MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
Orlando, Florida
Wednesday, February 15, 2023, 1:00-3:00 pm

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Incoming Co-Chair:	**Mazyar Shadman, MD, MPH, Fred Hutchinson Cancer Center, WA; Telephone: 206-667-5467; E-mail: mshadman@fredhutch.org**
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1. **Introduction**

   The CIBMTR Hodgkin and Non-Hodgkin Lymphoma Working Committee was called to order at 1 pm on Wednesday, February 15, 2023, by Dr. Mehdi Hamadani. Dr. Alex Herrera introduced the working committee leadership, and highlighted leadership's conflict of interest disclosures per CIBMTR policy. Dr. Herrera 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. Herrera also detailed the LYWC study life cycle and introduced PRO data collection effort of CIBMTR to audience followed by encouragement to propose studies that can encompass PRO data. Then Dr. Hamadani provided gratitude to outgoing chair - Dr. Kharfan Dabaja for his contributions to LYWC on behalf of CIBMTR. Dr. Hamadani provided an update on the Working Committee productivity including 2 publications, 2 presentations at EBMT 2022 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.

2. **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***

3. Studies in progress

(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.**

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

Dr. Mehdi Hamadani emphasized the availability of published datasets freely available to the public for secondary analysis. Also, explained the difference between the TED and CRF databases. It was emphasized that CRF is a subset of the TED database, and that the CRF forms collect all disease specific information such as lines of therapy, extranodal involvement, and prior radiation. If a study needs any of this information, CRF level data is needed on the study.

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

5. Future/proposed studies

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

(a) **Xia Bi:** Outcomes of allogenic stem cell transplant for large B-cell lymphoma progression after CAR T-cell therapy (Xia Bi/Dipenkumar Modi/Baldeep Wirk/Usama Gergis)
Dr Bi presented the concept in-person. The proposed study wants to look the outcomes of allo-HCT for large B-cell lymphoma (LBCL) progressing after commercial CAR-T cell therapy with the hypothesis that allo-HCT can provide long-term disease control and remains a viable option in selected patients with LBCL progressing after anti-CD19 CAR-T cell therapy. A total of 58 cases met the selection criteria for the study but impact of database transitioning on small number of cases found in retrieval was emphasized for which information for actual data file preparation

and study analysis was also provided that data for all cases reported to CIBMTR meeting eligibility criteria for study will be used if proposal is accepted.
The proposal was opened for questions from the audience. A clarification was requested if study is only focusing on allo-HCTs performed post CAR-T therapy relapse only and not with intent of consolidation which was responded as allo-HCT performed after relapse will be focused only. Another question raised was if therapies given to patients between post CAR-T therapy relapse and prior to auto-HCT will be looked upon. Frequencies of TED and CRF track patients for sample size was brought into attention. Requested data for CRF track patients can be provided. In addition to this, data collection on all CAR-Ts was also discussed with pivotal point that not all CAR-Ts are captured by CIBMTR but if they are captured followed by collection of subsequent transplant information, requested information will be available based on TED or CRF track assigned to the recipient**.** A suggestion from audience was received to wait for some years to get a greater number of patients and to avoid overlapping of patient data because there could be a possibility of data for these patients being reported to multi-centers. Another question was raised regarding identification of denominator which is not addressed in Dr. Zurko's paper about how many patients progressing after CAR-T infusion are receiving transplant. Dr. Hamadani emphasized importance of finding denominator number along with difficulties associated in the possible ways of finding it by prioritizing CAR-T over HCT database or by prioritizing HCT over CAR-T database along with limitation that not all CAR-Ts are reported to CIBMTR.

(b) **Razan Mohty**: Outcomes following CD19 Directed Chimeric Antigen Receptor (CAR) T-cell Therapy for Relapsed Refractory Follicular Lymphoma (Razan Mohty/ Aleksandr Lazaryan/ Swetha Kambhampati/ Alex Herrera)
Dr. Razan presented the proposal on behalf of study group. The proposed study hypothesizes that real-world safety and efficacy outcomes of CD19 CAR-T cell therapy as standard of care for relapsed/refractory follicular lymphoma are similar to data from pivotal clinical trials; and predictors of toxicity and efficacy following anti-CD19 CAR-T cell therapy for follicular lymphoma might be different from other types of non-Hodgkin lymphoma. A total of 333 patients met the eligibility criteria for the study.
The proposal was opened for questions from the audience. A member of audience asked about grades of follicular lymphoma included in the study. It includes patients of all grades of follicular lymphoma except transformed follicular lymphoma cases. A suggestion was received to present numbers in categories of follicular lymphoma grade for better understanding. Another question was raised regarding shorter median follow-up times and was answered as by the time study will be analyzed, there will be longer follow-up time. A question regarding assignment of 6 months' time-period for toxicity-free, progression free survival (TPFS) was raised. Dr. Mohty brought up toxicities included for TPFS outcome which are only grade III CRS and grade III ICANS that usually develops within specified time-period. A suggestion was received to include B-cell cytopenia aplasia in this outcome. Another question raised was if there are enough TED or CRF patients to perform study which was answered as cellular therapy cases are all research level patients so there is no categorization of TED and CRF track for cellular therapy cases. Question from virtual audience was also addressed regarding very few patients for Tisa-cell product in study which got excluded due to a contract with manufacturing company but can be added into the study once permission is received. Another question was raised if outcomes in research performed at Moffitt center were evaluated at earlier time-points of 3 and 6 months. Dr. Mohty responded that outcomes were only evaluated for diffuse large B-cell lymphoma (DLBCL) at earlier time-points and were also found strongly associated.

(c) **Amrita Goyal:** Allogeneic hematopoietic stem cell transplantation for advanced mycosis fungoides and Sezary syndrome (Amrita Goyal/Firas Safa/Nakhle Saba/ Francine Foss)
Dr. Goyal presented the concept to the audience. This study hypothesizes that allogenic HSCT is an effective treatment and curative modality for advanced mycosis fungoides (MF) and Sezary syndrome (SS). Advances in donor selection, GVHD prophylaxis, and supportive care over the last decade have resulted in improved outcomes of allo-transplant for MF/SS. A total of 349 and 150 cases were found for MF and SS respectively in CIBMTR database which were eligible for the study.
Study was opened for questions. A suggestion was received to start study years from 2008 instead of 2001 since there has been a lot of change in clinical practice since then and there were only 5% cases from those years so exclusion of those cases will not even cause much loss of follow-up. A concern was raised regarding frequencies of conditioning regimen where a very few cases received Myeloablative conditioning regimen and could be for younger patients only; all of which implies concern on the type and timing of complete or partial remission achieved corresponding to conclusion longer the time to transplant, more likely the response is slow. Dr. Hamadani responded that lines of therapies on CRF track and time interval from diagnosis to transplant can address this issue. A suggestion was received that looking on TBI and non-TBI frequencies can also be helpful for this. Dr. Goyal also informed that study would exclude CDA-positive aggressive epidermotropic CTCL. A suggestion was received that keeping transformation of disease can be an important factor to consider during the final analysis if that information is collected. Another question was asked if CRF forms collect MOGA usage and if that data will be included to shed light on GVHD. Dr. Hamadani informed about a pharma-funded study related to MOGA use in process and mentioned that required information related to MOGA can also be obtained from that study once complete.

Dr. Sauter presented last 3 proposal concepts.

(d) **Swetha Kambhampati:** Outcomes of novel therapies post CD19 CAR-T in DLBCL (Swetha Kambhampati/ Alex Herrera)
Dr. Kambhampati presented the proposal. The study hypothesizes that novel standard of care therapies such as Lonca-T, Pola-BR, Tafa-len, and Selinexor will be safe and efficacious in the post CT19 CAR-T setting but with limited duration of benefit. A total of 520 patients were eligible for study. The proposal was opened for questions and discussions.
A question was raised regarding quality of data collection for this topic since this data has never been looked before. Dr. Herrera answered that from collection of lines of therapies and sequencing data, response to each line of therapies can be looked upon. Dr. Hamadani explained forms capture response to therapy but how well that response is capture is unknown because of less usage of that data in CIBMTR research studies. Timeline at which forms are collected by CIBMTR was described and information related to consideration of 90% completeness index for research study was also provided. Another question was raised regarding collection of data on CD19 target biopsy results which was answered as no. It was discussed as a relevant topic because in practice, all cases go through biopsy, but no data collection of this result is one of the limitations. Dr. Dabaja suggested to look on number of patients who relapsed post CAR-T, survived for 12-18 months and got allogeneic transplant. A

question was asked by virtual audience if all prior lines of therapies are captured by CIBMTR which was answered as yes.

(e) **Sairah Ahmed:** Outcomes of Hematopoietic stem cell transplantation in patients with plasmablastic lymphoma (Adeel Masood/Sairah Ahmed)
Dr. Ahmed presented the concept to the audience that role of stem cell transplantation (SCT) is unclear with conflicting data of which patients may benefit from SCT as consolidation in first complete remission or in the salvage setting. The study hypothesize that analysis of patient and disease-related factor may help predict the patients who have improved outcomes after SCT for plasmablastic lymphoma. A total of 133 patients were eligible for study. The proposal was opened for questions and discussions.
Clarification was made that all transplants will be selected including first and beyond at patient level. A concern was raised on short duration of time from diagnosis to auto transplant. Dr. Ahmed proposed the possibility of transplant in first complete remission. She mentioned as per recent studies early-stage disease which has been found having better overall response post-transplant than overall survival and progression-free-survival. She also proposed the possibility of quick relapse post-transplant after achieving complete remission. Dr. Hamadani brought up lines of therapies and disease status prior to transplant for lymphoma captured on TED track from 2018 onwards and mentioned that information is accessible though TED track database.

(f) **Sushanth Gouni:** Secondary malignancies after CD-19 CAR-T cell therapy in Large B cell Lymphoma (Sushanth Gouni/Sairah Ahmed)
Dr. Gouni presented the concept to the audience. The study hypothesizes that the analysis of patient and disease-related factors may help predict the later development of secondary malignant neoplasms\subsequent myeloid neoplasms after CAR-T cell therapy. A total of 4751 patients met the eligibility criteria for the proposal. The proposal was opened for questions and discussions.
A comment was made for consideration of causation and association of events to ascertain correct recognition of secondary malignancies on carried-over malignancies for centralizing the analysis. A question was raised regarding which lines of therapies will be considered for the study for which a suggestion was that lines of therapies can be added in risk models. Another question was asked about ways to find out if secondary malignancies are developing causatively or co-incidentally. Shorter follow-up among cases was also a concern and was discussed. Another question was if forms are contemporary enough to capture next generation sequencing (NGS) data. Dr. Hamadani reported that NGS data is not collected but biopsy results can be requested from centers. Such reports are usually submitted to CIBMTR and in case of missingness, centers can be contacted via emails. Another question was raised if specificity of neoplasms will be reported in the results which was answered as yes.

Ongoing study presentation:

Mazyar Shadman: LY22-01- Outcome of patients with large cell lymphoma receiving ASCT vs. CAR-T therapy while in CR (Mazyar Shadman/Mehdi Hamadani):
The study hypothesizes that in patients with large B-cell lymphoma who are in a complete remission, autologous hematopoietic cell transplant (auto-HCT) consolidation provides a better progression-free survival (PFS) and overall survival (OS) compared to chimeric antigen receptor

(CAR) T-cell therapy (CAR-T). Primary objectives of the study are to evaluate PFS and OS along with secondary objectives looking at hematopoietic recovery, non-relapse mortality, cumulative incidence of disease relapse or progression and causes of death. A total of 79 and 282 patients met criteria for CAR-T and ASCT cohorts in study respectively.
Question was raised regarding validation of final numbers (n=79) out of around 6000 people who underwent cellular therapy. Attention was brought to non-CR exclusions in the selection criteria and was related to real-world scenarios of CR and non-CR disease status prior to transplant. Another question was raised regarding possible biasing based on difference in CR for ASCT and CAR-T which even goes beyond for partial remission patients. Dr. Hamadani mentioned it as one of the limitations but also suggested a way to look at nodal mass at time of transplant for determination. Other suggestion was received to monitor lines of therapies, response to last line of therapy, timings of therapies, and scanning results along with nodal mass monitoring. Another suggestion was provided regarding safety of lumping Kymriah and Yescarta in one cohort against ASCT because both products have different efficacy in the real-world.

Proposed studies; not accepted for consideration at this time

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

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

7. Other Business

After the proposals were presented, the voting process was reiterated, and the working committee leadership invite the attendees to rate each new proposal using the Tandem App. Without additional comments, the meeting was adjourned at 3:52 pm.

Working Committee Overview Plan 2023-2024		
Study number and title	**Status**	**Chairs priority**
LY20-02: Outcomes of allogeneic transplants in patients with hodgkin lymphoma in the era of checkpoint inhibitors: A joint CIBMTR and EBMT analysis.	Manuscript preparation	1
LY22-01: Outcomes of CD19 CAR-T in patients who achieve complete remission prior to lymphodepletion in patients with aggressive non-Hodgkins lymphoma.	Data file preparation	2
LY22-02: Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with primary and secondary central nervous system involvement.	Protocol development	3
LY23-01: Efficacy of hematopoietic stem cell transplantation in patients with plasmablastic lymphoma.	Protocol development	4