Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
Houston, TX
Thursday, February 21, 2019 12:15-2:15 pm

Co-Chair:	**Anna Sureda, MD, PhD, Hospital Duran i Reynals, Barcelona, Spain; Telephone: +34 9326 07750; E-mail: asureda@iconcologia.net**
Co-Chair:	**Timothy Fenske, MD, Medical College of Wisconsin, Milwaukee, WI; Telephone: 414-805-4633; E-mail: tfenske@mcw.edu**
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:	**Carlos Litovich, MPH, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0660; E-mail: clitovich@mcw.edu**

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1. **Introduction**
   a. Minutes and Overview Plan from February 2018 meeting (Attachment 1)

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

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

   a. **LY06-03** Sureda A, Zhang M-J, Dreger P, Carreras J, Fenske T, Finel H, Schouten H, Montoto S, Robinson S, Smith SM, Boumedil A, Hamadani M, Pasquini MC. Allogeneic hematopoietic stem cell transplantation for relapsed follicular lymphoma: A combined analysis on behalf of the Lymphoma Working Party of the EBMT and the Lymphoma Committee of the CIBMTR. **Cancer. 2018 Apr 15; 124(8):1733-1742.**
   b. **LY16-03** Dreger P, Sureda A, Ahn KW, Eapen M, Litovich C, Finel H, Boumendil A, Gopal A, Herrera AF, Schimd C, Diez-Martin JL, Fuchs E, Bolaños-Meade, J, Gooptu M, Al Malki MM, Castagna L, Ciurea SO, Dominetto A, Blaise D, Ciceri F, Tischer J, Corradini P, Montoto S, Robinson S, Gülbas Z, Hamadani M. Outcome of patients who have undergone haploidentical stem cell transplantation for diffuse large B cell lymphoma: A retrospective study of the CIBMTR Lymphoma WC and the EBMT Lymphoma WP (P Dreger/A Sureda) **Blood Advances (In Press).**
   c. **LY16-04** Smith SM, Godfrey J, Ahn KW, DiGilio A, Ahmed S, Agrawal V, Bachanova V, Bacher U, Bashey A, Bolaños-Meade J, Cairo M, Chen A, Chhabra S, Copelan E, Dahi PB, Aljurf M, Farooq U, Ganguly S, Hertzberg M, Holmberg L, Inwards D, Kanate AS, Karmali R, Kenkre VP, Kharfan-Dabaja MA, Klein A, Lazarus HM, Mei M, Mussetti A, Nishihori T, Ramakrishnan Geethakumari P, Saad A, Savani BN, Schouten HC, Shah N, Urbano-Ispizua A, Vij R, Vose J, Sureda A, Hamadani M.

Autologous transplantation versus allogeneic transplantation in patients with follicular lymphoma experiencing early treatment failure. **Cancer. 2018 Jun 15; 124(12):2541-2551.**

d. **LY17-01** Shah NN, Ahn KW, Litovich C, Fenske TS, Ahmed S, Battiwalla M, Bejanyan N, Dahi PB, Bolaños-Meade J, Chen AI, Ciurea SO, Bachanova V, DeFilipp Z, Epperla N, Farhadfar N, Herrera AF, Haverkos BM, Holmberg L, Hossain NM, Kharfan-Dabaja MA, Kenkre VP, Lazarus HM, Murthy HS, Nishihori T, Rezvani AR, D'Souza A, Savani BN, Ulrickson ML, Waller EK, Sureda A, Smith SM, Hamadani M. Outcomes of Medicare-age eligible NHL patients receiving RIC allogeneic transplantation: A CIBMTR analysis. **Blood Advances. 2018 Apr 24; 2(8):933-940.**

e. **LY17-03** Epperla N, Kwang AW, Litovich C, Kharfan-Dabaja MA, Smith SM, Sureda A, Fenske TS, Hamadani M. Impact of allogeneic hematopoietic cell transplantation on the outcomes of Angioimmunoblastic T-cell lymphoma. **Journal of Hematologic Oncology (In Press).**

f. **LY17-03** Impact of allogeneic hematopoietic cell transplantation on the outcomes of Angioimmunoblastic T-cell lymphoma (N Epperla) **Accepted for oral presentation at the 2018 American Society of Hematology Meeting in San Diego, December 2018.**

4. Studies in progress (Attachment 3)

a. **LY16-02** Comparison of alternative donor source stem cell transplant versus matched related donor stem cell transplant for hodgkin lymphoma (S Ahmed/J Kanakry) **Analysis**

b. **LY17-01b** Clinical outcomes of patients age >=65 undergoing allogeneic hematopoietic cell transplant for non-hodgkin lymphoma (N Shah) **Manuscript Preparation**

c. **LY17-02** Allografts in lymphoma following reduced intensity conditioning (N Ghosh/S Ahmed) **Data File Preparation**

d. **LY18-01** Outcomes in b cell non-hodgkin lymphoma patients who underwent autologous stem cell transplantation following rituximab containing conditioning regimens (D Jagadeesh/N Majhail/B Hill) **Protocol Development**

e. **LY18-02** Effect of time to relapse on overall survival in mantle cell lymphoma patients following frontline autologous stem cell transplant (P Riedell/S Smith) **Protocol Development**

f. **LY18-03** Does outcome after allogeneic hematopoietic stem cell transplant differ between patients with de novo diffuse large b-cell lymphoma and transformed diffuse large b cell lymphoma arising in the setting of indolent lymphoma (A Herrera) **Protocol Development**

g. **LY18-G1** Maintenance therapies for Hodgkin and non-Hodgkin lymphomas after autologous transplantation: a consensus project of ASBMT, CIBMTR and EBMT (M Hamadani) **Manuscript Preparation**

5. Future/proposed studies

a. **PROP 1808-02** Evaluating the efficacy of high-dose therapy and autologous hematopoietic cell transplantation for gray zone lymphoma or aggressive B-cell lymphoma with features intermediate between diffuse large B- cell and hodgkin lymphoma. (Kharfan-Dabaja, Ayala, Murthy) (Attachment 4)

b. **PROP 1809-01** Post-transplant cyclophosphamide-based haploidentical transplantation versus matched sibling or well matched unrelated donor transplantation for peripheral T-cell Lymphoma: A CIBMTR Lymphoma working committee & EBMT Lymphoma working party analysis (Dreger, Hamadani) (Attachment 5)

c. **PROP 1810-02/1811-56** Evaluating the impact of checkpoint inhibitor exposure on the outcomes of allogeneic hematopoietic cell transplantation in patients with hodgkin lymphoma; Outcomes of allogeneic HCT in patients with hodgkin lymphoma in the era of checkpoint inhibitors (Awan, Perales, Sureda) (Attachment 6)

d. **PROP 1810-07** Autologous transplantation vs allogeneic transplantation in patients with angioimmunoblastic t-cell lymphoma (Epperla) (Attachment 7)
e. **PROP 1811-08/1811-191** An evaluation of the use and impact of post-transplant brentuximab vedotin in patients with classical Hodgkin lymphoma; The use of hematopoietic stem cell transplant for hodgkin lymphoma: an analysis of treatment patterns in the modern era of novel agents (Cohen, Parsons, Kumar, Hahn; Smith) (Attachment 8)
f. **PROP 1811-19/1811-156** The impact of conditioning regimens on outcomes of autologous hematopoietic stem cell transplantation in peripheral t cell lymphoma; Impact of conditioning regimen on outcomes for patients with peripheral T-cell lymphoma undergoing high-dose therapy with autologous hematopoietic cell transplantation (Jagadeesh, Majhail, Hu; DHolaria, Savani, Kharfan-Dabaja) (Attachment 9)
g. **PROP 1811-40** Hematopoietic stem cell transplantation for relapsed/refractory primary mediastinal b cell lymphoma (Mussetti, Sureda) (Attachment 10)
h. **PROP 1811-89/1811-135** Determining the optimal conditioning regimen for patients with primary central nervous system lymphoma undergoing autologous hematopoietic cell transplantation; A comparison of thiotepa and busulfan (TB)-based vs. thiotepa and carmustine (TT-BCNU) conditioned autologous transplantation in the treatment of primary and secondary CNS lymphom. (Scordo, Sauter; Wang, Jiminez) (Attachment 11)
i. **PROP 1811-101** Outcomes in elderly patients (Age ≥ 70 years) received autologous hematopoietic stem cell transplant for non-hodgkin lymphoma (Zhou, Rabinowitz, Nath) (Attachment 12)

Dropped proposed studies

a. **PROP 1811-06** Outcomes of patients with relapsed/refractory hodgkin and non-hodgkin lymphoma treated with radiotherapy in addition to high-dose chemotherapy and stem cell transplantation. *Dropped with current CIBMTR study.*
b. **PROP 1811-25** Rate of large granular lymphocytosis in SCT and effect on the long-term prognosis of post-transplant patients. *Dropped due to feasibility.*
c. **PROP 1811-37** Clinical outcome of patients 50 years and older with hodgkin lymphoma receiving allogeneic hematopoietic stem cell transplantation. *Dropped due to feasibility.*
d. **PROP 1811-48** Evaluating the efficacy of high-dose therapy and autologous hematopoietic cell transplantation for primary effusion lymphoma. *Dropped due to feasibility..*
e. **PROP 1811-61** Impact of allogeneic hematopoietic cell transplantation on the outcomes of adult T cell Leukemia Lymphoma. *Dropped due to feasibility.*
f. **PROP 1811-65** Does BV maintenance after autoHCT decrease the chance and success of alloHCT in high risk HL patients. *Dropped due to feasibility.*
g. **PROP 1811-70** Role of consolidation therapy post auto transplant in T cell lymphomas. *Dropped due to feasibility.*
h. **PROP 1811-76** Outcomes of auto compared to allo transplants for diagnosis of high risk non Hodgkin lymphoma. *Dropped due to feasibility.*
i. **PROP 1811-80** Outcomes of long-term survivors of non-hodgkin lymphoma who underwent reduced intensity alloHCT: matched unrelated vs haploidentical donor (Dholaria, Savani, Kharfan-Dabaja). *Dropped due to feasibility.*
j. **PROP 1811-91** Evaluation of outcomes of patients with B-PLL undergoing allogeneic stem cell transplant**.** *Dropped due to feasibility.*
k. **PROP 1811-111** Clinical and pathologic factors predictive of refractoriness or early relapse (<12 months) to autologous stem cell transplant in patients with primary refractory DLBCL. *Dropped due to feasibility.*

l. **PROP 1811-122** The impact of adding Rituximab to BEAM conditioning for patients with DLBCL undergoing autoHCT. *Dropped due to overlap with current CIBMTR study (LY18-01).*
m. **PROP 1811-140** Donor and recipient t cell exhaustion markers before allogeneic transplantation in hodgkin lymphoma. *Dropped due to feasibility.*
n. **PROP 1811-152** Survival after autologous and allogeneic stem cell transplantation in peripheral T-cell lymphoma. *Dropped due to overlap with current CIBMTR study (LY06-05).*
o. **PROP 1811-164** Outcomes of autologous hematopoietic stem cell transplantation in primary effusion lymphoma. *Dropped due to small sample size.*
p. **PROP 1811-181** Hematopoietic cell transplantation outcomes for cutaneous T cell lymphoma. *Dropped due to overlap with current CIBMTR study (LY06-05).*
q. **PROP 1811-182** For post-transplant cyclophosphamide-based GVHD prophylaxis, is survival after matched unrelated donor allogeneic transplantation better than haploidentical transplantation for relapsed lymphomas. *Dropped due to feasibility.*
r. **PROP 1811-183** Retrospective study of blood or bone marrow transplantation for enteropathy-associated T-cell lymphoma and hepatosplenic T-cell lymphoma. *Dropped due to feasibility.*
s. **PROP 1812-11** To evaluate outcomes of HSCT with TBI vs. Flu/Mel conditioning in treatment of cutaneous T-cell lymphoma. *Drooped due to overlap with current CIBTMR study (LY17-02).*

7. **Other Business**

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
Salt Lake City, Utah
Wednesday, February 21, 2018, 2:45 – 4:45 pm

Co-Chair:	**Sonali Smith, MD, The University of Chicago, Chicago, IL; Telephone: 773-702-4400; E-mail: smsmith@medicine.bsd.uchicago.edu**
Co-Chair:	**Anna Sureda, MD, PhD, Institut Català d'Oncologia, Barcelona, Spain; Telephone: +34 9326 07353; E-mail: asureda@iconcologia.net**
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1. Introduction

The CIBMTR Hodgkin and Non-Hodgkin Lymphoma Working Committee was called to order at 2:45 pm on Wednesday, February 21, 2018 by Dr. Mehdi Hamadani. Dr. Anna Sureda introduced the working committee leadership as well as the EBMT representative, Dr. Stephen Robinson. Dr. Sureda also outlined the Working Committee goals, expectations, and limitations and provided an update on the Working Committee productivity including 7 publications, and 1 oral presentation at the 2018 BMT Tandem meetings. Dr. Sonali Smith went over the five studies in progress, and reviewed the voting guidelines. The guidelines are based on a scale from 1 to 9; 1=high scientific impact, 9=low scientific impact. Dr. Mehdi Hamadani explained the difference between the TED and CRF data collection forms, the study life cycle, and the rules for authorship: 1) substantial and timely contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; 3) final approval for the version to be published. Dr. Hamadani emphasized that WC authorship is open to any LYWC Tandem Meetings attendees and encouraged junior faculty, fellows and assistant professors to collaborate actively with the Lymphoma Writing Committee.

2. Accrual summary

Dr. Sonali Smith presented a slide with the accruals, highlighting autologous accruals. It was mentioned that the accrual summary was available in the LYWC materials, attachment 2.

3. Presentations, published or submitted papers

Dr. Sonali Smith listed the presentations and publications during 2017, highlighting the great productivity of the LYWC.

1. **LY06-03** Sureda A, Zhang M-J, Dreger P, Carreras J, Fenske T, Finel H, Schouten H, Montoto S, Robinson S, Smith S, Boumedil A, Hamadani M, Pasquini M. HLA identical sibling allogeneic stem cell transplantation versus HLA matched unrelated donor allogeneic stem cell transplantation in patients with follicular lymphoma. **Cancer (In Press).**
2. **LY15-03** Casulo C, Friedberg JW, Ahn KW, Flowers C, DiGilio A, Smith SM, Ahmed S, Inwards D, Aljurf M, Chen AI, Choe H, Cohen J, Copelan E, Farooq U, Fenske TS, Freytes C, Gaballa S, Ganguly S, Jethava Y, Kamble RT, Kenkre VP, Lazarus H, Lazaryan A, Olsson RF, Rezvani AR, Rizzieri D, Seo S, Shah GL, Shah N, Solh M, Sureda A, William B, Cumpston A, Zelenetz AD, Link BK, Hamadani M. Autologous transplantation in follicular lymphoma with early therapy failure: A NLCS and CIBMTR analysis. **Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. doi:10.1016/j.bbmt.2017.12.771. Epub 2017 Dec 11.**
3. **LY16-01a** Kanate AS, DiGilio A, Ahn KW, Al Malki M, Jacobsen E, Steinberg A, Hammerschlak N, Kharfan-Dabaja M, Salit R, Ball E, Bashir Q, Cashen A, Couriel D, Diez-Martin J, Katsanis E, Linhares Y, Mori S, Nash R, Pawarode A, Perales M-A, Phipps CD, Richman C, Savani BN, Shapira MY, Stiff P, Strair R, Fenske TS, Smith SM, Sureda A, Olteanu H, Hamadani M. Allogeneic haematopoietic cell transplantation for extranodal natural killer/T-cell lymphoma, nasal type: A CIBMTR analysis. **British Journal of Haematology. doi:10.1111/bjh.14879. Epub 2017 Aug 2.**
4. **LY16-01b** Hamadani M, Kanate AS, DiGilio A, Ahn KW, Smith SM, Lee JW, Ayala E, Chao N, Hari P, Bolaños-Meade J, Gress R, Smedegaard Anderson N, Chen Y-B, Farooq U, Schiller G, Yared J, Sureda A, Fenske TS, Olteanu H. Allogeneic hematopoietic cell transplantation for aggressive NK cell leukemia. A Center for International Blood and Marrow Transplant Research analysis. **Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2017 May 1; 23(5):853-856. doi:10.1016/j.bbmt.2017.01.082. Epub 2017 Feb 1. PMC5410937.**
5. **LY16-04** Smith S, Godfrey J, Ahn KW, DiGilio A, Ahmed S, Agrawal V, Bachanova V, Bacher U, Bashey A, Bolaños-Meade J, Cairo M, Chen A, Chhabra S, Copelan E, Dahi P, Aljurf M, Farooq U, Ganguly S, Hertzberg M, Holmberg L, Inwards D, Kanate A, Karmali R, Kenkre V, Kharfan-Dabaja M, Klein A, Lazarus H, Mei M, Mussetti A, Nishihori T, Ramakrishnan Geethakumari P, Saad A, Savani B, Schouten H, Shah N, Urbano-Ispizua A, Vij R, Vose J, Sureda A, Hamadani M. Utility of autologous vs allogeneic transplant as the first transplantation approach in follicular lymphoma patients with early chemoimmunotherapy failure. **Cancer (In Press).**
6. **LY16-05a** Epperla N, Ahn KW, Ahmed S, Jagasia M, DiGilio A, Devine SM, Jaglowski S, Kennedy V, Rezvani AR, Smith SM, Sureda A, Fenske TS, Kharfan-Dabaja MA, Armand P, Hamadani M. Rituximab-containing reduced-intensity conditioning improves progression-free survival following allogeneic transplantation in B cell non-Hodgkin lymphoma. **Journal of Hematology & Oncology. 2017 Jun 12; 10(1):117. doi:10.1186/s13045-017-0487-y. Epub 2017 Jun 12. PMC5469142.**
7. **LY16-05b** Epperla N, Ahn KW, Armand P, Jaglowski S, Ahmed S, Kenkre VP, Savani B, Jagasia M, Shah NN, Fenske TS, Sureda A, Smith SM, Hamadani M. Fludarabine and Busulfan versus Fludarabine, Cyclophosphamide, and Rituximab as Reduced-Intensity Conditioning for Allogeneic Transplantation in Follicular Lymphoma. **Biol Blood Marrow Transplant. 2018 Jan; 24(1):78-85. doi: 10.1016/j.bbmt.2017.10.011. Epub 2017 Oct 13. PMID: 29032272.**
8. **LY17-01** Allogeneic hematopoietic cell transplantation for Non-Hodgkin lymphoma patients age 65 or older compared to patients age 55-64 (N Shah) **Accepted for oral presentation at the 2018 BMT Tandem Meetings in Salt Lake City, February 2018.**

4. Studies in progress

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

a. **LY16-02** Comparison of alternative donor source stem cell transplant versus matched related donor stem cell transplant for Hodgkin Lymphoma (S Ahmed/J Kanakry) This study will be presented in the statistical meeting in May 2018.
b. **LY16-03** Outcome of patients who have undergone haploidentical stem cell transplantation for diffuse large B cell lymphoma: A retrospective study of the CIBMTR Lymphoma WC and the EBMT Lymphoma WP (P Dreger/A Sureda) **Manuscript Preparation.** Additional analysis is currently being performed in this study, and an abstract has been submitted to ASCO and EHA. **LY17-01** Allogeneic hematopoietic cell transplantation for Non-Hodgkin lymphoma patients age 65 or older compared to patients age 55-64 (N Shah) **Submitted.** Accepted for oral presentation at the 2018 BMT Tandem Meetings in Salt Lake City, February 2018.
c. **LY17-02** Allografts in lymphoma following reduced intensity conditioning (N Ghosh/S Ahmed) **Protocol Development.** This study will be presented in the statistical meeting in May 2018. **LY17-03** Impact of allogeneic hematopoietic cell transplantation on the outcomes of Angioimmunoblastic T-cell lymphoma (N Epperla) **Datafile Preparation.** This study will be presented at the statistical meeting in April 2018.

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

Dr. Mehdi Hamadani emphasized the difference between the TED and CRF databases. It was emphasized that CRF is a subset of the TED database, and that the CRF forms collect all disease specific information such as lines of therapy, extranodal involvement, and prior radiation. If a study needs any of this information, CRF level data is needed on the study.

6. Future/proposed studies

g. **PROP 1711-13/123** Outcomes of hematopoietic stem cell transplantation (HSCT) in rare T Cell lymphoma (TCL) subtypes – Hepatosplenic TCL (HSTCL) and Enteropathy Associated TCL (EATL) (Koshy, Jagadeesh, and Majhail) (Attachment 4)

During the presentation of PROP 1711-13/123, an audience member asked if there was a possibility of going back to the centers to get more data, due to low CRF numbers. Mehdi explained that although it is a possibility, studies in this nature are not favored due to increase cost, labor and thus possibly less cost-effectiveness.

Audience member asked if there was a possibility of collaboration to from the EBMT to pursue this project. Dr. Sureda mentioned that it could be possible, given interest in the project from audience and working committee.

h. **PROP 1711-19** Outcomes of elderly patients undergoing high-dose therapy and autologous stem cell transplantation for non-Hodgkin lymphoma (Murthy, Ayala, and Kharfan-Dabaja) (Attachment 5)

During the presentation of PROP 1711-19, an audience member asked if there was a need of CRF level data, which Dr. Hamadani explained that probably yes due to some variables of interest, like length of stay in hospital. Dr. Hamadani explained that the majority of endpoints do not need CRF level data.

Audience member asked presenter to clarify what modern paradigm of treatment for Follicular Lymphoma.

Audience member asked presenter if there are other ways to assess utilization of HCT in this population.

Audience member asked the purpose of including DLBCL and FL jointly, and if there was a possibility to separate these two disease into two different analysis.

i. **PROP 1711-52** Does outcome after allogeneic hematopoietic cell transplantation differ between patients with *de novo* diffuse large B-cell lymphoma (DLBCL) and transformed DLBCL arising in the setting of indolent lymphoma? (Herrera) (Attachment 6)

During the presentation of PROP 1711-52, the concept of what constitutes a transformed DLBCL case was discussed.
Audience member commented that it would be helpful to review the prior autologous population and possibly exclude them due to the different prognostic characteristics of these patients.
Audience member asked if it was possible to do this analysis on TED level data.

j. **PROP 1711-67** Allogeneic hematopoietic transplantation strategies for anaplastic large cell lymphoma in adult patients: current trends and impact of pre-transplant targeted therapy (Brentuximab, Vedotin, and Crizotinib) (Mussetti, Kanate, and Corradini) (Attachment 7)

During the presentation of PROP 1711-67, an audience member asked why is this concept being limited to allogeneic transplantations. Dr. Mussetti explained that the percentage of autologous patients with Brentixumab was low in the preliminary overview of data.
Audience member asked how many patients are found in EBMT registry- Dr. Hamadani suspects that virtually none.
Audience member asked if lines of therapy could be analyzed at TED level data. Dr. Hamadani explained that this information is only found in CRF patients.

k. **PROP 1711-69** Outcomes in B cell Non-Hodgkin's Lymphoma (NHL) patients who underwent autologous stem cell transplantation following Rituximab containing conditioning regimens (Jagadeesh, Majhail, and Hill) (Attachment 8)

During the presentation of PROP 1711-69, an audience member asked why are patients age 17 or younger included. Dr. Jagadeesh explored the possibility of excluding the pediatric population given the low number of Follicular Lymphoma pediatric patients, and if these patient's characteristics are different from the adult population.
Audience member suggested to separate DLBCL and FL into two different analysis or focusing on DLBCL.
Audience member asked if we had immune reconstitution data available, to which Dr. Hamadani responded that such details are currently unavailable.

l. **PROP 1711-102** Effect of time to relapse on overall survival in Mantle Cell lymphoma patients following frontline autologous stem cell transplant (Riedell and Smith) (Attachment 9)

During the presentation of PROP 1711-102, an audience member asked if we had information on KI67 molecular marker on these patients.

m. **PROP 1711-127** Outcomes of consolidation autologous hematopoietic cell transplantation in patients with Plasmablastic lymphoma (Mukherjee, Pingali, and Veeraputhiran) (Attachment 10)

During the presentation of PROP 1711-127, an audience member asked if this study could be feasible. Dr. Hamadani mentioned that this study could only be descriptive due to the low number of patients.
Audience member asked why are there low CRF numbers on a rare histology in Lymphoma. Dr. Hamadani explained that there are different parameters of CRF collection, determined internally.

n. **PROP 1711-156** Role of autologous hematopoietic cell transplantation in NK/T-Cell lymphomas (Badar) (Attachment 11)

During the presentation of PROP 1711-156, an audience member asked if this study would need additional data recollection from centers. Dr. Hamadani explained that it does, and reiterated that studies that require additional data collection from centers need higher justification and scientific impact than studies that do not.
Audience member asked if we had data on EBV infection on NK/T-cell lymphoma, and Dr. Hamadani clarified the definition of NK/T-cell lymphoma.
Audience member asked if we would have relapse information for the disease selection, and Dr. Hamadani explained that we have disease status available for these patients.

Eleven additional proposals were submitted to the committee but were not presented due to the following reasons:

a. **PROP 1710-12** Impact of auto SCT vs RIC allo SCT in mature T-NHL in CR1 in the most recent era. *Dropped due to committee scientific priority.*
b. **PROP 1710-18** Outcomes of allogeneic hematopoietic stem cell transplantation for marginal zone non-Hodgkin lymphoma. *Dropped due to feasibility.*
c. **PROP 1711-39** Autologous hematopoietic cell transplantation versus allogeneic hematopoietic cell transplantation in mantle cell lymphoma harboring 17p deletion or TP53 mutation. *Dropped due to feasibility.*
d. **PROP 1711-66** Outcomes after allogeneic hematopoietic cell transplantation in patients with aggressive B-cell non-Hodgkin lymphoma who previously received chimeric antigen receptor modified T-cells**.** *Dropped due to feasibility.*
e. **PROP 1711-70** Allogeneic transplant versus autologous transplant as first-line consolidation for patients with peripheral T-cell lymphoma. *Dropped due to committee scientific priority.*
f. **PROP 1711-81** Comparison of outcomes in first stem cell transplantation for DLBCL in CR2 or greater; autologous vs reduced intensity conditioning allogeneic stem cell transplantation. *Dropped due to committee scientific priority.*
g. **PROP 1711-93** Outcomes of allogeneic stem cell transplantation compared to autologous stem cell transplantation in patients with non-Hodgkin's lymphoma with central nervous system involvement. *Dropped due to feasibility.*
h. **PROP 1711-100** Outcomes with allogeneic transplantation in an era of novel therapies in Hodgkin lymphoma**.** *Dropped due to overlap with ongoing CIBMTR & EBMT study.*
i. **PROP 1711-101** Allogeneic Transplant Outcomes for Patients with Mature T-cell Malignancies Relapsed post-Autologous Transplant. *Dropped due to committee scientific priority.*
j. **PROP 1711-119** Outcomes of autologous hematopoietic cell transplantation (autoHCT) in CNS lymphoma (CNSL). *Dropped due to committee scientific priority.*
k. **PROP 1711-129** Outcomes of allogeneic stem cell transplantation compared to autologous stem cell transplant in patients with non-Hodgkin's lymphoma with central nervous system involvement. *Dropped due to feasibility.*

7. **Other Business**

After the proposals were presented, the voting process was reiterated, and each participant had the opportunity to rate each new proposal using paper ballots. Without additional comments, the meeting was adjourned at 4:42 pm.

Working Committee Overview Plan for 2018-2019

a. **LY16-02** Alternative donor source stem cell transplant vs matched donor stem cell transplant for Hodgkin lymphoma. This study is currently deferred and will be deferred until July 1, 2018. We anticipate this study to be in protocol development in July, 2018.

b. **LY16-03** Haploidentical transplantation in diffuse large B cell lymphoma: A CIBMTR and EBMT collaborative study. Abstract submitted to ASCO and EHA. We anticipate to submit to journal by June 2018.

c. **LY17-01** Allogeneic Hematopoietic Cell Transplantation for Non-Hodgkin Lymphoma patients age 65 or older compared to patients age 55-64. Submitted to JCO, estimate published date December 2018.

d. **LY17-02** Allografts in lymphoma following reduced intensity conditioning. We anticipate that this study will be in manuscript preparation by July 2018.

e. **LY17-03** Impact of allogeneic hematopoietic cell transplantation on the outcomes of Angioimmunoblastic T-cell lymphoma. We anticipate that this study will be submitted by July 2018.

f. **LY18-01 (Prop 1711-69)** Outcomes in Bcell non-Hodgkin's lymphoma patients who underwent autologous stem cell transplantation following rituximab containing conditioning Regimens. We anticipate that this study will be submitted by July 2019.

g. **LY18-02 (Prop 1711-102)** Effect of time to relapse on overall survival in mantle cell lymphoma patients following frontline autologous stem cell transplant. We anticipate that this study will be submitted by July 2019.

h. **LY18-03 (Prop 1711-52)** Does outcome after allogeneic hematopoietic stem cell transplant differ between patients with de novo diffuse large b-cell lymphoma and transformed diffuse. We anticipate that this study will be in analysis by July 2019.

Oversight Assignments for Working Committee Leadership (March 2018)

Tim Fenske	**LY17-01** Allogeneic Hematopoietic Cell Transplantation for Non-Hodgkin Lymphoma patients age 65 or older compared to patients age 55-64. **LY18-02** Effect of time to relapse on overall survival in mantle cell lymphoma patients following frontline autologous stem cell transplant.
Anna Sureda	**LY16-03** Haploidentical transplantation in diffuse large B cell lymphoma: A CIBMTR and EBMT collaborative study. **LY17-02** Allografts in lymphoma following reduced intensity conditioning. **LY16-02** Alternative donor source stem cell transplant vs matched donor stem cell transplant for Hodgkin lymphoma.
Sonali Smith	**LY17-03** Impact of allogeneic hematopoietic cell transplantation on the outcomes of Angioimmunoblastic T-cell lymphoma
Mohamed Kharfan-Dabaja	**LY18-01** Outcomes in Bcell non-Hodgkin's lymphoma patients who underwent autologous stem cell transplantation following rituximab containing conditioning Regimens. **LY18-03** Does outcome after allogeneic hematopoietic stem cell transplant differ between patients with de novo diffuse large b-cell lymphoma and transformed diffuse large Bcell lymphoma.

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2018

	HLA-Identical Sibling		Alternative Donor		Autologous	
	TED only	Research	TED only	Research	TED only	Research
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Anaplastic large cell	257	50	283	159	1538	181
PIF	33 (13)	8 (16)	34 (12)	23 (14)	146 (9)	10 (6)
CR1	35 (14)	6 (12)	38 (13)	24 (15)	571 (37)	71 (39)
Rel 1	27 (11)	7 (14)	19 (7)	10 (6)	158 (10)	22 (12)
CR2	75 (29)	17 (34)	80 (28)	41 (26)	364 (24)	45 (25)
Other/Unknown	87 (34)	12 (24)	112 (40)	61 (38)	299 (19)	33 (18)
Burkitt/small noncleaved	152	51	88	102	521	125
PIF	17 (11)	7 (14)	8 (9)	19 (19)	53 (10)	19 (15)
CR1	34 (22)	12 (24)	18 (20)	18 (18)	179 (34)	49 (39)
Rel 1	23 (15)	6 (12)	7 (8)	14 (14)	47 (9)	12 (10)
CR2	35 (23)	20 (39)	29 (33)	33 (32)	122 (23)	34 (27)
Other/Unknown	43 (28)	6 (12)	26 (30)	18 (18)	120 (23)	11 (9)
Diffuse large cell/Immunoblastic	1636	352	1618	870	19825	2739
PIF	288 (18)	83 (24)	266 (16)	209 (24)	2358 (12)	347 (13)
CR1	151 (9)	52 (15)	179 (11)	84 (10)	3455 (17)	523 (19)
Rel 1	260 (16)	48 (14)	167 (10)	93 (11)	3381 (17)	502 (18)
CR2	228 (14)	31 (9)	276 (17)	118 (14)	5551 (28)	762 (28)
Other/Unknown	709 (43)	138 (39)	730 (45)	366 (42)	5080 (26)	605 (22)
Follicular	1331	560	1126	717	4482	942
PIF	145 (11)	81 (14)	111 (10)	112 (16)	423 (9)	75 (8)
CR1	95 (7)	41 (7)	78 (7)	36 (5)	496 (11)	109 (12)
Rel 1	179 (13)	109 (19)	125 (11)	107 (15)	773 (17)	184 (20)
CR2	169 (13)	75 (13)	149 (13)	80 (11)	1061 (24)	214 (23)
Other/Unknown	743 (56)	254 (45)	663 (59)	382 (53)	1729 (39)	360 (38)
Lymphoblastic	169	52	123	108	270	42
PIF	18 (11)	7 (13)	8 (7)	12 (11)	14 (5)	2 (5)
CR1	48 (28)	13 (25)	20 (16)	19 (18)	118 (44)	23 (55)
Rel 1	28 (17)	8 (15)	9 (7)	17 (16)	23 (9)	1 (2)
CR2	31 (18)	13 (25)	35 (28)	34 (31)	34 (13)	6 (14)
Other/Unknown	44 (26)	11 (21)	51 (41)	26 (24)	81 (30)	10 (24)
Mantle	810	237	888	480	6958	948
PIF	101 (12)	43 (18)	76 (9)	76 (16)	531 (8)	82 (9)
CR1	157 (19)	47 (20)	129 (15)	74 (15)	4540 (65)	631 (67)

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2018

	HLA-Identical Sibling		Alternative Donor		Autologous	
	TED only	Research	TED only	Research	TED only	Research
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Rel 1	132 (16)	37 (16)	128 (14)	84 (18)	221 (3)	33 (3)
CR2	155 (19)	35 (15)	277 (31)	106 (22)	385 (6)	57 (6)
Other/Unknown	265 (33)	75 (32)	278 (31)	140 (29)	1281 (18)	145 (15)
Marginal	86	28	90	36	331	48
PIF	11 (13)	8 (29)	13 (14)	8 (22)	37 (11)	8 (17)
CR1	8 (9)	3 (11)	13 (14)	4 (11)	54 (16)	4 (8)
Rel 1	10 (12)	1 (4)	12 (13)	5 (14)	41 (12)	5 (10)
CR2	11 (13)	3 (11)	7 (8)	4 (11)	63 (19)	11 (23)
Other/Unknown	46 (53)	13 (46)	45 (50)	15 (42)	136 (41)	20 (42)
NK T cell	216	53	241	102	655	79
PIF	31 (14)	9 (17)	48 (20)	21 (21)	71 (11)	13 (16)
CR1	54 (25)	13 (25)	59 (24)	36 (35)	271 (41)	35 (44)
Rel 1	23 (11)	5 (9)	15 (6)	7 (7)	49 (7)	4 (5)
CR2	37 (17)	4 (8)	50 (21)	22 (22)	110 (17)	14 (18)
Other/Unknown	71 (33)	22 (42)	69 (29)	16 (16)	154 (24)	13 (16)
T cell	765	198	895	439	2841	393
PIF	182 (24)	58 (29)	201 (22)	143 (33)	300 (11)	44 (11)
CR1	137 (18)	39 (20)	163 (18)	82 (19)	1477 (52)	193 (49)
Rel 1	84 (11)	17 (9)	77 (9)	44 (10)	229 (8)	37 (9)
CR2	105 (14)	27 (14)	155 (17)	52 (12)	303 (11)	48 (12)
Other/Unknown	257 (34)	57 (29)	299 (33)	118 (27)	532 (19)	71 (18)
NHL Not specified	178	25	101	116	858	56
PIF	15 (8)	4 (16)	7 (7)	31 (27)	89 (10)	12 (21)
CR1	13 (7)	0	5 (5)	13 (11)	107 (12)	11 (20)
Rel 1	26 (15)	3 (12)	7 (7)	18 (16)	63 (7)	6 (11)
CR2	15 (8)	2 (8)	18 (18)	19 (16)	110 (13)	6 (11)
Other/Unknown	109 (61)	16 (64)	64 (63)	35 (30)	489 (57)	21 (38)
Other	503	189	504	280	3896	654
PIF	100 (20)	49 (26)	103 (20)	75 (27)	624 (16)	110 (17)
CR1	87 (17)	28 (15)	93 (18)	60 (21)	1142 (29)	215 (33)
Rel 1	52 (10)	19 (10)	53 (11)	26 (9)	460 (12)	70 (11)
CR2	59 (12)	13 (7)	85 (17)	33 (12)	824 (21)	128 (20)
Other/Unknown	205 (41)	80 (42)	170 (34)	86 (31)	846 (22)	131 (20)

Accrual Summary for Hodgkin and Non-Hodgkin Lymphoma Working Committee: 2000-2018

	HLA-Identical Sibling		Alternative Donor		Autologous	
	TED only	Research	TED only	Research	TED only	Research
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Hodgkin	1221	250	1395	820	15563	2077
PIF	186 (15)	38 (15)	166 (12)	136 (17)	2157 (14)	336 (16)
CR1	60 (5)	12 (5)	74 (5)	53 (6)	1629 (10)	221 (11)
Rel 1	145 (12)	44 (18)	157 (11)	103 (13)	2998 (19)	407 (20)
CR2	132 (11)	29 (12)	174 (12)	87 (11)	4372 (28)	575 (28)
Other/Unknown	698 (57)	127 (51)	824 (59)	441 (54)	4407 (28)	538 (26)
Graft type	7324	2045	7352	4229	57738	8284
BM	761 (10)	174 (9)	1240 (17)	919 (22)	651 (1)	72 (<1)
PBSC	6506 (89)	1864 (91)	5654 (77)	2668 (63)	56156 (97)	8059 (97)
Other/Unknown	57 (<1)	7 (<1)	458 (6)	642 (15)	931 (2)	153 (2)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	4379	1113	679
Source of data			
CRF	2117 (48)	474 (43)	329 (48)
TED	2262 (52)	639 (57)	350 (52)
Number of centers	187	131	165
Disease at transplant			
NHL	3579 (82)	951 (85)	559 (82)
Hodgkins Lymphoma	800 (18)	162 (15)	120 (18)
NHL Disease status at transplant			
CR1	446 (13)	158 (17)	58 (10)
CR2	664 (19)	166 (18)	93 (17)
CR3+	302 (9)	82 (9)	47 (8)
PR	431 (12)	108 (11)	78 (14)
Advanced	1655 (47)	419 (44)	271 (49)
Missing	50 (1)	9 (1)	9 (2)
Recipient age at transplant			
0-9 years	47 (1)	6 (1)	11 (2)
10-19 years	204 (5)	34 (3)	32 (5)
20-29 years	536 (12)	125 (11)	82 (12)
30-39 years	616 (14)	151 (14)	97 (14)
40-49 years	835 (19)	217 (19)	145 (21)
50-59 years	1221 (28)	300 (27)	167 (25)
60-69 years	862 (20)	248 (22)	137 (20)
70+ years	58 (1)	32 (3)	8 (1)
Median (Range)	50 (2-79)	51 (3-76)	49 (2-74)
Recipient race/ethnicity			
Caucasian, non-Hispanic	3803 (88)	943 (87)	540 (88)
African-American, non-Hispanic	187 (4)	40 (4)	20 (3)
Asian, non-Hispanic	68 (2)	27 (2)	20 (3)
Pacific islander, non-Hispanic	4 (<1)	2 (<1)	0
Native American, non-Hispanic	4 (<1)	7 (1)	1 (<1)
Hispanic	232 (5)	65 (6)	33 (5)
Other	1 (<1)	4 (<1)	1 (<1)
Unknown	80 (N/A)	25 (N/A)	64 (N/A)
Recipient sex			
Male	2743 (63)	741 (67)	444 (65)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Female	1636 (37)	372 (33)	235 (35)
Karnofsky score			
10-80	1462 (33)	396 (36)	231 (34)
90-100	2697 (62)	632 (57)	404 (59)
Missing	220 (5)	85 (8)	44 (6)
HLA-A B DRB1 groups - low resolution			
<=3/6	3 (<1)	3 (<1)	0
4/6	8 (<1)	8 (1)	1 (<1)
5/6	517 (12)	119 (12)	66 (10)
6/6	3793 (88)	884 (87)	583 (90)
Unknown	58 (N/A)	99 (N/A)	29 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	39 (1)	6 (1)	1 (<1)
6/8	108 (3)	14 (2)	6 (1)
7/8	818 (20)	151 (19)	104 (22)
8/8	3185 (77)	642 (79)	362 (77)
Unknown	229 (N/A)	300 (N/A)	206 (N/A)
HLA-DPB1 Match			
Double allele mismatch	679 (29)	46 (21)	34 (28)
Single allele mismatch	1309 (56)	113 (52)	61 (50)
Full allele matched	347 (15)	60 (27)	27 (22)
Unknown	2044 (N/A)	894 (N/A)	557 (N/A)
High resolution release score			
No	18 (1)	11 (37)	22 (61)
Yes	2449 (99)	19 (63)	14 (39)
Unknown	1912 (N/A)	1083 (N/A)	643 (N/A)
KIR typing available			
No	3613 (83)	1101 (99)	677 (>99)
Yes	766 (17)	12 (1)	2 (<1)
Graft type			
Marrow	909 (21)	213 (19)	158 (23)
PBSC	3469 (79)	892 (80)	521 (77)
PBSC+UCB	1 (<1)	8 (1)	0
Number of cord units			
Unknown	4379 (N/A)	1113 (N/A)	679 (N/A)
Conditioning regimen			
Myeloablative	1803 (41)	408 (37)	255 (38)
RIC/Nonmyeloablative	2545 (58)	698 (63)	419 (62)
TBD	31 (1)	7 (1)	5 (1)
Donor age at donation			
To Be Determined/NA	16 (<1)	194 (17)	9 (1)
0-9 years	1 (<1)	0	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
10-19 years	115 (3)	25 (2)	18 (3)
20-29 years	1910 (44)	432 (39)	272 (40)
30-39 years	1277 (29)	254 (23)	202 (30)
40-49 years	827 (19)	159 (14)	125 (18)
50+ years	233 (5)	49 (4)	53 (8)
Median (Range)	31 (3-69)	30 (18-68)	32 (19-59)
Donor/Recipient CMV serostatus			
+/+	1007 (23)	256 (24)	141 (21)
+/-	523 (12)	167 (16)	112 (17)
-/+	1293 (30)	285 (27)	189 (29)
-/-	1504 (35)	350 (33)	219 (33)
CB - recipient -	0	1 (<1)	0
Unknown	52 (N/A)	54 (N/A)	18 (N/A)
GvHD Prophylaxis			
Ex vivo T-cell depletion	53 (1)	10 (1)	13 (2)
CD34 selection	53 (1)	12 (1)	4 (1)
Tacrolimus + MMF +- others	776 (18)	155 (14)	130 (19)
Tacrolimus + MTX +- others (except MMF)	1945 (44)	523 (47)	220 (32)
Tacrolimus + others (except MTX, MMF)	279 (6)	96 (9)	50 (7)
Tacrolimus alone	151 (3)	49 (4)	16 (2)
CSA + MMF +- others (except Tacrolimus)	460 (11)	92 (8)	79 (12)
CSA + MTX +- others (except Tacrolimus, MMF)	371 (8)	88 (8)	95 (14)
CSA + others (except Tacrolimus, MTX, MMF)	66 (2)	18 (2)	13 (2)
CSA alone	41 (1)	6 (1)	21 (3)
Other GVHD prophylaxis	76 (2)	21 (2)	13 (2)
Missing	108 (2)	43 (4)	25 (4)
Donor/Recipient sex match			
Male-Male	2006 (46)	512 (47)	298 (44)
Male-Female	1030 (24)	222 (20)	127 (19)
Female-Male	725 (17)	209 (19)	141 (21)
Female-Female	598 (14)	137 (13)	106 (16)
CB - recipient M	0	5 (<1)	0
CB - recipient F	1 (<1)	3 (<1)	0
Unknown	19 (N/A)	25 (N/A)	7 (N/A)
Year of transplant			
1986-1990	3 (<1)	1 (<1)	1 (<1)
1991-1995	44 (1)	12 (1)	13 (2)
1996-2000	228 (5)	56 (5)	39 (6)
2001-2005	721 (16)	139 (12)	155 (23)
2006-2010	1369 (31)	256 (23)	184 (27)
2011-2015	1572 (36)	431 (39)	219 (32)
2016-2019	442 (10)	218 (20)	68 (10)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Follow-up among survivors, Months			
N Eval	1826	513	270
Median (Range)	61 (3-312)	44 (2-243)	51 (0-218)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	460	106	101
Source of data			
CRF	350 (76)	78 (74)	62 (61)
TED	110 (24)	28 (26)	39 (39)
Number of centers	87	37	49
Disease at transplant			
NHL	367 (80)	81 (76)	80 (79)
Hodgkins Lymphoma	93 (20)	25 (24)	21 (21)
NHL Disease status at transplant			
CR1	56 (15)	5 (6)	17 (22)
CR2	68 (19)	17 (21)	20 (25)
CR3+	42 (12)	10 (12)	9 (11)
PR	65 (18)	12 (15)	10 (13)
Advanced	133 (37)	36 (44)	22 (28)
Missing	0	1 (1)	1 (1)
Recipient age at transplant			
0-9 years	19 (4)	5 (5)	3 (3)
10-19 years	34 (7)	4 (4)	6 (6)
20-29 years	59 (13)	13 (12)	13 (13)
30-39 years	86 (19)	15 (14)	21 (21)
40-49 years	78 (17)	28 (26)	17 (17)
50-59 years	112 (24)	18 (17)	21 (21)
60-69 years	68 (15)	23 (22)	19 (19)
70+ years	4 (1)	0	1 (1)
Median (Range)	45 (1-73)	45 (5-70)	45 (7-71)
Recipient race/ethnicity			
Caucasian, non-Hispanic	262 (58)	73 (70)	54 (60)
African-American, non-Hispanic	89 (20)	19 (18)	15 (17)
Asian, non-Hispanic	30 (7)	3 (3)	6 (7)
Pacific islander, non-Hispanic	1 (<1)	0	0
Native American, non-Hispanic	6 (1)	0	0
Hispanic	60 (13)	9 (9)	15 (17)
Unknown	12 (N/A)	2 (N/A)	11 (N/A)
Recipient sex			
Male	271 (59)	64 (60)	58 (57)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Female	189 (41)	42 (40)	43 (43)
Karnofsky score			
10-80	130 (28)	27 (25)	22 (22)
90-100	309 (67)	67 (63)	76 (75)
Missing	21 (5)	12 (11)	3 (3)
HLA-A B DRB1 groups - low resolution			
<=3/6	15 (3)	3 (4)	0
4/6	225 (51)	40 (49)	49 (52)
5/6	172 (39)	31 (38)	37 (39)
6/6	27 (6)	8 (10)	9 (9)
Unknown	21 (N/A)	24 (N/A)	6 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	239 (64)	41 (68)	54 (70)
6/8	92 (25)	13 (22)	13 (17)
7/8	33 (9)	5 (8)	7 (9)
8/8	11 (3)	1 (2)	3 (4)
Unknown	85 (N/A)	46 (N/A)	24 (N/A)
HLA-DPB1 Match			
Double allele mismatch	42 (36)	1 (20)	1 (14)
Single allele mismatch	63 (54)	4 (80)	5 (71)
Full allele matched	11 (9)	0	1 (14)
Unknown	344 (N/A)	101 (N/A)	94 (N/A)
High resolution release score			
No	8 (9)	1 (25)	0
Yes	84 (91)	3 (75)	0
Unknown	368 (N/A)	102 (N/A)	101 (N/A)
KIR typing available			
No	382 (83)	106 (100)	101 (100)
Yes	78 (17)	0	0
Cord blood number of units			
1	276 (60)	0	57 (56)
2	183 (40)	0	44 (44)
3	1 (<1)	0	0
Unknown	0 (N/A)	106 (N/A)	0 (N/A)
Graft type			
UCB	424 (92)	98 (92)	98 (97)
PBSC+UCB	36 (8)	8 (8)	3 (3)
Conditioning regimen			
Myeloablative	189 (41)	43 (41)	35 (35)
RIC/Nonmyeloablative	271 (59)	62 (58)	66 (65)
TBD	0	1 (1)	0
Donor age at donation			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
To Be Determined/NA	11 (2)	12 (11)	7 (7)
0-9 years	403 (88)	82 (77)	89 (88)
10-19 years	20 (4)	4 (4)	3 (3)
20-29 years	6 (1)	1 (1)	0
30-39 years	7 (2)	2 (2)	1 (1)
40-49 years	6 (1)	2 (2)	1 (1)
50+ years	7 (2)	3 (3)	0
Median (Range)	4 (0-68)	5 (0-68)	3 (1-43)
Donor/Recipient CMV serostatus			
+/+	103 (22)	18 (17)	23 (23)
+/-	59 (13)	11 (10)	13 (13)
-/+	77 (17)	22 (21)	15 (15)
-/-	49 (11)	14 (13)	15 (15)
CB - recipient +	107 (23)	22 (21)	22 (22)
CB - recipient -	60 (13)	13 (12)	9 (9)
CB - recipient CMV unknown	5 (1)	6 (6)	4 (4)
GvHD Prophylaxis			
Ex vivo T-cell depletion	4 (1)	1 (1)	1 (1)
CD34 selection	25 (5)	5 (5)	1 (1)
Tacrolimus + MMF +- others	153 (33)	26 (25)	29 (29)
Tacrolimus + MTX +- others (except MMF)	13 (3)	4 (4)	1 (1)
Tacrolimus + others (except MTX, MMF)	31 (7)	7 (7)	5 (5)
Tacrolimus alone	26 (6)	10 (9)	3 (3)
CSA + MMF +- others (except Tacrolimus)	170 (37)	47 (44)	50 (50)
CSA + MTX +- others (except Tacrolimus, MMF)	3 (1)	1 (1)	1 (1)
CSA + others (except Tacrolimus, MTX, MMF)	11 (2)	1 (1)	3 (3)
CSA alone	1 (<1)	0	1 (1)
Other GVHD prophylaxis	16 (3)	2 (2)	2 (2)
Missing	7 (2)	2 (2)	4 (4)
Donor/Recipient sex match			
CB - recipient M	271 (59)	64 (60)	58 (57)
CB - recipient F	189 (41)	42 (40)	43 (43)
Year of transplant			
2001-2005	6 (1)	6 (6)	2 (2)
2006-2010	154 (33)	33 (31)	34 (34)
2011-2015	246 (53)	52 (49)	50 (50)
2016-2019	54 (12)	15 (14)	15 (15)
Follow-up among survivors, Months			
N Eval	213	44	39
Median (Range)	57 (3-139)	37 (6-134)	48 (2-97)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	765	102	75
Source of data			
CRF	235 (31)	26 (25)	23 (31)
TED	530 (69)	76 (75)	52 (69)
Number of centers	57	23	19
Disease at transplant			
NHL	631 (82)	84 (82)	58 (77)
Hodgkins Lymphoma	134 (18)	18 (18)	17 (23)
NHL Disease status at transplant			
CR1	103 (16)	19 (23)	8 (14)
CR2	124 (20)	14 (17)	11 (19)
CR3+	70 (11)	6 (7)	2 (3)
PR	58 (9)	11 (13)	6 (10)
Advanced	270 (43)	32 (39)	31 (53)
Missing	2 (<1)	1 (1)	0
Recipient age at transplant			
0-9 years	7 (1)	1 (1)	0
10-19 years	40 (5)	5 (5)	1 (1)
20-29 years	76 (10)	12 (12)	6 (8)
30-39 years	76 (10)	13 (13)	11 (15)
40-49 years	134 (18)	13 (13)	19 (25)
50-59 years	230 (30)	29 (28)	23 (31)
60-69 years	192 (25)	27 (26)	14 (19)
70+ years	10 (1)	2 (2)	1 (1)
Median (Range)	52 (5-74)	53 (2-73)	51 (20-72)
Recipient race/ethnicity			
Caucasian, non-Hispanic	529 (71)	53 (55)	52 (71)
African-American, non-Hispanic	73 (10)	13 (14)	9 (12)
Asian, non-Hispanic	31 (4)	14 (15)	2 (3)
Pacific islander, non-Hispanic	2 (<1)	1 (1)	0
Native American, non-Hispanic	3 (<1)	0	0
Hispanic	108 (14)	15 (16)	10 (14)
Unknown	19 (N/A)	6 (N/A)	2 (N/A)
Recipient sex			
Male	481 (63)	68 (67)	46 (61)
Female	284 (37)	34 (33)	29 (39)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Karnofsky score			
10-80	235 (31)	34 (33)	21 (28)
90-100	503 (66)	65 (64)	48 (64)
Missing	27 (4)	3 (3)	6 (8)
Graft type			
Marrow	90 (12)	17 (17)	10 (13)
PBSC	675 (88)	84 (82)	65 (87)
BM+PBSC	0	1 (1)	0
Conditioning regimen			
Myeloablative	300 (39)	36 (35)	26 (35)
RIC/Nonmyeloablative	462 (60)	65 (64)	49 (65)
TBD	3 (<1)	1 (1)	0
Donor age at donation			
To Be Determined/NA	6 (1)	0	1 (1)
0-9 years	15 (2)	1 (1)	0
10-19 years	41 (5)	4 (4)	0
20-29 years	77 (10)	17 (17)	9 (12)
30-39 years	107 (14)	12 (12)	15 (20)
40-49 years	158 (21)	20 (20)	16 (21)
50+ years	361 (47)	48 (47)	34 (45)
Median (Range)	49 (0-81)	49 (0-71)	48 (0-74)
Donor/Recipient CMV serostatus			
+/+	315 (42)	52 (52)	28 (39)
+/-	94 (12)	11 (11)	8 (11)
-/+	138 (18)	18 (18)	16 (23)
-/-	207 (27)	19 (19)	19 (27)
Unknown	11 (N/A)	2 (N/A)	4 (N/A)
GvHD Prophylaxis			
Ex-vivo T-cell depletion	7 (1)	2 (2)	0
CD34 selection	3 (<1)	0	0
Post-CY + other(s)	129 (17)	17 (17)	13 (17)
Post-CY alone	4 (1)	1 (1)	0
TAC + MMF +- other(s) (except post-CY)	108 (14)	13 (13)	3 (4)
TAC + MTX +- other(s) (except MMF, post-CY)	344 (45)	29 (28)	39 (52)
TAC + other(s) (except MMF, MTX, post-CY)	82 (11)	32 (31)	13 (17)
TAC alone	8 (1)	1 (1)	1 (1)
CSA + MMF +- other(s) (except post-CY)	9 (1)	1 (1)	0
CSA + MTX +- other(s) (except MMF, post-CY)	18 (2)	0	0
CSA + other(s) (except MMF, MTX, post-CY)	11 (1)	5 (5)	0
CSA alone	2 (<1)	0	0
Other(s)	19 (2)	0	1 (1)
Missing	21 (3)	1 (1)	5 (7)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Donor/Recipient sex match			
Male-Male	292 (38)	41 (40)	29 (39)
Male-Female	138 (18)	17 (17)	11 (15)
Female-Male	188 (25)	27 (26)	17 (23)
Female-Female	146 (19)	17 (17)	18 (24)
Unknown	1 (N/A)	0 (N/A)	0 (N/A)
Year of transplant			
2006-2010	105 (14)	10 (10)	13 (17)
2011-2015	430 (56)	59 (58)	36 (48)
2016-2019	230 (30)	33 (32)	26 (35)
Follow-up among survivors, Months			
N Eval	482	68	54
Median (Range)	36 (3-126)	25 (3-101)	37 (3-109)

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CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Lymphoma Working Committee Members

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

RE: Studies in Progress Summary

LY16-02: Comparison of alternative donor source stem cell transplant versus matched related donor stem cell transplant for Hodgkin Lymphoma (S Ahmed/J Kanakry) This study looks to compare haploidentical, cord blood, 8/8 unrelated donors, 7/8 unrelated donors, and HLA identical sibling donors in patients with Hodgkin Lymphoma. This study is currently under analysis. The goal of this study is to submit the study for publication by June 2019.

LY17-01b: **Clinical outcomes of patients age >=65 undergoing allogeneic hematopoietic cell transplant for non-hodgkin lymphoma** (N Shah) This study describes the post-allogeneic transplant outcomes of patients with NHL aged ≥ 65 years in comparison to patients aged 55-64 years. This study is currently under manuscript preparation. The goal of this study is to submit the study for publication by June 2019.

LY17-02: Allografts in lymphoma following reduced intensity conditioning (N Ghosh/S Ahmed) This study looks to describe post-allogeneic transplant outcomes in Hodgkin's disease and Non-Hodgkin lymphoma patients following reduced intensity or non-myeloablative conditioning. This study is currently under data file preparation. The goal of this study is to submit the study for publication by June 2019.

LY18-01: Outcomes in b cell non-hodgkin lymphoma patients who underwent autologous stem cell transplantation following rituximab containing conditioning regimens (D Jagadeesh/N Majhail/B Hill) This study evaluates outcomes of rituximab containing conditioning regimen for in DLBCL patients undergoing auto-HCT compared to non-rituximab conditioning regimen. This study is currently under protocol development. The goal of this study is to finalize the analysis by June 2019.

LY18-02: Effect of time to relapse on overall survival in mantle cell lymphoma patients following frontline autologous stem cell transplant (P Riedell/S Smith) This study compares post-relapse survival among patients relapsing <2 years and ≥2 years following frontline autologous stem cell transplant for mantle cell lymphoma. This study is currently under protocol development. The goal of this study is to finalize the analysis by June 2019.

LY18-03: Does outcome after allogeneic hematopoietic stem cell transplant differ between patients with de novo diffuse large b-cell lymphoma and transformed diffuse large b cell lymphoma arising in the setting of indolent lymphoma (A Herrera) This study evaluates whether there is a difference in post-alloHCT PFS among patients with TIL as compared to patients with *de novo* DLBCL. This study is currently under protocol development. The goal of this study is to finalize the protocol by June 2019.

LY18-G1: Maintenance therapies for Hodgkin and non-Hodgkin lymphomas after autologous transplantation: a consensus project of ASBMT, CIBMTR and EBMT (M Hamadani) This study is currently under manuscript preparation. The goal of this study is to submit the study for publication by June 2019.

Proposal: 1808-02

Title:
Evaluating the efficacy of high-dose therapy and autologous hematopoietic cell transplantation for Gray Zone Lymphoma or aggressive B-cell lymphoma with features intermediate between diffuse large B- cell and Hodgkin lymphoma.

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Hypothesis:
High-dose therapy (HDT) followed by autologous hematopoietic cell transplant (auto-HCT) is associated with durable remissions in patients with Gray Zone Lymphoma (GZL), comparable to outcomes of auto-HCT in cHL and DLBCL.

Specific aims:
- To determine the 3-year progression-free survival (PFS) following auto-HCT
- To determine the 3-year overall survival (OS) following auto-HCT
- To determine the 3-year cumulative incidence of relapse/progression following auto-HCT
- To determine the 1-year and 3-year non-relapse mortality (NRM) following auto-HCT
- To compare 3-year PFS and OS of patients with GZL vs. a matched-controlled cohort of patients who received an auto-HCT for cHL or DLBCL.

Scientific justification:
HDT followed by auto-HCT represents the standard of care and the most optimal treatment for chemosensitive relapsed DLBCL and cHL [1-3]. GZL is a recently recognized entity which demonstrates histologic features between DLBCL and cHL [4,5]. Owing to its rarity, the treatment of GZL poses a real therapeutic challenge. To date, no randomized data exist comparing conventional chemotherapy or chemoradiotherapy vs. auto-HCT whether as front-line consolidation or in the relapsed and/or refractory setting. The main reason is due to the relatively low incidence of GZL and probably misdiagnosis and underreporting.
A small multicenter observational study which included 32 patients, median age of 38 (18-70) years, who received an auto-HCT at 1 of 9 transplant centers in the United States showed a 3-year PFS and OS for all patients of 69% and 78%, respectively [6]. Encouragingly, the 3-year PFS and OS were 100% for patients who had received only 1 line of therapy prior to autografting; in contrast, for patients who had received > 1 line of therapy, the 3-year PFS and OS were 65% and 75%, respectively [6]. The authors reported a cumulative incidence of relapse at 3-years post-autografting was 31% [6]. This study is limited by the small sample size and its retrospective nature.
Because it is unlikely that a randomized controlled trial will be ever conducted for GZL, observational studies involving larger datasets are definitely needed to confirm the efficacy of auto-HCT in patients with GZL and better inform clinical decision in this disease. Accordingly, we propose to utilize the Center for International Blood and Marrow Transplantation Research (CIBMTR) database to evaluate outcomes of patients with GZL who are offered and auto-HCT. Moreover, we propose to compare outcomes of auto-HCT in GZL against a matched-controlled cohort of patients autografted for cHL or DLBCL for the same time period.

Patient eligible population:
Adult patients older than 18 years of age who received an auto-HCT for GZL or cHL or DLBCL between 01/2006 and 12/2016.

Confirmation of diagnosis:
Centralized pathology review if possible; otherwise, review of pathology reports.

Variables to be analyzed:
Patient-related:

- Age at auto-HCT, years (stratified by decade)
- Gender
- Race: Caucasian vs. African American vs. others
- Karnofsky performance score
- HCT comorbidity index

Disease-related:

- Remission status at time of auto-HCT: CR1 vs. PR1 vs. CR2 vs. PR2 vs. SD vs. PD
- Disease stage at diagnosis
- Interval from diagnosis to auto-HCT (in months)
- Number of pre-transplant lines of therapies
- Treatments prior to auto-HCT (first line CHOP- vs. ABVD vs. others)

Transplant-related:

- BEAM/BEAC vs. others
- Year of transplantation: 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015
- CD34 cell dose
- Cell source: PBSC vs. BM
- Post-transplant maintenance therapy: yes vs. no

Data requirement:
patient baseline data, pre-HCT data, 100-day post-HCT data, six months to 2-year post-HCT data, patient's death data.

Study design:
This study will investigate the efficacy of auto-HCT in patients with GZL and compare survival outcomes (PFS, OS) with a matched-controlled cohort of patients autografted for cHL and DLBCL. Descriptive tables of patient, disease-, and transplant-related factors will be developed. The tables will list median and range for continuous variables and percent of total for categorical variables. Probabilities of PFS and OS will be calculated from time of auto-HCT (day 0) using the Kaplan-Meier estimator. Cumulative incidence of relapse/progression and NRM will be calculated using the Fine and Gray competing risk regression model.
If sample size and number of events allow, a multivariate analysis will be performed using Cox proportional hazards models for various outcomes. A stepwise model building approach will then be used to identify the significant risk factors associated with the outcomes. Factors, which are significant at a 5% level, will be kept in the final model. The potential interactions between main effect and all significant risk factors will be tested.

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The below selection criteria was applied	# excluded	N
Adult patients who underwent 1st auto-HCT for NHL/HL from 2006-2016		40917
Disease: GZL, DLBCL, cHL	23534	17383
EXCLUSION:		
Exclude missing survival status	1215	16168
Exclude patients without consent	192	15976
Exclude embargoed centers	294	15682

Baseline characteristics of adult patients who underwent first auto-HCT for GZL, cHL or DLBCL, 2006-2016

	Grey Zone Lymphoma	cHL	DLBCL
Number of patients	**110**	**8634**	**13582**
Research level data	12	818	1418
Number of centers	64	309	280
Age at HCT, median(range), yrs			
Age at HCT, yrs	39 (19-76)	34 (18-84)	59 (18-84)
18-29	26 (24)	3246 (38)	552 (4)
30-39	32 (29)	2228 (26)	935 (7)
40-49	14 (13)	1453 (17)	1834 (14)
50-59	18 (16)	978 (11)	3995 (29)
60-69	17 (15)	623 (7)	4866 (36)
≥ 70	3 (3)	106 (1)	1400 (10)
Sex			
Male	71 (65)	4741 (55)	8224 (61)
Female	39 (35)	3890 (45)	5355 (39)
Missing	0	3 (<1)	3 (<1)
Patient race			
Caucasian	91 (83)	6465 (75)	10955 (81)
African American	6 (5)	917 (11)	757 (6)
Other	4 (4)	349 (4)	744 (5)
Missing	9 (8)	903 (10)	1126 (8)
Karnofsky score			
≥ 90	82 (75)	5222 (60)	7274 (54)
< 90	26 (24)	2524 (29)	5201 (38)
Missing	2 (2)	888 (10)	1107 (8)

	Grey Zone Lymphoma	cHL	DLBCL
Number of patients	**110**	**8634**	**13582**
Disease status			
CR	60 (55)	3922 (45)	7314 (54)
PR	41 (37)	3394 (39)	5035 (37)
Resistant	9 (8)	794 (9)	834 (6)
Untreated	0	74 (<1)	47 (<1)
Unknown	0	450 (5)	352 (2)
Year of transplant			
2006	2 (2)	878 (10)	1081 (8)
2007	0	679 (8)	899 (7)
2008	1 (<1)	744 (9)	980 (7)
2009	4 (4)	796 (9)	1161 (9)
2010	7 (6)	804 (9)	1202 (9)
2011	5 (5)	843 (10)	1365 (10)
2012	4 (4)	807 (9)	1389 (10)
2013	13 (12)	787 (9)	1393 (10)
2014	33 (30)	795 (9)	1337 (10)
2015	17 (15)	782 (9)	1428 (11)
2016	24 (22)	719 (8)	1347 (10)
Median follow-up of survivors (range), months	37 (1-96)	50 (<1-150)	52 (<1-149)

Proposal: 1809-01

Title:
Post-transplant cyclophosphamide-Based Haploidentical Transplantation versus Matched Sibling or Well-matched Unrelated Donor Transplantation for peripheral T cell lymphoma: A CIBMTR Lymphoma Working Committee & EBMT Lymphoma Working Party Analysis

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Mehdi Hamadani, MD, mhamadani@mcw.edu, CIBMTR

Study type:
Retrospective registry-based analysis.

Objective:
To analyse the outcome of ptCY haplo-HCT in comparison to alloHCT from MSD, WMUD TCD+, and WMUD TCD- in patients with PTCL

Rationale:
- PTCL is now the largest indication for alloHCT in patients with lymphoma
- alloHCT will remain a key therapeutic tool in PTCL because there are no competing drug or cellular therapies at the doorstep (except for ALCL)
- PTCL is basically GVL-sensitive; but the effect may vary with entity (1, 2), immunogenetic barrier and GVHD prophylaxis
- To date, only a small study comparing haploHCT with conventional donors has been published (18 haplos, 2013)(3), but there is no larger PTCL-specific analysis on haploHCT available
- Because of often rapid disease kinetics, haploHCT may have particular advantages over MUDs in this entity
- Would be largest study on alloHCT in PTCL ever (1, 2, 4-10)
- Restriction to AITL and PTCL-NOS, as the largest sub-entities, avoids conflicts with diagnostic imprecision and, with regard to ALCL, ALK status and targeted therapy competition

Eligibility:
Inclusion criteria:
- Allogeneic HCT
- First allogeneic HCT (previous auto-HCT allowed)
- Diagnosis of angioimmunoblastic T cell lymphoma (AITL) or peripheral T cell lymphoma, not otherwise specified (PTCL-NOS) (other entities to be discussed)
- Age ≥18y at transplant
- Allografted 2008-2017
- Haplo donor, or HLA-identical sibling (MSD) or well-matched unrelated donor (WMUD, 8/8)
- Haplo donor: Use of ptCY as GVHD prophylaxis
- MSD or WMUD: Use of CNI-based GVHD prophylaxis
- All types of conditioning

Exclusion criteria:
- MMUD
- UCB

- CIBMTR: patients not from U.S or Canada (to avoid duplication)
- ptCY in MSD / WMUD
- TCD in MSD

Primary endpoints:

- Progression-free survival (PFS): Comparison of time from HCT to relapse, progression, or death from any cause
- Overall survival (OS): Comparison of time from HCT to death from any cause

Secondary endpoints:

- Non-Relapse mortality (NRM): Comparison of time from HCT to death without previous disease relapse or progression (taking into account relapse as competing risk)
- Disease relapse or progression incidence (RI): Comparison of time from HCT to relapse or progression, or death from any cause (taking into account NRM as competing risk)
- Time to engraftment: Comparison of days from autoSCT to ANC >0.5/nl / PLT >20/nl
- Incidence and severity of acute and chronic GVHD
- GVHD- and relapse-free survival (GRFS): Comparison of time from HCT to severe acute or chronic GVHD, relapse, progression, or death from any cause
- Primary cause of death (descriptive only)
- Optional: to study the effect of TCD in the MUDs

Data items to be collected:
Med-A if not indicated differently

Baseline characteristics:

- Age at allo-HCT
- Sex
- Diagnosis
- Date of diagnosis
- Previous auto-HCT
- Reporting registry (CIBMTR vs EBMT)
- (HCT-CI score, if available)

HCT details:

- Date of transplant
- Time from diagnosis to transplant
- Disease status at transplant (CR1/PR1/VGPR1 vs CR>1/PR>1/VGPR>1/sensitive_relapse vs SD/PD/ref)
- Performance status at transplant
- Conditioning regimen details
- Conditioning intensity
- Use of in-vivo TCD with ATG or alemtuzumab
- Graft source: BM vs. PB
- GVHD prophylaxis including ptCY
- Donor sex

- Donor HLA match
- Patient and donor CMV status

Outcomes:

- Status at last follow-up
- Date of last follow-up
- Time to durable ANC >0.5/nl
- Best response after SCT
- Relapse – y/n
- Date of relapse, if applicable
- Cause of death, if applicable
- Date of death, if applicable
- Secondary malignancy
- Acute GVHD: no/yes and maximum grade
- Chronic GVHD: maximum extent and date of diagnosis

Sample size:

A PM download on August 1, 2018, identified 85 ptCY haplos, 463 MSD and 342 WMUD who meet all the inclusion criteria (if only AITL and PTCL-NOS were considered) in the EBMT registry. A CIBMTR database download on July 16, 2018, identified 37 ptCY haplos, 269 MSD and 190 WMUD who meet all the inclusion criteria (if only AITL and PTCL-NOS were considered) not corrected for a few patients <18 and/or form outside U.S./Canada.*

In total, we can work with approximately 120 haplos, 720 MSD, and 530 MUD if both datasets are pooled and the analysis is restricted to AITL and PTCL-NOS.

*The enclosed raw data are confidential and represent a preliminary review of information submitted to the CIBMTR. If used publicly, the following statement must be included: 'The data presented here are preliminary and were obtained from the Statistical Center of the Center for International Blood and Marrow Transplant Research. The analysis has not been reviewed or approved by the Advisory or Scientific Committees of the CIBMTR.' The data may not be published without the approval of the Advisory Committees.

Statistical work program and statistical methods:

<u>Work program:</u>

- Analyze the impact of graft source and conditioning intensity univariately and after multivariate adjustment for confounders separately for each of the 3 donor groups
- Compare the 3 donor groups for the 4 standard endpoints by matching and/or standard multivariate adjustment. The following factors will be considered for matching (1:2 ratio) or adjustment
    - Gender
    - Age (+/- 10 years)
    - Previous auto yes/no
    - Diagnosis (PTCL vs AITL)
    - Time from diagnosis to transplant (+/- 10 months)
    - Disease status at transplant
    - Year of allo-HSCT
    - Performance status (including a missing category)
    - center where the patient is transplanted

- conditioning intensity
- graft source (BM vs PBSC)

Methods:
Descriptive statistics will be used to summarize patient's characteristics. The Chi-square test or the Fisher exact test for categorical variables and the t-test or Mann-Whitney U-test for continuous variables will be used for comparisons. Time to relapse, time to death and time to GVHD are measured from the date of stem cell transplantation. Cumulative incidence curves for GVHD will be constructed and will take into account for the competing risk of death. Cumulative incidence curves for relapse will be estimated and will take into account the competing risk of death. Potential prognostic factors for relapse, and NRM will be examined in a Cox proportional hazards model and a competing-risks regression model.
Time to death, relapse or last follow-up will be calculated from the time of stem cell transplant. The probabilities of overall survival (OS) and progression free survival (PFS) will be estimated using the Kaplan-Meier product-limit estimate. Comparison between groups will use the log-rank test. Cox multivariate regression analysis will be performed to estimate the risk factors for survival. All factors differing significantly between the groups and all prognostic factors in univariate analysis ($p < 0.2$) will be included in the multivariate analysis.
Statistical analysis will be performed at the EBMT data office in Paris.

Data collection:
Data to be collected from Med A forms plus Med B levels items to be requested from the centres if not already available due to previous requests.

Central review of written histology reports:
Will not be performed for the purposes of this study.

Time frame:
To be approved at the September 2018 LWP ORF and the LWC BM at the 2019 Tandems.
Targeted deadline for final data retrieval: March 31, 2019. It is envisaged that data analysis may be completed to be presented at the ASH meeting 2019 and the 2020 Tandem / EBMT Annual meetings and be prepared for publication in parallel. Optional presentation split between MSD and WMUD comparisons.

Participating centres:
All centres with appropriate baseline and follow-up data on eligible patients in the database.

Administration and budget:
- Study Coordinator: Hervé Finel
- Statistician: Ariane Boumendil
- WP chairperson: Silvia Montoto
- Envisaged staff time: tbc

Publication:
See TIME FRAME. Authorship has to be discussed and decided before launch of the study.

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Selection criteria

Inclusion/Exclusion	Excluded	CIBMTR Total	EBMT excluded	EBMT total	Total
First allogeneic HCT for NHL in US or Canada from 2008-17		8351		11274	19625
Age ≥ 18 years	272	8079	554	10720	18799
Restrict graft type to peripheral blood or bone marrow	507	7572	350	10370	17942
PTCL, AITL, or ALCL disease histology	6491	1081	8841	1529	2610
Restrict to HLA-identical sibling, MUD or haploidentical donors	117	964	391	1138	2102
Restrict haploidentical donors to PT-CY GVHD prophylaxis	17	947	17	1121	2068
Restrict MUD and MRD to CNI-based GVHD prophylaxis	54	893	66	1055	1948
Restrict to patients who consented for research	50	843	28	1027	1870
Exclude centers embargoed for research	19	824	0	1027	1851

Table 1. Baseline characteristics of adult patients receiving 1st allogeneic HCT for PTCL, AITL and ALCL registered at the CIBMTR during 2008-2017

	HLA-identical sibling	Matched Unrelated donor	Haploidentical donor
Number of patients	**918**	**757**	**176**
Research level data; CIBMTR	44 (12)	63 (17)	24 (32)
Number of centers	310	227	92
Patient age, years: Median(range)	52 (18-77)	53 (18-75)	55 (18-74)
Male sex	595 (65)	476 (63)	110 (63)
KPS ≥ 90	592 (64)	482 (64)	95 (54)
Missing KPS	621 (68)	498 (66)	98 (56)
Patient race; CIBMTR			
Caucasian	284 (75)	335 (90)	46 (62)
African American	45 (12)	12 (3)	20 (27)
Other	20 (5)	16 (4)	5 (7)
Missing	28 (7)	10 (3)	3 (4)
Peripheral blood as graft type	854 (93)	704 (93)	115 (65)
NHL subtype			
PTCL	484 (53)	378 (50)	87 (49)
AITL	270 (29)	231 (30)	45 (26)
ALCL	164 (18)	148 (20)	44 (25)
Remission status			
CR	450 (49)	372 (49)	96 (55)
PR	266 (28)	213 (28)	53 (30)
Resistant	170 (19)	149 (20)	16 (9)
Unknown	32 (4)	23 (3)	2 (1)
Median follow-up of survivors (range), months	56 (3-123)	48 (5-122)	24 (3-97)

Proposals: 1810-02 & 1811-56

Title:
Outcomes of Allogeneic HCT in patients with Hodgkin Lymphoma in the era of Checkpoint Inhibitors.

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Hypothesis:
Results of allogeneic transplant for Hodgkin Lymphoma in the recent era have improved in part because prior exposure to checkpoint inhibitors improves post-transplant outcomes through decreased relapse.

Specific aims:
The specific aims are:

- Assess outcomes in adult patients with Hodgkin lymphoma undergoing reduced intensity allo-HCT with or without prior exposure to checkpoint inhibitors.
- General Outcomes to be examined include:
    - Primary objective:
        - Overall Survival.
    - Secondary objectives:
        - Engraftment (neutrophil, platelet), graft failure
        - NRM
        - acute GVHD (II-IV and II-IV)
        - chronic GVHD
        - relapse/progression
        - PFS/DFS
- To identify factors predictive of outcomes with the use of CPI prior to HCT.
- To describe and identify factors predictive of response and outcomes with the use of CPI post HCT.

Scientific impact:
Although the approvals of new and highly effective drugs such as brentuximab vedotin (BV) and checkpoint inhibitors (CPI) have resulted in lower numbers of patients with Hodgkin lymphoma being referred for allo-HCT, results in the modern era suggest a significant improvement in overall survival in those patients with Hodgkin Lymphoma who undergo allo-HCT. Understanding factors that impact HCT outcomes including prior use of checkpoint inhibitors, which has now become standard, will be important in optimal patient selection and choice of transplant approach.

Scientific justification:
Hodgkin lymphoma (HL) is a rare malignancy that has a bimodal distribution of incidence with most patients diagnosed between 15 and 30 years of age and another peak in those older than 55 years. It is estimated that in 2014, approximately 9,190 people were diagnosed with HL in the United States.[1] Despite high success rates with initial chemotherapy, relapse occurs in 10-20% of patients with HL and a small minority is nonresponsive to initial chemotherapy. The standard management of these patients includes high-dose chemotherapy (HDT) followed by autologous stem cell transplant (ASCT). For patients who relapse following ASCT, eligible candidates have historically been offered allogeneic SCT.[2,3]

The past decade has been notable for the approval by the FDA of highly effective novel therapies in patients with HL, including brentuximab vedotin (BV) and the checkpoint inhibitors (CPI).[4-11] This has likely resulted in decreased utilization of allo-HCT in this patient population (A Sureda, EHA 2018). Prior studies have shown improved outcomes of allo-HCT in HL in the brentuximab era,[12] although an EBMT report showed that prior BV did not directly affect OS after HCT.[13] Interestingly recent preliminary data suggests that outcomes in patients with HL who were treated with CPI are improved compared to historical controls.[9] While there is currently limited published data regarding the use of CPI prior to or after HCT, a few preliminary studies have been reported.[9,14] Merryman et al described 39 patients, including 31 with HL, who underwent allo-HCT after prior CPI.[14] The 1-year OS and PFS were 89% (95% confidence interval [CI], 74-96) and 76% (95% CI, 56-87), respectively, whereas the 1-year cumulative incidences of relapse (CIR) and NRM were 14% (95% CI, 4-29) and 11% (95% CI, 3-23), respectively. More recently, Armand et al reported outcomes of 44 patients who proceeded to allo-HCT after treatment with nivolumab.[9] At the time of publication, the 6-month PFS estimate was 82% and the 6-month OS estimate 87%. These results are markedly better than previously published CIBMTR data, where Devetten et al reported probabilities of PFS and OS of 30% and 56% at 1 year and 20% and 37% at 2 years, respectively.[15] Finally the potential benefit of choosing a haploidentical donor over other graft sources remains controversial with conflicting data in the literature.[16,17] It is possible that the results of these studies do not correct for prior CPI use, which in part coincides with the increasing use of haploidentical HCT.

Patient eligibility population:
This study will include adult patients with Hodgkin Lymphoma who received a first allogeneic using a reduced intensity conditioning between 01/2012 and 12/2017.
Inclusion criteria:

- first allo-HCT between 2008 and 2017
- Age $\geq$ 18
- Donors include MSD, MUD and HLA-haploidentical
- GVHD prophylaxis (CNI/MTX, CNI/MMF, PTCY/CNI/MMF) – exclude ex vivo T cell depletion
- Reduced intensity conditioning

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

Table 1 Data Requirements:

Type of data	Data point	Specific data
Patient Specific	Patient specific characteristics	• Age at transplant (Date of birth) • Gender • Race • Significant comorbidities • Prior autologous transplant • Remission status (CR1, CR2, etc) • Karnofsky performance status at transplant: ≥ 90 vs. < 90 vs. missing • HCT-CI • HCT-CI/age • Prior use of checkpoint drug (nivolumab, pembrolizumab) and time from last dose.
Transplant Specific	Transplant date	• Transplant date
	Preparative regimen used	• Reduced Intensity/ non-myeloablative
	GVHD prophylaxis	• Calcineurin inhibitor based (cyclosporin, tacrolimus) • Sirolimus • PTCY • Other
	Graft characteristic	• Donor-recipient HLA match
	Donor source	• Sibling • Unrelated • Haploidentical
Outcome Measures	Engraftment	• Time to absolute neutrophil count $\geq$500 cells/mm^3 for 3 consecutive laboratory readings • Time to unsupported platelets $\geq$20 x 10^9 cells/L and $\geq$50 x 10^9 cells/L • Donor-recipient chimerism • Graft failure (primary and secondary)
	GVHD	• Acute GVHD (aGVHD) o Incidence of grade II-IV acute GVHD (aGVHD) (subset evaluating grade III-IV aGVHD) o Time to aGVHD • GVHD after day 100 o Incidence of chronic GVHD (cGVHD) o Severity of GVHD after day 100
	Mortality	• Time to mortality • Day 100, 6 months and 1 year mortality • Treatment related mortality at 6 months and 1 year • Cause of mortality
	Disease relapse	• Incidence of disease relapse • Time to disease relapse

Study design:

A retrospective study will be conducted utilizing CIBMTR data. Patients will be eligible for inclusion if they are ≥ 18 and who received a first allogeneic HCT for Hodgkin Lymphoma using a MSD, MUD or haploidentical donor between 01/2012 and 12/2017. The objectives of this analysis are to determine outcomes in patients undergoing HCT with or without prior checkpoint exposure treatment.

Descriptive tables of patient, disease-, and transplant-related factors will be created and compared for both cohorts. The tables will list median and range for continuous variables and percent of total for categorical variables. Cumulative incidence of chronic GVHD, relapse/progression, and NRM will be calculated while accounting for competing events. Probabilities of OS will be calculated using the Kaplan-Meier estimator. Multivariate analysis will be performed using Cox proportional hazards models for outcomes for chronic GVHD, relapse/progression, NRM, PFS, and OS and logistic regression for acute GVHD. A stepwise model building approach will then be used to identify the significant risk factors associated with the outcomes. Factors which are significant at a 5% level will be kept in the final model. The potential interactions between main effect and all significant risk factors will be tested. The proportional hazards assumption will be checked for the Cox model. If violated, it will be added as time-dependent covariates.

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Conflict of interest disclosures:

Miguel Perales MD:

- Member, Scientific Advisory Board:
  - MolMed, NexImmune
- Ad hoc Advisory Board:
  - Abbvie, Bellicum, Incyte, Nektar Therapeutics, Novartis
- Consulting:
  - Merck
- Member, DSMB:
  - Medigene, Servier
- Research Funding (to institution):
  - Incyte (clinical trial), Miltenyi (clinical trial)
- Academic/Not-for-Profit:
  - Board Member: ASBMT, Be The Match (NMDP)
  - CIBMTR Advisory Committee
  - Tufts Cancer Center DSMB, University of Barcelona CAR T trial DSMB

Anna Sureda MD:

- Takeda: Consultancy, Advisory Board, Travel Grants, Educational Activities / Symposia
- BMS: Consultancy, Advisory Board, Travel Grants, Educational Activities / Symposia
- MSD: Advisory Board, Educational Activities / Symposia
- Roche: Travel Grants
- Celgene: Advisory Boards, Travel Grant
- Janssen: Travel Grants, Advisory Board
- Sanofi: Travel Grants, Advisory Boards
- Gilead: Advisory Board, Consultancy
- Novartis, Advisory Board, Consultancy

Farrukh Awan MD:

- Member, Speakers Bureau:
  - Astrazeneca, Abbvie
- Ad hoc Advisory Board:
  - Abbvie, Astrazeneca, Genentech, Gilead, Sunesis, Pharmacyclics, Janssen
- Research Funding (to institution):
  - Innate Pharma, Pharmacyclics

Selection criteria

	Excluded	N
Number of adult patients underwent 1st ALLO HCT for HL from 2008-2017 in CIBMTR CRF Jan 2019 retrieval		511
Haplo donor, or HLA-identical sibling (MSD) or well-matched unrelated donor (WMUD, 8/8)	200	311
Reduced intensity	108	203
GVHD prophylaxis: exclude ex vivo T cell depletion	16	187
Consent	2	185
Exclude embargo centers	3	182

Table 1. Baseline characteristics of CRF patients receiving a reduced intensity alloHCT for HL from 2008-2017

	No prior CKI	**CKI***
Number of patients	**151**	**31**
Number of centers	68	22
Patient age, years		
Median (range)	35 (18-70)	30 (19-65)
18- 29	57 (38)	16 (52)
30- 39	42 (28)	6 (19)
40- 49	27 (18)	4 (13)
50 - 59	18 (12)	2 (6)
≥ 60	7 (5)	3 (10)
Sex		
Male	90 (60)	19 (61)
Female	61 (40)	12 (39)
KPS		
≥ 90	107 (71)	21 (68)
< 90	35 (23)	10 (32)
Missing	9 (6)	0
Race		
White	121 (80)	24 (77)
Black	11 (7)	3 (10)
Asian	6 (4)	2 (6)
Others	2 (1)	0
Missing	11 (7)	2 (6)

	No prior CKI	CKI*
Remission status at HCT		
Sensitive	121 (80)	26 (84)
Resistant	26 (17)	5 (16)
Untreated	2 (1)	0
Unknown	2 (1)	0
Donor type		
HLA-identical sibling	33 (22)	10 (32)
Matched unrelated donor	69 (46)	8 (26)
Haploidentical donor	49 (32)	13 (42)
GVHD prophylaxis		
CNI/MTX	52 (34)	9 (29)
CNI/MMF	33 (22)	6 (19)
PTCY/CNI/MMF	66 (44)	16 (52)
Transplant year		
2008	15 (10)	0
2009	14 (9)	0
2010	10 (7)	0
2011	3 (2)	0
2012	8 (5)	0
2013	11 (7)	0
2014	23 (15)	0
2015	11 (7)	2 (6)
2016	22 (15)	9 (29)
2017	34 (23)	20 (65)
Median follow-up of survivors (range), months	35 (3-121)	12 (3-36)

*CKI: Nivolumab, Pembrolizumab, Ipilimumab

Proposal: 1810-07

Title:
Autologous transplantation vs allogeneic transplantation in patients with Angioimmunoblastic T-cell Lymphoma

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Hypothesis:
We hypothesize that allogeneic hematopoietic cell transplantation (allo-HCT) will provide durable remission for angioimmunoblastic T cell lymphoma (AITL) compared to autologous hematopoietic stem cell transplantation (auto-HCT).

Specific objectives:

- To compare auto-HCT with allo-HCT as the first transplantation approach for patients with AITL undergoing auto-HCT or allo-HCT in early disease (first complete or partial remission [CR1/PR1]) during 2000-2017. The following outcomes will be evaluated:
    - Primary objective
        - Overall Survival
    - Secondary objectives
        - Cumulative incidence of acute and chronic graft versus host disease (GVHD)
        - Cumulative incidence of non-relapse mortality (NRM)
        - Cumulative incidence of disease relapse or progression
        - Progression Free Survival
        - Cause of death
- To compare auto-HCT vs allo-HCT for patients with AITL undergoing auto-HCT or allo-HCT in late disease (chemosensitive beyond CR1/PR1) during 2000-2017. The following outcomes will be evaluated:
    - Primary objective
        - Overall Survival
    - *Secondary Objectives*
        - Cumulative incidence of acute and chronic GVHD
        - Cumulative incidence of NRM
        - Cumulative incidence of disease relapse or progression
        - Progression Free Survival
        - Cause of death
- To identify factors predictive of outcome in AITL.

Scientific justification:
Among the nodal peripheral T-cell lymphomas, angioimmunoblastic T-cell lymphoma (AITL) represents a distinct clinicopathologic entity, accounting for approximately 1-2% of all non-Hodgkin's lymphomas (NHLs). Patients typically present with generalized lymphadenopathy, hepatosplenomegaly, anemia, and hypergammaglobulinemia. AITL is characterized by an aggressive clinical behavior and carries a poor prognosis even when treated intensively (1, 2).
First-line therapy mostly consists of anthracycline-based chemotherapy (2, 3). With this approach, overall survival (OS) is a little over 30% at 5 years. In an attempt to improve both CR rate and long-term survival, auto-HCT in AITL was investigated. Several studies evaluated the role of auto-HCT in AITL (4-11).

Table 1 shows both retrospective and prospective studies with n ≥10 (4, 6, 8-11). Though the response rates (CR rate=68-87%) and PFS (49-55%) are better, the cumulative incidence of relapse was high (40-50%).

Allo-HCT may result in a lower risk of relapse in part due to a *graft-versus-lymphoma* effect mediated by the alloreactive donor cells (12-14). Several retrospective studies (12, 15-17) have reported excellent disease control with low rates of relapse and a 1-year NRM ranging from 8 to 25% with allo-HCT in AITL patients. However, these analyses were done mainly in peripheral T-cell lymphoma (PTCL) patients with AITL as a subgroup or reported only a small number of patients with AITL (range N=9-45 patients). We recently evaluated the role of allo-HCT in AITL patients using the CIBMTR registry (n=249). In our study we noted that patients who underwent allo-HCT in CR1 (n=33), the 1-year NRM was 6% while 4 year PFS and OS were 58% and 70% respectively. Patients who underwent allo-HCT in CR>1, PR and even chemorefractory disease had good outcomes (unpublished findings, Epperla et al). However, auto-HCT vs allo-HCT comparison has not been done in patients with AITL.

Some of the relevant clinical questions that need to be answered in the AITL patient population include, determining the appropriate transplant modality and the timing of the transplant (auto-HCT vs allo-HCT, and early vs late disease, respectively).

In the absence of a prospective, randomized data, analysis of a large retrospective cohort can provide valuable information to answer these questions. Herein we propose a registry analysis to analyze two different questions. First, to compare the outcomes of patients with AITL who underwent auto-HCT vs allo-HCT in early (CR1/PR1) disease and second to compare the outcomes of AITL patients who underwent auto-HCT vs allo-HCT in late disease (chemosensitive beyond CR1/PR1).

Table 1: Outcomes of patients with AITL who underwent auto-HCT upfront (n>10)

[1]14 of the total 29 patients' analyzed received auto-HCT upfront. 93% (n=13/14) were chemosensitive at the time of auto-HCT (CR=7/14, PR=6/14).

[2]15 of the 19 patients' analyzed underwent auto-HCT upfront. 87% (n=13/15) were chemosensitive at the time of auto-HCT (CR=8/15, PR=5/15).

[3]101 of the 146 received auto-HCT in first CR or PR. The outcomes reported is for the entire study population (146).

[4]27 of the 83 patients were AITL. The outcomes reported is for the study population who underwent auto-HCT and not restricted to AITL (n=55 of the 83 received auto-HCT).

[5]30 of the total 160 patients were AITL. Of the 160 patients, 115 underwent auto-HCT (breakdown by histology not provided). CR rate and NRM reported is for the entire cohort.

[6]30 of the total 111 patients were AITL. Of the 111 patients 75 received auto-HCT. The outcomes reported is for the study population who underwent auto-HCT (n=75) and not restricted to AITL.

Authors (year)	**Study type**	**N**	**Conditioning regimen**	**CR rate**	**NRM**	**Progression/ Relapse**	**PFS**	**OS**
Schetelig (2003)	Retrosp study	14[1]	BEAM/BEAM like=56% ICE/ICE like=24% Others= 20%	86%	-	5 yr: 41%*	5 yr: 37%**	5 yr: 60%
Rodriguez (2007)	Retrosp study	15[2]	BEAM/BEAM like=79% Others= 21%	79%	-	-	3 yr: 55%	3 yr: 60%
Kyriakou C (2008)	Retrosp study	101[3]	BEAM/BEAM like=84% Others=16%	70%	1 yr: 5% 2 yr:7%	1 yr: 40% 2 yr: 51%	1 yr: 53% 2 yr: 42%	1 yr: 67% 2 yr: 59%
Reimer P (2009)	Prosp study	27[4]	BEAM Others	87%	3.6%	1 yr: 40%	-	3 yr: 71%
d'Amore (2012)	Prosp study	30[5]	BEAM/BEAC	78%	4%	-	5 yr: 49%	5 yr: 52%
Wilhelm (2016)	Prosp study	37[6]	BEAM Cy/TBI	68%	3.6%	43%	5 yr: 39%	5 yr: 57%

*Depicts the outcome of the entire cohort who had CR after auto-HCT (n=22)

**Indicates Event free survival

Table 2: Outcomes of patients with AITL who underwent allo-HCT (n≥ 9)

Authors (year)	Study type	N	Preparative regimens	aGVHD (2-4)	cGVHD (1 yr)	NRM	Prog/ Relapse	PFS	OS
Le Gouill (2008)	Retrosp study	11	MAC=55% NMA=45%	-	-	1 yr: 9%	5 yr: 9%	5 yr: 80%[1]	5 yr: 80%
Kyriakou C (2009)	Retrosp study	45	MAC=56% RIC=44%	29%	52%	1 yr: 25% 3 yr: 27%	1 yr: 13% 3 yr: 20%	1 yr: 62% 3 yr: 53%	1 yr: 66% 3 yr: 64%
Dodero (2012)	Retrosp study	9	MAC=64%[2] RIC=36%	21%[2]	17%[2]	5 yr: 12%[2]	5 yr: 49%[2]	5 yr: 44%	5 yr: 66%
Smith SM (2013)	Retrosp study	12	-	8%	27%	1 yr: 8% 3 yr: 8%	1 yr: 25% 3 yr: 25%	1 yr: 67% 3 yr: 67%	1 yr: 92% 3 yr: 83%
Epperla N (2018)*	Retrosp study	249	MAC=64% RIC=36%	36%[3]	12%[3]	1 yr: 19%	1 yr: 15% 4 yr: 21%	1yr: 66% 4 yr: 47%	1 yr: 73% 4 yr: 56%

Abbreviations: Retrosp=retrospective; aGVHD=acute graft versus host disease; cGVHD= chronic graft versus host disease;
NRM=non-relapse mortality; Prog=progression; PFS=progression-free survival; OS= overall survival;
MAC=myeloablative
conditioning; RIC=reduced-intensity conditioning.

[1]Indicates Event-free survival

[2]Depicts the outcome of the entire PTCL cohort (n=52)

[3]Depicts day 180 acute and chronic GVHD

*Unpublished findings

Study population:

Inclusion criteria:

- Adult (age ≥18 years) T-cell NHL patients (restricted to AITL), undergoing first transplantation (auto-HCT or allo-HCT) during 2000-2017.
- Any donor source
- Any graft source (BM/PB/CB)

Exclusion criteria:

- Non-AITL cases
- Chemo-refractory disease at transplant

Outcomes:

Primary outcome:

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

Secondary outcomes:

- Incidence of acute and chronic GVHD: Cumulative incidence of grade II-IV and grade III-IV acute GVHD per consensus criteria at day +100, with death as competing risk. One year cumulative incidence of limited and extensive chronic GVHD, with death as competing risk
- Non-relapse mortality (NRM): Cumulative incidence of NRM. NRM is defined as death without preceding disease relapse/progression. Relapse and progression are competing events
- Relapse/Progression: Cumulative incidence of disease relapse/progression with NRM as competing event
- Progression-free survival (PFS): 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
- Primary cause of death: descriptive only

Variables to be described:

Patient related:

- Age at HCT, decades
- Gender: male vs. female
- Karnofsky performance score: ≥90 vs. <90 vs. missing
- HCT Co-morbidity index: 0 vs. 1-2 vs. ≥ 3 vs. missing (after 2007)
- Race: White vs. African American vs. Others [Analyze as White vs. others vs. missing]

Disease related:

- Time from diagnosis to HCT: ≥1 year vs. <1 year
- Chemosensitivity at HCT: CR vs PR vs untreated/ missing
- Disease risk index at HCT: Low vs intermediate vs high vs missing

Transplant related:

- Graft type: bone marrow vs peripheral blood vs cord blood
- Donor type: HLA-identical sibling vs. matched unrelated donor vs mismatched unrelated donor (for allo-HCT)
- Year of HCT: Continuous to find the appropriate cut point for the survival model

- Donor/Recipient gender match: male-male vs. male-female vs. female-male vs. female-female (analyzed as M-M vs M-F vs F-M vs F-F) (for allo-HCT)
- Donor/Recipient CMV status: +/+ vs. +/- vs. -/+ vs. -/- vs. missing (analyzed as -/+ vs. others) (for allo-HCT)

Study design:

A retrospective multicenter study will be conducted utilizing CIBMTR dataset. Patients will be eligible if they satisfied the criteria detailed in the "Study population" section. Patients will then be stratified according to auto-HCT vs allo-HCT. The objective of this analysis is to compare these two approaches (in early and late disease) and their effects on the outcomes.

Descriptive tables of patient, disease-, and transplant-related factors will be created. The tables will list median and range for continuous variables and percent of total for categorical variables. Cumulative incidence of GVHD will be calculated while accounting for competing events. Probabilities of OS will be calculated using the Kaplan-Meier estimator. Multivariate analysis will be performed using Cox proportional hazards models for various outcomes. A stepwise model building approach will then be used to identify the significant risk factors associated with the outcomes. Factors which are significant at a 5% level will be kept in the final model. The potential interactions between main effect and all significant risk factors will be tested. The proportional hazards assumption will be checked. If violated, it will be added as time-dependent covariates.

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Selection Criteria:

Inclusion/Exclusion	Excluded #	AlloHCT N	Excluded #	AutoHCT N	Total #
1st HCT for AITL from 2000-2017		454		1157	1611
Age ≥ 18	3	451	4	1153	1604
Exclude resistant remission status at HCT	70	381	45	1108	1489
Exclude if survival status missing	20	361	75	1033	1394
Exclude patients without consent	23	338	10	1023	1361
Exclude embargoed centers	6	332	20	1003	1335

Baseline Characteristics of adult patient who received fist alloHCT or autoHCT for AITL registered in CIBMTR during 2000-2017

	AlloHCT	AutoHCT
Number of patients	332	1003
Research level data		
Number of centers	119	181
Patient age at transplant, years		
Median (range)	56 (21-77)	60 (21-81)
18-29	4 (1)	14 (1)
30-39	24 (7)	41 (4)
40-49	69 (21)	141 (14)
50-59	126 (38)	295 (29)
60-69	100 (30)	419 (42)
≥ 70	9 (3)	93 (9)
Patient sex		
Male	194 (58)	576 (57)
Female	138 (42)	427 (43)
Karnofsky performance score		
≥ 90	167 (50)	546 (54)
< 90	141 (42)	377 (38)
Missing	24 (7)	80 (8)
Patient race		
Caucasian	265 (80)	786 (78)
African-American	12 (4)	63 (6)
Others	15 (5)	66 (7)
Missing	40 (12)	88 (9)

Remission status at HCT

	AlloHCT	AutoHCT
CR1	61 (18)	576 (57)
Other CR	117 (35)	148 (15)
PR	135 (41)	254 (25)
Untreated	7 (2)	7 (<1)
Unknown	12 (4)	18 (2)
Year of HCT		
2000	5 (2)	17 (2)
2001	2 (<1)	10 (<1)
2002	5 (2)	22 (2)
2003	5 (2)	16 (2)
2004	11 (3)	21 (2)
2005	15 (5)	33 (3)
2006	7 (2)	30 (3)
2007	10 (3)	31 (3)
2008	8 (2)	38 (4)
2009	21 (6)	64 (6)
2010	29 (9)	68 (7)
2011	35 (11)	78 (8)
2012	30 (9)	81 (8)
2013	34 (10)	92 (9)
2014	17 (5)	98 (10)
2015	28 (8)	114 (11)
2016	33 (10)	85 (8)
2017	37 (11)	105 (10)
Median follow-up of survivors (range), months	49 (<1-170)	48 (<1-216)

Proposal: 1811-08

Title:
An Evaluation of the Use and Impact of Post-Transplant brentuximab vedotin in patients with classical Hodgkin lymphoma

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Hypothesis:
- Brentuximab vedotin use post auto transplant in high risk classical HL will be increased in the era post-AETHERA and FDA approval
- Use of brentuximab vedotin in patients with high risk classical HL will be associated with improved progression-free and overall survival

Specific aims:
- To characterize the incidence of "high risk" relapsed classical Hodgkin lymphoma within the CIBMTR data set defined as patients with early relapse, residual disease at transplant, and/or extranodal disease
- To describe the use of brentuximab vedotin after autologous transplantation as consolidation before and after the publication of the AETHERA study and FDA approval for all patients and for the high-risk subset.
- To describe the progression-free and overall survival for all patients receiving post-transplant BV compared to those that don't.
- To describe the progression-free and overall survival for high risk patients receiving post-transplant as compared to historical cohort of high risk patients pre-AETHERA as well as contemporaneous patients who were high risk but did not receive it.

Scientific impact:
Although the AETHERA study suggested a benefit of brentuximab vedotin in PFS for patients with classical Hodgkin lymphoma who have high risk disease prior to transplant it is unclear how frequently this approach is currently being utilized and whether or not the findings from the trial are being seen when adopted outside the setting of the trial. This study would first improve our understanding of current treatment patterns at CIBMTR sites and second would potentially validate the findings from the AETHERA study. Depending on the findings, this may significantly impact treatment patterns if it does appear that utilization of brentuximab vedotin truly shows a benefit in high risk patients. We will also evaluate its use in non-high risk patients to see if it is being utilized in that setting and what, if any, impact it may have on PFS in that setting.

Scientific justification:
Fortunately, classical HL is cured in most patients with currently available therapies, including ABVD or brentuximab vedotin + AVD. However up to 25% of patients will relapse and require additional therapy, and in that setting, autologous stem cell transplantation is curable in up to 50% of cases. Unfortunately, high risk subsets of patients have predicted inferior outcome post-transplant, including patients with extranodal disease at relapse, early time to progression, and residual disease after salvage therapy. Several years ago, the AETHERA study compared outcomes for patients with high risk relapsed Hodgkin lymphoma who received brentuximab vedotin post-transplant for 1 year vs placebo and have found a significant improvement in PFS although no OS benefit to date. It is unclear how this finding has been

adopted at centers throughout the world since the publication nor has there been a validation of these findings in a "real world" setting. I am proposing a CIBMTR project designed to evaluate the actual use of this approach at transplant centers as well as what impact it may be having on PFS and OS.

Patient eligibility population:
We will include patients with classical Hodgkin lymphoma who underwent autologous transplantation after at least one relapse OR who required > 1 line of treatment to achieve CR1. We will divide patients between those transplanted Jan 1, 2010 – Aug 31, 2015 and Sep 1, 2015 – December 31, 2017. All patients will be included in the analysis. High risk patients will be defined as: patients who required > 1 line of therapy to achieve CR1, patients whose date of relapse is <18 months from the time of treatment initiation (ie, < 12 months of response duration), and patients with extranodal disease at relapse (we may utilized pre-transplant PET/CT as well as baseline staging to identify patients with extranodal disease if the sites of disease pre-salvage therapy are not available). In the AETHERA study, > 90% of high risk patients had either primary refractory disease or early relapse so we should capture nearly all patients with those two criteria if extranodal sites of disease is not available. Patients with disease progression or death within 30 days of auto transplant shall be excluded.

Data requirements:
<u>All data will be obtained from the following forms:</u>

- Recipient Baseline Data
- Hodgkin and Non-Hodgkin Lymphoma Pre-HSCT Data
- Pre-Transplant Essential Data
- Post-Transplant Essential Data
- 100 Days Post-HSCT Data
- Six Months to Two Years Post-HSCT Data
- Yearly Follow-Up for Greater Than Two Years Post-HSCT Data
- Recipient Death Data

<u>Variables to be analyzed:</u>

- Diagnosis
- Bulky disease
- Stage at diagnosis and at relapse
- Labs at diagnosis, including LDH and ESR
- Bone marrow involvement
- Presence of B-symptoms
- Date of diagnosis
- Date of first Relapse
- Date of Transplant
- Date of post-transplant relapse
- Date of death
- Post-transplant consolidation/maintenance and treatment used (Form 2118)
- Pre-transplant performance status
- BMI
- Organ impairment (CV, renal, hepatic)
- HCT comorbidity index
    - Number of prior therapies
- Type of prior therapies

- Chemo sensitivity of disease (question 151 on form 2018)
- Disease status at transplant
- Conditioning regimen
- Patient education level
- Race /ethnicity
- Gender
- Patient income

Outcomes we intend to capture include (as able using the day 100, 6 months, and yearly forms):

- Date and cause of death (including progressive disease and TRM)
- Use of post-transplant brentuximab vedotin
- Frequency of high risk relapsed Hodgkin lymphoma
- Post-transplant disease status at day 100
- Progression-free survival at 12 months, 24 months, and 60 months
- Overall survival at 12 months, 24 months, and 60 months

Study design:

There are two primary goals for this study. The first is to characterize the frequency of high risk relapsed HL as defined by the AETHERA study and to describe the use of brentuximab vedotin post-autologous transplantation in that setting. For this portion of the project, we will identify patients meeting one of the following criteria: primary refractory disease (defined by never achieving a CR prior to transplant OR requiring > 1 line of therapy to achieve CR1) or patients who experience progression < 18 months after initiation of therapy. The 18 month cutoff is used as we assume that most patients will complete 6 months of therapy and therefore a relapse prior to the 18 month cutoff would suggest that the patients had a relapse duration of < 12 months. We will also attempt to identify patients with extranodal disease at relapse. We will describe the incidence of high risk HL and also describe the use of brentuximab vedotin as consolidation/maintenance before vs after the FDA approval. As a secondary portion of this part of the project, we will describe the use of maintenance in patients who do NOT meet the criteria for high risk.

For the second portion of the study, we will evaluate for differences in survival outcome for high risk patients who receive post-transplant brentuximab vedotin vs those who do not. We will divide the group into those transplanted before September 2015 and those transplanted afterwards. We will identify a contemporaneous high risk cohort of untreated patients as well as evaluate high risk patients treated prior to September 2015 and compare these untreated patients to those high risk patients who have received maintenance therapy since FDA approval. We will compare non-relapse mortality as well as PFS and OS at predetermined timepoints between the treated and untreated patients (1 year, 2 year, 5 year). We will also build a multivariable model to evaluate the impact of other factors on these outcomes and to see if use of brentuximab vedotin remains independently predictive of PFS when controlling for additional factors like performance status, bulky disease, and other baseline prognostic factors.

As an exploratory endpoint, we will attempt to identify predictors of BV use vs non-use among eligible patients as well as any potential patient subsets that do not appear to benefit from this therapy.

Selection criteria table

	Excluded	N
Number of adult patients underwent 1st AUTO and 1st ALLO* HCT for HL in US from 2005-2017 registered with CIBMTR Jan 2019 retrieval		10099
High risk HL: at least one relapse OR who required > 1 line of treatment to achieve CR1	3379	6720
Post transplant maintenance*: yes or no	309	6411
Consent	278	6133
Exclude embargo centers	163	5970

*1st ALLO: didn't include prior AUTO

Table 1. Baseline characteristics of HL patients receiving autoHCT or alloHCT in US registered in the CIBMTR from 2005-2017

	ALLO 2005-2011 N(%)	ALLO 2012-2017 N(%)	AUTO 2005-2011 N(%)	AUTO 2012-2017 N(%)
Number of patients	125	141	2586	3118
Research level data	49 (39)	52 (37)	430 (17)	416 (13)
Number of centers	47	65	168	174
Patient age, years				
Median (range)	35 (19-63)	34 (18-68)	36 (18-84)	35 (18-83)
18-29	38 (30)	59 (42)	856 (33)	1093 (35)
30-39	43 (34)	37 (26)	700 (27)	758 (24)
40-49	21 (17)	21 (15)	504 (19)	495 (16)
50-59	22 (18)	17 (12)	305 (12)	432 (14)
≥ 60	1 (<1)	7 (5)	221 (9)	340 (11)
Patient sex				
Male	67 (54)	81 (57)	1442 (56)	1750 (56)
Female	58 (46)	60 (43)	1144 (44)	1368 (44)
Karnofsky performance score				
≥ 90	49 (39)	102 (72)	1045 (40)	2245 (72)
<90	56 (45)	37 (26)	1006 (39)	828 (27)
Missing	20 (16)	2 (1)	535 (21)	45 (1)
Patient race				
Caucasian	106 (85)	119 (84)	2052 (79)	2458 (79)
African-American	11 (9)	15 (11)	337 (13)	399 (13)
Asian	1 (<1)	2 (1)	52 (2)	81 (3)
Native American	0	0	3 (<1)	8 (<1)
Pacific islander	0	0	8 (<1)	13 (<1)
Other	3 (2)	0	62 (2)	0
Multiple race	0	0	4 (<1)	20 (<1)
Missing	4 (3)	5 (4)	68 (3)	139 (4)
Remission status				
Chemosensitive	75 (60)	96 (68)	2100 (81)	2762 (89)
Resistant	47 (38)	44 (31)	421 (16)	342 (11)
Untreated	1 (<1)	1 (<1)	17 (<1)	4 (<1)
Missing	2 (2)	0	48 (2)	10 (<1)

	ALLO 2005-2011 N(%)	ALLO 2012-2017 N(%)	AUTO 2005-2011 N(%)	AUTO 2012-2017 N(%)
Number of patients	125	141	2586	3118
BV maintenance				
No maintenance given	116 (93)	131 (93)	2304 (89)	2464 (79)
BV given	0	2 (1)	26 (1)	385 (12)
Other maintenance drugs (No BV)	9 (7)	8 (6)	256 (10)	269 (9)
Year of HCT				
2005	25 (20)	0	373 (14)	0
2006	26 (21)	0	411 (16)	0
2007	19 (15)	0	337 (13)	0
2008	13 (10)	0	355 (14)	0
2009	13 (10)	0	350 (14)	0
2010	16 (13)	0	362 (14)	0
2011	13 (10)	0	398 (15)	0
2012	0	12 (9)	0	388 (12)
2013	0	20 (14)	0	437 (14)
2014	0	29 (21)	0	578 (19)
2015	0	22 (16)	0	609 (20)
2016	0	28 (20)	0	531 (17)
2017	0	30 (21)	0	575 (18)
Median follow-up of survivors (range), months	102 (3-147)	29 (5-73)	86 (<1-154)	29 (<1-80)

Proposal: 1811-156 & 1811-19

Title:
Impact of Conditioning Regimen on Outcomes for Patients with Peripheral T-cell Lymphoma Undergoing High-Dose Therapy with Autologous Hematopoietic Cell Transplantation

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Hypothesis:
The choice of conditioning regimen will not significantly influence the outcomes of peripheral T-cell lymphoma (PTCL) patients undergoing high-dose therapy followed by autologous hematopoietic cell transplantation (auto-HCT)

Specific aims:
- Primary: Evaluate the effect of conditioning regimen on overall survival (OS) of the patients with PTCL who underwent high-dose chemotherapy therapy followed by auto-HCT.
- Secondary:
    - Compare 2-year cumulative incidence of relapse, progression-free survival (PFS), non-relapse mortality (NRM); between TBI- vs. non-TBI based and BEAM vs. non-BEAM-based conditioning regiments in patients with PTCL who underwent auto-HCT.
    - Evaluate the Incidence of idiopathic pneumonia syndrome (IPS), neutrophil and platelet engraftment, cause of death between different conditioning regiments in patients with PTCL who underwent auto-HCT.
    - Impact of conditioning regimens on PFS and OS will be analyzed by major PTCL subtypes (i.e. PTCL NOS, angioimmunoblastic T-cell lymphoma, anaplastic large cell lymphoma) if sample size allows.

Scientific impact:
Optimal conditioning regimen for the patients with PTCL undergoing auto-HCT is not well defined. These patients are at higher risk for relapse with poor long-term survival compared to the other B-cell non-Hodgkin lymphoma after high-dose chemotherapy and auto-HCT(1). The proposed observational study will explore the outcomes associated with different conditioning regimens commonly being used (i.e.-BEAM-like, CBV-like, TBI-based) for PTCL patients. The results of this study could influence clinical practice if there are significant findings.

Scientific justification:
Peripheral T-cell lymphomas are a heterogenous group of non-Hodgkin lymphomas (NHL) with aggressive clinical course characterized by frequent relapses and shorter long-term survival compared to B-cell NHLs(1). The common histological subtypes include peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), anaplastic large cell lymphoma (ALCL) and angioimmunoblastic T-cell lymphoma (AITL). Other uncommon histologies are Extranodal NK/T cell lymphoma (ENKTL), nasal type, subcutaneous panniculitis-like T cell lymphoma (SPTCL), enteropathy associated T cell lymphoma (EATL) and hepatosplenic T cell lymphoma(2). The median progression-free survival (PFS) in PTCL following CHOP chemotherapy is 12 to 14 months with approximately 30 percent of patients being alive and free of disease five years after treatment(2). Consolidation with high-dose chemotherapy and auto-HCT is increasingly being utilized after front-line combination chemotherapy or in the relapsed PTCL.

Different conditioning regimens have variable toxicity profile and influence on auto-HCT outcomes of NHL. Chen et al. performed one of the largest analysis using CIBMTR cohort of 4917 NHL patients who underwent auto-HCT. There was a significant interaction between histology, conditioning regimen, and outcomes of auto-HCT. In Hodgkin lymphoma, CBV (cyclophosphamide, BCNU, etoposide [VP-16]), TBI and BuCy (busulfan, cyclophosphamide) were associated with higher NRM compared with BEAM (BCNU, etoposide, cytarabine, melphalan). In diffuse large B-cell lymphoma (DLBCL), high-dose CBV was associated with higher NRM compared to BEAM. However, T-cell NHL were not included in PFS, OS and NRM analysis(3). In other retrospective single center study of NHL, there was no difference in relapse-free survival, OS and NRM between TBI and BEAM regimens(4). T cell lymphomas are biologically, and clinically distinct entities compared to B cell and Hodgkin lymphomas. This makes it difficult to extrapolate from previously published data to determine the impact of conditioning regimen in PTCL subtypes. In a previous CIBMTR analysis by Smith et al., 115 patients with mature T-cell NHL underwent auto-HCT between 2000-2006. Three-year PFS and overall survival (OS) were 47% and 59%, respectively(5). In this study, TBI and BEAM conditioning were used in 23% and 57% of the patients, respectively. The impact of conditioning regimens on PFS, OS and non-relapse mortality (NRM) was not evaluated in that study. To our knowledge, there is no published study specifically looking at post-auto-HCT outcomes of PTCL patients stratified by conditioning regimens.
This study hopes to provide insight into post-auto-HCT PTCL outcomes stratified by conditioning regimen. Given the rarity of PTCL and heterogenous histologies, it is difficult to conduct a prospective study. However, CIBMTR based observational study will provide enough power to detect the interaction between conditioning regimen and PFS, OS and NRM post-auto-HCT in PTCL patients.

Patient eligibility population:
Inclusion:

- Adult patients (ages ≥18 years) who underwent first auto-HCT through 2008- 2016.
- Diagnosis of mature T-cell NHL: PTCL-NOS, AITL, ALCL (ALK-positive and negative), ENKTL, SPTCL, EATL, hepato-splenic lymphoma
- Patients who had received BEAM, CBV, BuCy, TBI based containing regimens prior to auto-HSCT

Exclusion:

- Patients with diagnosis of, precursor T-cell neoplasms, cutaneous T-cell lymphoma
- Second transplantations, allogeneic HCT
- Pediatric patients aged <18 years will be excluded

Data requirements:
We will utilize the following CIBMTR data forms:

- 2400: Pre-Transplant Essential Data
- 2450: Post-Transplant Essential Data
- 2018: Hodgkin and Non-Hodgkin Lymphoma Pre-HCT Data
- 2118: Hodgkin and Non-Hodgkin Lymphoma Post-HCT Data
- 3500: Subsequent Neoplasms

Outcomes:
Relapse/progression: Progressive disease or recurrence of disease would be counted as an event. NRM, defined as death without relapse or progression, is the competing event. Those who survive without recurrence or progression would be censored at the time of last contact.

Progression-free survival (PFS): Survival without recurrence or tumor progression starting following auto-HCT. Recurrence of progression of disease and death would be counted as events. Those who survive without recurrence or progression would be censored at the time of last contact.
Overall survival (OS): Time to death following auto-HCT. Death from any cause will be considered an event. Surviving patients will be censored at the time of last follow up.
Chronic GVHD: Cumulative incidence of chronic GVHD.
Non-relapse mortality (NRM): Death without relapse or progression, where relapse or progression would be competing risks. Those who survive without recurrence or progression would be censored at the time of last contact.
Neutrophil and platelet engraftment: Neutrophil recovery defined as the first of 3 successive days with absolute neutrophil count (ANC) ≥500/μL after post-transplantation nadir. Platelet recovery defined as achieving platelet counts ≥20,000/μL for at least 7 days, unsupported by transfusion. For neutrophil and platelet recovery, death without the event is considered a competing risk.

Variables to be analyzed:
Patient-related:

- Age at transplant- continuous variable, by decades
- Gender- female vs. male
- Karnofsky performance status at transplant: < 90% vs. ≥ 90%
- HCT comorbidity index at transplant 0, 1, 2, and ≥ 3
- Race – Caucasian, African American, others, missing

Disease-related:

- Prognostic index of T-cell non-Hodgkin lymphoma(6)
- Ann-arbor stage at diagnosis – early (I-II) vs advanced (III-IV)
- Disease risk index(7)
- Number of prior therapy (before transplant): 1 vs. 2 vs. ≥ 3
- LDH at diagnosis– normal, elevated, missing
- B symptoms at diagnosis – yes vs no
- BM involvement at transplant – yes vs no
- CNS involvement any time prior to transplant – yes vs no
- Extranodal involvement at the time of diagnosis - yes vs no
- Pre-transplant chemotherapy regimens (if known)
- Disease status at the time of transplant: complete remission vs. partial response vs. stable disease vs. refractory disease vs. untreated vs. unknown

Transplant-related:

- Year of transplant
- Conditioning regimens: TBI vs. non-TBI; BEAM vs. non-BEAM
- Response to transplant (if data available) – CR, PR, SD, refractory, unknown
- Days to neutrophil recovery, median, and at 28 days
- Days to platelet recovery – median and at 28 days
- Time from diagnosis to transplantation: months- median, <24 months ≥24 months
- Graft type: bone marrow vs. peripheral blood stem cell
- Cell dose (bone marrow, total nucleated cells or peripheral blood, $CD34^+$ cell dose)
- Duration of follow up from auto-HCT in survivors-months

Study design:
This will be an observational study based on CIBMTR database. The goal of this study is to analyze outcomes of PTCL patients following their first auto-HCT, stratified by their conditioning regimen. We plan to group conditioning regimens as follows: TBI vs. non-TBI; BEAM vs. non-BEAM. CBV will be divided into CBV^{high} and CBV^{low} based on BCNU dose as described previously.(3) Descriptive tables of patient, disease-, and transplant-related factors will be created. The tables will list median and range for continuous variables and percent of total for categorical variables. Probabilities of relapse/progression, OS and PFS will be calculated using the Kaplan-Meier estimator, with the variance estimated by Greenwood's formula. Values for other endpoints will be generated using cumulative incidence estimates to account for competing risks. Multivariate analysis will be performed using Cox proportional hazards models for various outcomes. A stepwise model building approach will then be used to identify the significant risk factors associated with the outcomes. A backward stepwise model selection approach will be used to identify all significant risk factors. Factors which are significant at a 5% level will be kept in the final model. The potential interactions between main effect and all significant risk factors will be tested.

Non-CIBMTR data source:
For this study, we will utilize the CIBMTR Research Database.

Conflicts of interest:
None

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The below selection criteria were applied	# excluded	N
1st auto-HCT for PTCL-NOS/AITL/ALCL/ENKTL/SPTCL/EATL/hepato-splenic lymphoma from 1996-2016		3618
Age >= 18	39	3579
Received BEAM, CBV, BuCy, TBI based containing regimens	750	2829
EXCLUSION:		
Exclude planned auto-allo package	15	2814
Exclude patients without consent	89	2725
Exclude embargoed centers	35	2690

Baseline characteristics of adult patients who underwent 1st auto-HCT for PTCL-NOS/AITL/ALCL/ ENKTL/ SPTCL/EATL/hepato-splenic lymphoma and received BEAM/CBV/BuCy/TBI based conditioning regimens, 1996-2016

	N (%)
Number of patients	**2690**
Research level data	311
Number of centers	206
Age at HCT, median(range), yrs	57 (18-83)
Age at HCT, yrs	
18-29	150 (6)
30-39	216 (8)
40-49	454 (17)
50-59	769 (29)
60-69	902 (34)
≥70	199 (7)
Patient sex	
Male	1630 (61)
Female	1060 (39)
Karnofsky score	
≥ 90	1432 (53)
< 90	717 (27)
Missing	541 (20)
Disease status	
CR	1794 (67)
PR	737 (27)
Resistant	91 (3)
Untreated	14 (<1)
Unknown	54 (2)

	N (%)
Number of patients	**2690**
Graft source	
Bone marrow	17 (<1)
Peripheral blood	2672 (99)
Others	1 (<1)
Conditioning regimen	
TBI ± others	206 (8)
Bu/Cy ± others	236 (9)
CBV	348 (13)
BEAM or BEAM-like	1900 (71)
Year of transplant	
1996-1997	16 (<1)
1998-1999	44 (2)
2000-2001	73 (3)
2002-2003	86 (3)
2004-2005	126 (5)
2006-2007	161 (6)
2008-2009	299 (11)
2010-2011	374 (14)
2012-2013	471 (18)
2014-2015	679 (25)
2016	361 (13)
Median follow-up of survivors (range), months	48 (<1-219)

Proposal: 1811-40

Title:
Hematopoietic Stem Cell Transplantation for Relapsed/Refractory Primary Mediastinal B-Cell Lymphoma

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Hypothesis and scientific justification:
Patients affected by primary mediastinal B-cell lymphoma (PMBCL) have high chances to be cured with first-line therapy. Latest studies using a chemo-intensive approach such as R-DA-EPOCH reported a 5-year event-free survival and an overall survival rate of 93% and 97% respectively.(1)
Patients with relapsed/refractory PMBCL are treated similarly to other forms of relapsed DLBCL with the use of non-cross-resistant chemotherapy followed by auto-HCT as consolidation.(2,3)However, second-line overall response rates for patients with relapsed/refractory PMBCL are inferior to patients with relapsed diffuse large B cell lymphoma (25% vs 48%, p=0.01).(4)This lower rate of response affects the execution of salvage auto-HCT. In a recent study by Vardhana and colleagues, only 65% of transplant-eligible patients reached a response after second-line chemotherapy.(5) This means that 1 out of 3 transplant-eligible patients won't be eligible for auto-HCT due to chemorefractory disease. These results resemble what happens in the real-life setting with peripheral T-cell lymphoma more than DLBCL.(6) Moreover, of the patients who received auto-HCT as consolidation, 25% had chemorefractory disease and 29% had partial response carrying a higher risk of relapse after the procedure. In a similar study by EBMT, but limited to patients who received auto-HCT as salvage therapy, disease status before transplant conditioned survival outcomes.(7) In fact, 3-year survival was 100%, 85%, 41% for patients in CR1-PR1, CR-PR>1 and refractory disease, respectively. At ASH 2018, Herrera and colleagues presented data regarding 28 patients with PMBCL who received salvage allo-HCT.(abstract #2177). Despite the heavily pretreated population (4 median previous lines of therapy, 75% and 21% with PR and refractory disease at transplant respectively and 71% previous auto-HCT failure), most patients in PR had a 2-year PFS and OS of 50% and 58%, respectively.
The aim of our study is to analyze outcomes of transplantation (auto-HCT and/or allo-HCT) for relapsed/refractory PMBCL. Due to the low number of patients reported in literature and different applications of auto-HCT and/or allo-HCT, it is difficult to understand the role of transplant as a therapeutic strategy in this setting. This is true especially for that significant fraction of patients who cannot reach a major response after salvage chemotherapy and before transplant.
Considering the rarity of the disease, a registry study is the **appropriate methodology** to perform this analysis.
The **innovation** of this study relies on the absence of studies analyzing the outcomes of both auto-HCT and allo-HCT in a large cohort of relapsed/refractory PMBCL patients.
The **clinical significance** of this study consists in improving the medical knowledge regarding the real-life outcomes of these specific group of patients.

Objectives:
Primary objective:

- To describe the overall survival (OS) of patients with relapsed/refractory PMBCL receiving auto-HCT and/or allo-HCT during the course of their therapy.

Secondary objectives:

- Progression Free Survival (PFS)
- Cumulative incidence of Treatment Related Mortality (TRM)
- Cumulative incidence of relapse/progression
- Neutrophil and platelet recovery
- Descriptive analysis of the allo-HCT cohort in terms of both acute and chronic Graft versus Host Disease (GVHD)

Study population:

Inclusion criteria:

- Relapsed/refractory PMBCL patients, age ≥18 years, receiving autologous HCT and/or allo-HCT between 2000-2017, reported to the CIBMTR. Patients who received a previous auto-HCT and eventually an allo-HCT will be studied as part of the allo-HCT cohort.
- For the allo-HCT cohort, eligible donors include HLA-identical siblings or well-matched unrelated donors (HLA 8/8) and haploidentical donor transplants
- For the allo-HCT cohort both myeloablative (MAC) and reduced intensity/non myeloablative (RIC/NMA) conditioning regimen will be permitted
- Bone marrow and/or peripheral blood as graft source
- For the allo-HCT cohort, previous auto-HCT is allowed

Exclusion criteria:

- Patients receiving auto-HCT during their first line of therapy will be excluded
- Patients not receiving rituximab before HCT will be excluded
- Identical twin transplants will be excluded
- Allo-HCT using cord blood will be excluded

Outcomes:

- Hematopoietic recovery: The primary measures for hematopoietic recovery will be:
    - Time to neutrophils (ANC) > 0.5 $x10^9$/L sustained for three consecutive days. This endpoint will be evaluated at 28-day and 100-day after HCT.
    - 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. This endpoint will be evaluated at 28-day and 100-day after HCT.
- TRM: Cumulative incidence of TRM at day +100 and 1, 3 and 5 years. TRM is defined as death without preceding disease relapse/progression. Relapse/progression are competing events.
- RI/POD: Cumulative incidence of disease relapse/progression at 1, 3 and 5 years, with TRM as competing event.
- PFS: survival without relapse/progression or death at 1, 3 and 5 years. Relapse or progression of disease and death are events. Those who survive without recurrence or progression are censored at last contact.
- OS: time to death at 1, 3 and 5 years. Death from any cause will be considered an event. Surviving patients will be censored at time of last follow-up.
- Acute GVHD: Cumulative incidence of grade II-IV acute GVHD per consensus criteria at day +100 and +180, with death as competing risk.
- Chronic GVHD: Cumulative incidence of limited and extensive chronic GVHD at 1 and 3 years.

With death as competing risk.

Data requirements:
Utilizing data collected by CIBMTR from pre and post HCT, which includes pre-transplant essential data form #2400, post-transplant essential data form #2450, selective post-transplant selective data form #2455 and 100 day post-HCT data form #2100, Six Months to Two Years Post-HCT Data #2200. The parameters to be assessed are outlined in **table 1** below.

Table 1 Data Requirements:

Type of data	Data point	Specific data
Patient-specific	Patient-specific characteristics	Age at transplant (Date of birth) Gender Race Significant comorbidities Primary disease type (PMBCL) Remission status pre transplant (CR vs PR vs Refractory)
Transplant Specific	Transplant date	Transplant date
	Transplant information (allo cohort)	Matched related, matched unrelated, full haploidentical
	Preparative regimen used (allo cohort)	MAC, RIC
	GVHD prophylaxis (allo cohort)	Calcineurin based T cell depletion Others
	Graft characteristic (allo cohort)	Stem cell source (BM or PBSC)
Outcome Measures	Engraftment (allo cohort)	Time to absolute neutrophil count $\geq$500 cells/mm^3 for 3 consecutive laboratory readings Time to unsupported platelets $\geq$20 x 10^9 cells/L and $\geq$50 x 10^9 cells/L Graft failure (primary and secondary)
	GVHD (allo cohort)	Acute GVHD (aGVHD) Incidence of grade II-IV acute GVHD (aGVHD) (subset

		evaluating grade III-IV aGVHD) Time to aGVHD GVHD after day 100 Incidence of chronic GVHD at 2 years (cGVHD) Severity of GVHD after day 100
	Mortality (allo cohort)	Time to mortality Day 100, 6 months and 2 year mortality Treatment related mortality at 6 months and 1 year Cause of mortality
	Disease relapse	Incidence of disease relapse Time to disease relapse

Variables to be analyzed:

Main effect:

- Auto-HCT vs allo-HCT (+ subanalysis Auto-HCT vs allo-HCT as first transplant strategy)

Patient-related:

- Age at HCT, years: 18-29; 30-39; 40-49, 50-59, ≥60 years and continuous
- Sex: male vs female
- Karnofsky performance score: ≥90% vs. <90% vs. missing
- Race: White vs. Black vs. Asian/pacific islander vs. Hispanic vs. others

Disease-related:

- Ann Arbor stage at diagnosis: I/II vs III/IV
- IPI stage at diagnosis: <2 vs ≥ 2
- Extranodal disease at diagnosis: yes vs no
- Bulky disease at diagnosis: yes vs no
- Bulky disease at transplant: yes vs no
- B-symptoms at diagnosis: yes vs no
- B-symptoms at transplant: yes vs no
- Elevated LDH at diagnosis: yes vs no
- Time from diagnosis to HCT: <1year vs. ≥1 year and continuous
- PET positive at HCT: yes vs no (when available)
- Disease status at HCT: CR vs PR vs chemorefractory
- Number of prior chemotherapy regimens received: continuous
- Prior radiotherapy: yes vs no
- Chemosensitivity at HCT: chemosensitive vs. chemoresistant vs. untreated
- BM involvement at HCT: yes vs no

Transplant-related (allo-cohort):

- Donor type: HLA-identical siblings vs unrelated transplantation vs haploidentical donors
- Conditioning regimen: TBI-based vs no TBI
- Conditioning regimen: MAC vs RIC/NMA
- Graft type: bone marrow vs peripheral blood vs cord blood
- GVHD prophylaxis: calcineurin inhibitors based vs other groups
- Year of HCT: Continuous (auto and allo cohorts)
- DLI post allogeneic HCT: yes vs no
- Female donor/Male recipient: yes vs no
- Negative donor/Positive recipient CMV status: yes vs no
- ATG or alemtuzumab use for *in vivo* T cell depletion

Study design:

The aim of this study is to describe the clinical outcomes of relapsed/refractory PMBCL patients who received a transplant during their disease history.

Patients will be grouped between auto-HCT or allo-HCT as last transplant procedure.

Patient-, disease- and transplant- related factors will be compared between groups using the Chi-square test for categorical variables and the Wilcoxon two sample test for continuous variables.

OS and PFS probabilities will be calculated using Kaplan-Meier estimator. Neutrophil engraftment, platelets engraftment, acute GVHD (only allo-HCT cohort), chronic GVHD (only allo-HCT cohort), TRM, RI/POD will be calculated using cumulative incidence estimates to account for competing risks. Cox proportional hazards regression will be used to compare the two HCT types for, NRM, relapse/progression, PFS, and OS. The assumption of proportional hazards for each factor in the Cox model will be tested using time-dependent covariates. When the test indicated differential effects over time (non-proportional hazards), models will be constructed breaking the post-transplant time course into two periods, using the maximized partial likelihood method to find the most appropriate breakpoint. The proportionality assumptions will be further tested. A backward stepwise model selection approach will be used to identify all significant risk factors. Each step of model building contained the main effect for conditioning regime. Factors, which are significant at a 5% level, will be kept in the final model. The potential interactions between main effect and all significant risk factors will be tested.

A first subset analysis will be performed for the allo-HCT group regarding specific allogeneic transplant outcomes and variables.

In case of a sufficient number of patients, a second subanalysis will be performed between auto-HCT vs allo-HCT as **first-transplant procedure** will be performed.

Potential pitfalls:

PMBCL cohort may be too small to perform meaningful statistical analysis. In this scenario, additional data could be requested from European Bone Marrow Transplantation (EBMT) registry.

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Selection criteria table

	Exclude	N
Number of patients underwent ALLO or AUTO HCTs for NHL US from 2000-2017 registered with CIBMTR Nov 2018 retrieval		51781
Age ≥ 18	811	50970
Graft type: BM, PB	396	50574
Select 1st AUTO and 1st ALLO(including prior AUTO) HCT	2980	47594
Primary mediastinal large B-cell lymphoma	47387	207
Further select allo donor: Matched sibling, matched unrelated donor (MUD 8/8) or mismatched related(haplo)[1]	4	203
Consent	8	195
Exclude embargo centers	4	191

Patient number	ALLO	AUTO	Total
Ted (registration) patient	14	133	147
cRF (Research) patient	14	30	44
Total	28	163	191

Notes:
*No chemotherapy data available in TED retrieval
[1]Haplo: ≥1 mismatch at allele level

Characteristics of Primary mediastinal large B-cell lymphoma patients

Characteristic	ALLO	AUTO
Number of patients	**28**	**163**
Number of centers	22	85
CRF (Research) level patient	14	30
Age at transplant, year		
Median(range)	37 (20-61)	35 (18-72)
18-29	10 (36)	50 (31)
30-39	5 (18)	69 (42)
40-49	10 (36)	24 (15)
50-59	2 (7)	12 (7)
≥ 60	1 (4)	8 (5)
Sex		
Male	10 (36)	71 (44)
Female	18 (64)	91 (56)
Not answered	0	1 (<1)
KPS		
≥ 90	19 (68)	87 (53)
<90	8 (29)	54 (33)
Missing	1 (4)	22 (13)
Race		
Caucasian	25 (89)	124 (76)
African-American	0	15 (9)
Asian	2 (7)	11 (7)
Native American	0	1 (<1)
Pacific islander	0	1 (<1)
Other	0	3 (2)
Missing	0	2 (1)
Disease status		
Sensitive	19 (68)	141 (87)
Resistant	8 (29)	21 (13)
Untreated	1 (4)	0
Missing	0	1 (<1)
Graft type		
Bone marrow	6 (21)	2 (1)
Peripheral blood	22 (79)	161 (99)
Donor type		
Autologous HSCT	0	163

Characteristic	ALLO	AUTO
Number of patients	**28**	**163**
HLA-identical sibling	11 (39)	0
Matched unrelated donor	12 (43)	0
Haplo	5 (18)	0
Transplant year		
2000	1 (4)	17 (10)
2001	2 (7)	9 (6)
2002	1 (4)	3 (2)
2003	1 (4)	0
2004	1 (4)	1 (<1)
2005	1 (4)	3 (2)
2006	0	2 (1)
2007	0	2 (1)
2008	0	1 (<1)
2009	1 (4)	0
2010	0	1 (<1)
2011	1 (4)	5 (3)
2012	0	3 (2)
2013	2 (7)	11 (7)
2014	4 (14)	19 (12)
2015	5 (18)	29 (18)
2016	3 (11)	28 (17)
2017	5 (18)	29 (18)
Median follow-up of survivors (range), months	35 (6-197)	24 (3-193)

Proposal: 1811-89

Title:
Determining the Optimal Conditioning Regimen for Patients with Primary Central Nervous System Lymphoma Undergoing Autologous Hematopoietic Cell Transplantation

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Hypothesis:
We hypothesize that patients with primary CNS lymphoma (CNSL) undergoing thiotepa and busulfan- (Bu/Thio-) based high-dose therapy and autologous hematopoietic cell transplantation (AHCT) have superior progression-free (PFS) and overall survival (OS) compared to patients receiving other conditioning regimens.

Specific aims:
- Aim 1: Determine the optimal conditioning regimen that results in superior PFS and OS in patients undergoing AHCT for CNSL.
- Aim 2: Evaluate the differences in non-relapse mortality (NRM) based on conditioning regimen received in patients undergoing AHCT for CNSL.
- Aim 3: Compare the incidences of relapse, organ toxicities and adverse events (if available), and causes of death based on based on conditioning regimen received in patients undergoing AHCT for CNSL.

Scientific impact:
Patients with primary CNSL have high likelihood of disease recurrence and poor outcomes without optimal consolidation after induction therapy.[1,2] Several consolidation strategies have been proposed over the years, with whole-brain radiotherapy (WBRT) and high-dose therapy and autologous hematopoietic cell transplantation (AHCT) emerging as the most commonly utilized. AHCT may abrogate the need for WBRT and its associated risk of long-term neurotoxicity.[2,3] In recent years, AHCT has emerged as a highly effective consolidative treatment strategy in patients with CNSL resulting in favorable long-term outcomes in both the upfront and salvage settings. While earlier studies using standard lymphoma conditioning such as carmustine, etoposide, cytarabine, and melphalan (BEAM) resulted in suboptimal outcomes, the results of multiple single-arm phase II studies suggest that CNS penetrant chemotherapy agents used in the conditioning platform, such as thiotepa, busulfan, cyclophosphamide, and BCNU, are particularly active in this setting.[3–12] Our centers and others have highly successfully utilized thiotepa, busulfan and cyclophosphamide (TBC)-AHCT in first and subsequent remissions in patients with CNSL, and it has become an internal standard approach for physiologically appropriate patients.[6,7,13–17] BCNU/Thio-conditioned AHCT has also demonstrated to result in favorable long-term disease control and tolerability. In a recent meta-analysis, BCNU/Thio-based regimens had the lowest rates of NRM; however, Bu/Thio-based regimens (namely TBC) had superior PFS and OS.[18]

However, the optimal conditioning regimen remains to be established as there are no randomized studies. Determination of the optimal conditioning regimen may allow for less heterogeneity in the conditioning regimens used for these patients and would determine the conditioning regimen to be used in future prospective clinical studies. Moreover, an understanding of the outcomes of patients after various conditioning regimens would allow for more precise patient selection and potentially a higher proportion of patients referred to AHCT for CNSL. To our knowledge, no large registry studies have addressed this question to date.

Scientific justification:
As discussed above, the optimal conditioning regimen for patients undergoing AHCT for CNS lymphoma remains to be determined as there are no randomized studies. In this setting, the use of large registry data is essential to determining the optimal conditioning regimen in this rare disease. Moreover, an understanding of the outcomes of patients after various conditioning regimens would allow for more precise patient selection and potentially a higher proportion of patients referred for AHCT.

Patient eligibility population:
- Adult patients (≥ 18 years old) with primary non-Hodgkin lymphoma (NHL) of the CNS.
- Patients must have undergone AHCT between 2008 – 2016.
- Absence of systemic NHL at the time of diagnosis.
- Exclusion criteria: Patients with secondary CNSL (i.e., systemic NHL at the time of diagnosis) and diagnoses other than NHL.

Data requirements:
Data collected by CIBMTR before and after AHCT, including essential pre-AHCT data forms such as:
- 2000
- 2018
- 2100
- 2118
- 2402

<u>Patient-specific characteristics:</u>
- Age at the time of AHCT
- Sex
- Race
- Karnofsky performance status or ECOG performance status
- Hematopoietic cell transplantation-comorbidity index
- Disease risk
- NHL histology
- Disease status prior to AHCT (CR/CRu, PR, etc)
- Number of lines of therapy prior to AHCT
- Previous treatments, including WBRT, if available
- HIV status

<u>Transplantation-specific characteristics:</u>
- Conditioning regimen used (including total doses of chemotherapies, if available)
- Stem cell dose
- Year of AHCT

- Time from diagnosis to AHCT
- Use of WBRT after AHCT, if available
- Length of hospital stay, if available

Outcome measures:

- Date of relapse or progression of disease, if applicable
- Date of last follow-up
- Date of death, if applicable
- Organ toxicities and adverse events, if available
- Causes of death

Study design:
This study is retrospective analysis using observational CIBMTR registry data from a large cohort of patients with primary CNSL who underwent consolidative AHCT to compare the outcomes based on the conditioning regimen received. For the purposes of statistical analysis, the patients will be stratified into the following groups based on conditioning regimen used:
Group 1: Bu/Thio-based regimens.
Group 2: BCNU/Thio-based regimens.
Group 3: All other non-thiotepa containing regimens.

Study endpoints:

- PFS at 1 and 2 years post-AHCT in groups 1, 2, and 3.
- OS at 1 and 2 years post-AHCT in groups 1, 2, and 3.
- NRM at 1 and 2 years post-AHCT in groups 1, 2, and 3.
- Cumulative incidence of relapse in groups 1, 2, and 3.
- Cumulative incidence of organ toxicities and adverse events, if available, in groups 1, 2, and 3.

Non-CIBMTR data source:
Non-CIBMTR data sources will be required for this study.

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Conflicts of interest:
There are no relevant conflicts of interest pertinent to this proposal.

Disclosures:
Michael Scordo: Is an ad-hoc consultant for McKinsey & Company, and a consultant for Angiocrine Bioscience, Inc.

Craig S. Sauter: Is a consultant for Juno Therapeutics, Sanofi-Genzyme, Spectrum Pharmaceuticals, Novartis, Precision Biosciences, Kite – a Gilead Company. He receives research funds from Juno Therapeutics and Sanofi-Genzyme.

Selection criteria table

	Exclude	N
Number of patients underwent 1st AUTO HCT for NHL lymphoma in US from 2008-2016 registered with CIBMTR Nov 2018 retrieval		21854
Age ≥ 18	130	21724
Lymphoma with primary CNS involvement	21228	496
Consent	36	460
Exclude embargo centers	3	457

Table 1. Baseline characteristics for primary CNS lymphoma patients registered in the CIBMTR during 2008-2016

	Thio based	Others
Number of patients	357	100
Number of centers	72	55
CRF level patients	33 (9)	15 (15)
Age at transplant, years		
Median(range)	58 (20-78)	58 (23-75)
18-29	15 (4)	4 (4)
30-39	14 (4)	7 (7)
40-49	150 (14)	11 (11)
50-59	120 (34)	32 (32)
≥ 60	158 (44)	46 (46)
Patient sex		
Male	186 (52)	54 (54)
Female	171 (48)	46 (46)
Karnofsky performance score		
≥ 90	179 (50)	37 (37)
<90	157 (44)	62 (62)
Missing	21 (6)	1 (1)
Patient race		
Caucasian	305 (85)	86 (86)
African-American	9 (3)	4 (4)
Asian	25 (7)	8 (8)
Native American	2 (<1)	0
Pacific islander	2 (<1)	1 (1)
Other	2 (<1)	0
Missing	12 (3)	1 (1)
Disease status		
CR1	178 (50)	36 (36)
CR2+	77 (22)	25 (25)
PR	30 (8)	11 (11)
Relapse	32 (9)	14 (14)
PIF/Untreated	40 (11)	14 (14)

	Thio based	Others
Number of patients	357	100
Year of HCT		
2008	8 (2)	5 (5)
2009	5 (1)	2 (2)
2010	22 (6)	6 (6)
2011	39 (11)	13 (13)
2012	37 (10)	14 (14)
2013	34 (10)	18 (18)
2014	50 (14)	13 (13)
2015	73 (20)	11 (11)
2016	89 (25)	18 (18)
Median follow-up of survivors (range), months	36 (1-122)	49 (3-119)

Proposal: 1811-101

Title:
Outcomes in Elderly Patients (Age ≥ 70 years) Received Autologous Hematopoietic Stem Cell Transplant for non-Hodgkin Lymphoma

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Hypothesis:
- Elderly patients with NHL (age ≥ 70 years) who received autologous hematopoietic stem cell transplant (AHSCT) have similar outcomes compared to younger age counterpart, in terms of relapse/ non-relapse mortality, and overall survival.
- Among elderly NHL patients (age ≥ 70 years), type of conditioning regimen with either standard or modified dosing for AHSCT may have an impact on these short- and long-term outcomes

Specific aims:
To study short and long-term outcomes in elderly patients (age ≥ 70 years) who received autologous stem cell transplant, and for these outcomes in comparison to younger age counterparts

Scientific impact:
Current knowledge is limited on the outcomes in elderly patients undergoing high dose chemotherapy and autologous hematopoietic stem cell transplant for treatment (AHSCT) of non-Hodgkin lymphoma (NHL). With the increase in both incidence and the median age of NHL diagnosis (65 years), there are more elderly patients with NHL who have relapsed after induction chemo-immunotherapy and may require AHSCT.
Despite a trend in increasing numbers of such transplant performed in the past decade, there is a lack of large-scale clinical study in examining short and long-term outcomes among elderly NHL patients, especially those who are very old (age ≥ 70 years) with regard to the risk and benefit of AHSCT.
This study will address a relatively simple question, yet has measurable clinical significance in guiding treatment decision in caring for elderly patients with NHL in terms of feasibility and safety of AHSCT. Outcomes of the study remain relevant and informative even in the era of immunotherapy for comparative effectiveness.

Scientific justification:
Although it would be expected that treatment-/ non-treatment related morbidity and mortality may be higher among seniors undergoing AHSCT for NHL, it is unclear whether such a difference exists and to what extent. The transplant course including complications and transplant outcomes that could be unique to this special group of elderly patients (≥ 70 years) have not been well captured.
In addition, there is a lack of evidence-based study on how these outcomes would compare between those very old (≥ 70 years) and relatively younger age counterpart (≥ 65-69 years) undergoing AHSCT.

Patient eligibility population:
The study population will be defined from CIBMTR retrospective transplant database. Elderly patients aged ≥70 years who received AHSCT for NHL between 2005-2015 will be included with at least 1 year follow-up data. Histology type will include most common types of NHL.
The primary study population will be elderly NHL patients whose age ≥ 70 years.
Elderly patients with aged ≥ 65 years will be enrolled for further comparative analysis.

Data requirements:
Please refer to data collection form (excel sheet)

- Patient (e.g. age, sex, demographic, HCT-CI)
- Disease (e.g. NHL histology type, stage, risk category, prior lines of treatment, disease status prior to treatment)
- Transplant related characteristics (e.g. condition regimen, dose of individual drug)

Study design:
Descriptive analysis:

- Will be performed with regard to patient, disease, prior treatment and transplant related characteristics (HCT-CI, stage, risk category), disease status prior to transplant (CR/PR), previous lines of therapy.
- Conditioning regimen (e.g. BEAM, BEAM with various etoposide dose, melphalan alone; +/- Zevalin, Z-BEAM); as well as dose intensity reported, for example, standard versus low etoposide dose adjustment or melphalan doses.

Primary endpoints:

- Overall survival at 1 and 3 years
- Non-relapse mortality at day 100 and 1 year

Secondary endpoints:

- Relapse at 1 year and 3 years
- Lymphoma free survival at 1 and 3 years
- Engraftment of Neutrophils and platelets at day 30 and 100

Comparative analysis:

- Above outcomes will be studied comparing patients with NHL aged between ≥ 70 years versus ≥ 65-69 years using multivariate adjustment (Cox model) and/or matching strategy.
- Also plan to examine high risk versus low risk elderly NHL patients defined by their lymphoma *within* Age ≥ 70 years group for respective outcomes. High risk defined by histology type, grade, transformation and less than CR prior to transplant.

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The below selection criteria were applied	# excluded	N
1st auto-HCT for NHL, 2005-2015		29969
Age ≥ 65	23155	6814
At least 1-year follow-up data	489	6325
Exclude patients without consent	66	6259
Exclude embargoed centers	132	6127

Baseline characteristics of patients over 65 years old who underwent 1st auto-HCT for NHL, 2005-2015

Characteristic	Age 65-69	Age ≥ 70
Number of patients	**4048**	**2079**
Research level data	547	251
Number of centers	213	166
Age at HCT, median(range), yrs	67 (65-70)	72 (70-84)
Patient sex		
Male	2602 (64)	1380 (66)
Female	1443 (36)	699 (34)
Missing	3 (<1)	0
Karnofsky score		
≥ 90	2022 (50)	972 (47)
< 90	1292 (32)	738 (35)
Missing	734 (18)	369 (18)
Disease status		
CR	2360 (58)	1172 (56)
PR	1421 (35)	760 (37)
Resistant	158 (4)	102 (5)
Untreated	17 (<1)	9 (<1)
Unknown	92 (2)	36 (2)
Graft source		
Bone marrow	27 (<1)	11 (<1)
Peripheral blood	4011 (99)	2067 (99)
Others	10 (<1)	1 (<1)
Year of transplant		
2005-2006	432 (11)	226 (11)
2007-2008	553 (14)	240 (12)
2009-2010	719 (18)	332 (16)
2011-2012	887 (22)	452 (22)
2013-2014	952 (24)	524 (25)
2015	505 (12)	305 (15)
Median follow-up of survivors (range), months	62 (12-155)	61 (12-146)