less well described but include sustained cytopenias and immunosuppression(1,2). One such long term-adverse income of interest is the development of therapy related development of secondary neoplasms (SN) and subsequent myeloid neoplasms (SMN), a well described event after the receipt of agents such as chemotherapy, radiation, and stem cell transplantation (3,4).

The pivotal CAR-T studies leading to the approval of CD-19 CAR-T directed therapies did not report the development of SN or SMN as an adverse event (5-7). Long-term safety data from ZUMA-1 reported development of myelodysplastic syndrome (MDS) in one patient at 19 months, which was attributed to prior cytotoxic therapy (8). Long-term follow up in the JULIET cohort reported 3 cases of prostate cancer (2%), 1 case of invasive breast ductal carcinoma (0.8%) and 1 case of neuroendocrine carcinoma (0.8%). 9 2 cases of MDS (1.7%) and 1 case of AML (0.8%) were also reported as adverse events after Tisa-cel infusion, regardless of study drug relationship. Long-term data for TRANSCEND study are still pending, but preliminary results of 2 year follow up suggest no signal related to SMN and SN.

A study cohort of 86 patients with relapsed/refractory ALL, NHL and CLL treated with CD-19 directed CAR-T cells in a phase I/II clinical trial reported a 15% incidence (13 patients) of subsequent malignancies (10). 5 patients (6%) developed hematological cancers including 4 cases of MDS and 1 case of multiple myeloma. 8 patients developed solid tumors including 6 (7%) with non-melanoma skin cancer, 1(1%) with melanoma and 1 (1%) with non-invasive bladder cancer. It is unclear at this time if a causal relationship can be established between the development of secondary malignancy and CAR-T exposure as a subset of these patients had prior cytogenic abnormalities and extensive prior cytotoxic therapies including auto/allogenic stem cell transplantation. More recently, Alkhateeb and colleagues reported on therapy-related myeloid (t-MN) neoplasms following CAR-T cell therapy (11). Here, of the 189 patients that received commercially available CAR-T products, 10 (5.3%) developed t-MN and had a short-interval from CAR-T infusion to the development of t-MN (median time 9.1 months) with 60% of patients developing t-MN within 1 year of CAR-T infusion.

Since secondary malignancies are relatively rare events, and there is a theoretical risk of malignancies due to genetically modified cellular therapies and sustained immunosuppression, follow up of ongoing clinical trials and epidemiologic data are needed to accurately estimate the risk of second cancers after CAR-T cell therapy such that appropriate measures are taken for screening and preventative care.

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

N/A

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

1. Adult patients (age >/= 18) who received CAR-T cell therapy for LBCL between 2013-2022.
2. Eligible Diagnosis: DLBCL, t-FL, high grade B cell lymphoma, and PMBCL
3. CD19 CAR-T cell therapy with either axi-cel, tisa-cel or liso-cel

Q21. Does this study include pediatric patients?

- No

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

N/A

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

Patient- Related Variables:
- Age at lymphoma diagnosis: 18-29, 30-39, 40-49, 50-59, 60-69, >=70
- Age at CAR T-cell infusion: 18-29, 30-39, 40-49, 50-59, 60-69, >=70
- Gender: male vs female
- Race: Caucasian vs. African American vs. Hispanic vs. Asian vs. other vs. missing
- Body Mass Index
- Karnowski Performance Status Score: <80% vs 80% vs 90-100%
- Comorbidities: as defined by the Y/N, details of comorbidities
- HCT-CI: 0 vs 1-2 vs >=3 vs missing

Lymphoma Disease- Related Variables:
- Disease histology / subtype Disease classification: Diffuse, large B-cell lymphoma vs. T-cell/histiocytic rich large B-cell lymphoma vs. Primary mediastinal (thymic) large B-cell lymphoma vs. Diffuse, large B-cell lymphoma - germinal center B-cell type vs. Diffuse, large B-cell lymphoma - activated B-cell type vs. EBV+ DLBCL, NOS vs. High-grade B-cell lymphoma, NOS vs. High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements
- Double/triple hit at initial diagnosis of the primary disease: neither vs. double/triple hit
- Transformed lymphoma: Y/N, follicular vs non-follicular

-Disease burden prior to CAR T-cell infusion:
- % involvement of the bone marrow; bulky

- Size of the largest nodal mass at the time of CT disease)
- Disease stage-, IPI score at diagnosis
- Presence of central nervous system disease at diagnosis / CT infusion: Y/N,
- Presence of extra-medullary disease at diagnosis / CT infusion: Y/N
- Laboratory Markers at diagnosis / CT infusion:
- C-reactive protein
- LDH
- ferritin (all baseline / prior to CAR T-cell infusion)
- LDH prior to CT
- Prior lines of therapy including HCT: 1-2 vs 3-4 vs >4

-Prior treatment:
- systemic chemotherapy: Y/N,
- radiotherapy: Y/N,
- Prior HCT: autologous vs and / or allogeneic HCTvs both

-Disease status prior to CAR T-cell therapy: CR, PR, relapse, refractoryCR1 vs CR2 vs >CR2 vs 1st relapse vs >1st relapse

-Prior acute or chronic graft versus host disease, max grade

-Bridging systemic therapy (Y/ N)

-Bridging radiotherapy (Y/ N)

CAR T-cell therapy Related Variables:
- CAR T-cell product
- Time from diagnosis to treatment CT infusion
- Year of CT, CAR T-cell dose
- Costimulatory domain
- Lympho-depletion chemotherapy (Y/ N)
- Flu/Cy, Bendamustine other
- D30 response: CR vs PR vs Progressive disease,
- D30: Hemoglobin, WBC, ANC and Platelet counts
- D100 response: CR vs Progressive disease
- D100: Hemoglobin, WBC, ANC and Platelet counts

Bone marrow evaluation at time of SMN diagnosis:
- Bone Marrow Blasts%
- Bone marrow cellularity
- Cytogenetics
- NGS mutations
- % of BM involvement by lymphoma

SN variables
- Age at secondary malignancy diagnosis
- Phenotype of disease/ Tumor histology
- Stage of disease
- Site of disease
- Cytogenetics
- NGS mutations
- Primary cause of death.

Outcomes

1. CAR T-cell Toxicity: Overall incidence of toxicities, including CRS, ICANS and prolonged cytopenias at Day +30 and Day +100

a.CRS: will be graded according to ASTCT criteria and reported as all grades and grades > 3. Grades III-V CR Time to develop CRS and time to resolution will also be described. Additionally, overall treatment, maximum grade and duration of CRS will also be used to determine severity.

b.ICANS: will be graded according to ASTCT criteria and reported as all grades and grades > 3. Time to develop ICANS and time to resolution will also be described. Additionally, overall treatment, maximum grade and duration of ICANS will also be used to determine severity.

c.Grades III-V hematologic toxicity Prolonged Cytopenias: it is defined as lack of hematologic recovery (ANC>500 and Plt>20,000/mcl) by day 30 post CAR T cell.

d.Hematologic Recovery: time to hematologic recovery including ANC >500 and Plt >20,000 will be described. The proportion of patients who recover but subsequently develop grade 4 cytopenias will be described as well.

2. Treatment-related mortality (TRM): Deaths occurring in patients without disease relapse at Day +100 and Day +365
3. Relapse: cumulative incidence of relapse (at Day +365)
4. Overall response rate and complete remission rate: this is defined as the best response either as a CR or CR and partial response (CR+PR) after CAR T cell infusion.
5. Duration of Response: this outcome are for patients who achieve a CR or PR and it is defined as the time from achieving these responses to the time of treatment failure, i.e. disease relapse or progression, or death.
6. Disease-free survival: composite endpoint with disease relapse and death of any cause
7. Overall survival: time to death of any cause

8. Cause of death: primary and contributing cause of death

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

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

N/A

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

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

N/A

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

N/A

Q26. REFERENCES:

1. Penack O, Koenecke C. Complications after CD19+ CAR T-Cell Therapy. Cancers (Basel). Nov 19 2020;12(11)doi:10.3390/cancers12113445
2. Chakraborty R, Hill BT, Majeed A, Majhail NS. Late Effects after Chimeric Antigen Receptor T cell Therapy for Lymphoid Malignancies. Transplant Cell Ther. 03 2021;27(3):222-229. doi:10.1016/j.jtct.2020.10.002
3. Ziegler AK, Abend M, Port M, et al. Cumulative dosages of chemotherapy and radiotherapy exposure, and risk of secondary malignancies after allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant. 04 2019;54(4):635-640. doi:10.1038/s41409-018-0359-2
4. Xu Y, Wang H, Zhou S, et al. Risk of second malignant neoplasms after cyclophosphamide-based chemotherapy with or without radiotherapy for non-Hodgkin lymphoma. Leuk Lymphoma. Jul 2013;54(7):1396-404. doi:10.3109/10428194.2012.743657
5. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 01 03 2019;380(1):45-56. doi:10.1056/NEJMoa1804980
6. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. N Engl J Med. 12 28 2017;377(26):2531-2544. doi:10.1056/NEJMoa1707447
7. Abramson JS, Palomba ML, Gordon LI, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. Lancet. 09 19 2020;396(10254):839-852. doi:10.1016/S0140-6736(20)31366-0
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9. Schuster SJ, Tam CS, Borchmann P, 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. 10 2021;22(10):1403-1415. doi:10.1016/S1470-2045(21)00375-2
10. Cordeiro A, Bezerra ED, Hirayama AV, et al. Late Events after Treatment with CD19-Targeted Chimeric Antigen Receptor Modified T Cells. Biol Blood Marrow Transplant. 01 2020;26(1):26-33. doi:10.1016/j.bbmt.2019.08.003
11. Alkhateeb HB, Mohty R, Greipp P, et al. Therapy-related myeloid neoplasms following chimeric antigen receptor T-cell therapy for Non-Hodgkin Lymphoma. Blood Cancer J. 07 26 2022;12(7):113. doi:10.1038/s41408-022-00707-4

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

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

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

Q27a. If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.

N/A

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

Embedded Data:

N/A

Table 1. Baseline characteristics of adult patients who received CAR-T for DLBCL, T-FL, HGBCL and PMBCL with Kymriah, Yescarta, and Breyanzi

Characteristic	**N (%)**
No. of patients	4751
No. of centers	121
Level Age at CT Treatment - median (min-max)	64 (18-91)
Age at CAR-T cell infusion - no. (%)	
18-29	130 (3)
30-39	233 (5)
40-49	427 (9)
50-59	1010 (21)
60-69	1652 (35)
>=70	1299 (27)
Gender - no. (%)	
Male	3008 (63)
Female	1742 (37)
Not reported	1 (0)
Performance score prior to CT - no. (%)	
90-100	1855 (39)
80	1472 (31)
<80	988 (21)
Not reported	436 (9)
HCT-CI - no. (%)	
0	1382 (29)
1	922 (19)
2	640 (13)
3+	1733 (36)
TBD, unclear lineage of prior hematologic malignancies	23 (0)
TBD, inconsistencies between parent and child-questions	3 (0)
Not reported	48 (1)
Recipient race - no. (%)	
White	3876 (82)
African American	268 (6)
Asian	245 (5)
Pacific Islander	8 (0)
Natice American	18 (0)
More than one race	30 (1)
Unknown	218 (5)
Not reported	88 (2)

Characteristic	N (%)
Recipient ethnicity - no. (%)	
Hispanic or Latino	520 (11)
Non-Hispanic or non-Latino	4022 (85)
N/A - Not a resident of the U.S.	46 (1)
Unknown	162 (3)
Not reported	1 (0)
Disease status prior to CT - no. (%)	
CR	240 (5)
PR	1033 (22)
resistant	3010 (63)
untreated	247 (5)
unknown	221 (5)
Product - no. (%)	
Kymriah	1029 (22)
Yescarta	3379 (71)
Breyanzi	343 (7)
Bridging therapy - no. (%)	
No	3025 (64)
Yes	1152 (24)
Not reported	574 (12)
Time from diagnosis to CT - no. (%)	
1-12 months	1987 (42)
>12 months	2762 (58)
Not reported	2 (0)
Subsequent neoplasms - no. (%)	
No	3796 (80)
Yes	184 (4)
Not reported	771 (16)
Year of CT - no. (%)	
2017	5 (0)
2018	497 (10)
2019	943 (20)
2020	1064 (22)
2021	1048 (22)
2022	1194 (25)
Follow-up among survivors - median (range)	14 (0-52)