Not for publication or presentation

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR LYMPHOMA
Honolulu, Hawaii
Friday, February 19, 2016, 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, 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**
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:	**Alyssa DiGilio, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0660; E-mail: adigilio@mcw.edu**

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1. **Introduction**
   The CIBMTR Hodgkin and Non-Hodgkin Lymphoma Working Committee was called to order at 2:45 pm on Friday, February 19, 2016 by Dr. Sonali Smith. Working Committee Leadership was introduced and the members were asked to introduce themselves as well. Dr. Smith also outlined the Working Committee goals, expectations, and limitations. Dr. Anna Sureda provided an update on the Working Committee productivity including 6 publications, and 7 abstracts: 1 at the 2015 European Hematology Association conference in Vienna, Austria, 1 at ASCO 2015, 3 at the 2015 ASH conference, and 1 at the 2016 BMT Tandem Meetings in Honolulu, Hawaii. Dr. Tim Fenske reviewed the voting guidelines. The guidelines are based on a scale from 1 to 9; 1=high scientific impact, 9=low scientific impact. Dr. Fenske also described 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. Fenske also announced our Working Committee twitter hashtag: #LYWCIBMTR.

2. **Accrual summary**
   Dr. Fenske presented a slide with the accruals on it. Due to the full agenda, there was not much discussion on the numbers, but it was mentioned that the committee has them in attachment 2.

3. **Presentations, published or submitted papers**
   Due to the full agenda, the 2015 presentations and published papers were mentioned by Dr. Sureda, but they were not presented.

   a. **LY12-01** Bachanova V, Burns LJ, Ahn KW, Laport GG, Akpek G, Kharfan-Dabaja MA, Nishihori T, Agura E, Armand P, Jaglowski SM, Cairo MS, Cashen AF, Cohen JB, D'Souza A, Freytes CO, Gale RP, Ganguly S, Ghosh N, Holmberg LA, Inwards DJ, Kanate AS, Lazarus HM, Malone AK, Munker

R, Mussetti A, Norkin M, Prestidge TD, Rowe JM, Satwani P, Siddiqi T, Stiff PJ, William BM, Wirk B, Maloney DG, Smith SM, Sureda AM, Carreras J, Hamadani M. Impact of real-world interpretation of pre-transplant FDG-PET status on outcomes after allogeneic hematopoietic cell transplantation for non-Hodgkin lymphoma. ***Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. doi:10.1016/j.bbmt.2015.05.007.***

b. **LY13-02** Satwani P, Ahn KW, Carreras J, Abdel-Azim H, Cairo MS, Cashen A, Chen AI, Cohen JB, Costa LJ, Dandoy C, Fenske TS, Freytes CO, Ganguly S, Gale RP, Ghosh N, Hertzberg MS, Hayashi RJ, Kamble RT, Kanate AS, Keating A, Kharfan-Dabaja MA, Lazarus HM, Marks DI, Nishihori T, Olsson RF, Prestidge TD, Rolon JM, Savani BN, Vose JM, Wood WA, Inwards DJ, Bachanova V, Smith SM, Maloney DG, Sureda A, Hamadani M. A prognostic model predicting autologous transplantation outcomes in children, adolescents and young adults with Hodgkin lymphoma. ***Bone Marrow Transplantation. 2015 Nov 1; 50(11):1416-1423. doi:10.1038/bmt.2015.177. PMCID:PMC4633349.***

c. **LY13-03a** Klyuchnikov E, Bacher U, Kröger NM, Hari PN, Ahn KW, Carreras J, Bachanova V, Bashey A, Cohen JB, D'Souza A, Freytes CO, Gale RP, Ganguly S, Hertzberg MS, Holmberg LA, Kharfan-Dabaja MA, Klein A, Ku GH, Laport GG, Lazarus HM, Miller AM, Mussetti A, Olsson RF, Slavin S, Usmani SZ, Vij R, Wood WA, Maloney DG, Sureda AM, Smith SM, Hamadani M. Reduced-intensity allografting as first transplantation approach in relapsed/refractory grade 1-2 follicular lymphoma provides improved outcomes in long-term survivors. ***Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2015 Dec 1; 21(12):2091-2099. doi:10.1016/j.bbmt.2015.07.028. PMCID:PMC4639453. Oral presentation at the 2015 European Hematology Association conference in Vienna, Austria, June 2015.***

d. **LY13-03b** Klyuchnikov E, Bacher U, Woo Ahn K, Carreras J, Kröger NM, Hari PN, Ku GH, Ayala E, Chen AI, Chen Y-B, Cohen JB, Freytes CO, Gale RP, Kamble RT, Kharfan-Dabaja MA, Lazarus HM, Martino R, Mussetti A, Savani BN, Schouten HC, Usmani SZ, Wiernik PH, Wirk B, Smith SM, Sureda A, Hamadani M. Long-term survival outcomes of reduced-intensity allogeneic or autologous transplantation in relapsed grade 3 follicular lymphoma**. *Bone Marrow Transplantation. doi:10.1038/bmt.2015.223. Epub 2015 Oct 5. Oral presentation at the 2015 American Society of Clinical Oncology conference in Chicago, IL, June 2015.***

e. **LY15-01** Kanate AS, Mussetti A, Kharfan-Dabaja MA, Ahn KW, DiGilio A, Beitinjaneh A, Chhabra S, Fenske TS, Freytes C, Gale RP, Ganguly S, Hertzberg M, Klyuchnikov E, Lazarus H, Olsson R, Perales MA, Rezvani A, Riches M, Saad A, Slavin S, Smith SM, Sureda A, Yared J, Ciurea S, Armand P, Salit R, Bolanos-Meade J, Hamadani M. Reduced-intensity transplantation for lymphomas using haploidentical related donors versus HLA-matched unrelated donors. ***Blood. Epub 2015 Dec 15. PMCID:26670632. Oral presentation at the 2015 American Society of Hematology Conference in Orlando, FL, December 2015.***

f. **LY14-02** Fenske TS, Ahn KW, Graff TM, DiGilio A, Bashir Q, Kamble RT, Ayala E, Bacher U, Brammer JE, Cairo M, Chen A, Chen YB, Chhabra S, D'Souza AD, Farooq U, Freytes C, Ganguly S, Hertzberg M, Inwards D, Jaglowski S, Kharfan-Dabaja MA, Lazarus HM, Nathan S, Pawarode A, Pereles MA, Reddy N, Seo S, Sureda A, Smith SM, Hamadani M. Allogeneic transplantation provides durable remission in a subset of DLBCL patients relapsing after autologous

transplantation. ***Submitted. Oral presentation at the 2015 the American Society of Hematology Conference in Orlando, FL, December 2015.***

g. **LY15-02** Ghosh N, Karmali R, Rocha V, Ahn KW, DiGilio A, Hari P, Bachanova V, Bacher U, Dahi P, deLima M, D'Souza A, Fenske TS, Ganguly S, Kharfan-Dabaja MA, Prestidge TD, Savani BN, Smith SM, Sureda AM, Waller EK, Jaglowski S, Herrera AF, Armand P, Salit RB, Wagner-Johnston ND, Bolanos-Meade J, Hamadani M. Reduced-intensity transplantation for lymphomas using haploidentical related donors versus HLA-matched sibling donors. ***Submitted. Oral presentation at the 2016 BMT Tandem Meetings in Honolulu, HI, February 2016.***

h. **LY06-03** Sureda A, Zhang MJ, Dreger P, Carreras J, Fenske TS, Finel H, Schouten HC, Montoto S, Robinson S, Smith SM, Boumendil A, Hamadani M, Pasquini M. Allogeneic stem cell transplantation for relapsed/refractory follicular lymphoma: a joint study between the EBMT and the CIBMTR. ***Oral presentation at the 2015 American Society of Hematology Conference in Orlando, FL, December 2015.***

4. Studies in Progress

Update on the current status of studies in progress was provided by Dr. Fenske.

a. **LY06-03** HLA identical sibling allogeneic stem cell transplantation versus HLA matched unrelated donor allogeneic stem cell transplantation in patients with follicular lymphoma (A Sureda/H Schouten) **Manuscript preparation**

b. **LY15-03** Does autologous hematopoietic cell transplant overcome the increased risk of death in patients with follicular lymphoma relapsing early after first line chemo-immunotherapy? (C Casulo/J Friedberg) **Protocol development**

c. **LY14-03** Multi-center retrospective study of outcomes of autologous hematopoietic cell transplantation for patients with EBER-ISH/LMP positive relapsed/refractory Hodgkin lymphoma (P Satwani) **Deferred** *currently collecting data from centers*

5. Future/proposed studies

a. **PROP 1511-16** Role of allogeneic hematopoietic cell transplantation in NK/T cell lymphoma (A Kanate) (Attachment 4)
Dr. Kanate presented this study. This study will look at allogeneic HCT in aggressive NK/T cell leukemia and nasal type lymphoma. There are 109 patients with extranodal, nasal type NK/T cell lymphoma and 38 patients in aggressive NK/T Cell leukemia. There are no data published on this from outside Asia. The Working Committee asked if there would be a center effect for this study. Dr. Hamadani explained that we have extensively tested for center effect in the past and have not found a significant one to date, but we will look at it for this study. Another member of the Working Committee suggested looking at the length of remission in these patients.

b. **PROP 1511-33** Utility of autologous vs allogeneic transplant as first transplantation approach in FL patients with early chemoimmunotherapy failure (J Godfrey/S Smith) (Attachment 5)
Dr. Smith presented this study. This study aims to look at patients who received either a first autoHCT or first alloHCT after failing front line chemotherapy plus rituximab treatment within two years of the start of treatment. The hypothesis is that patients receiving an alloHCT will

have better outcomes than those receiving an autoHCT. There were 210 patients in the auto cohort, and 165 in the allo cohort. Another parallel hypothesis was to look at the early failure autoHCT patients in comparison to patients who had a late failure then received an autoHCT. One member of the Working Committee thought that the late autoHCT group was a distraction from the main hypothesis by pointing out that we do not know the true denominator of these patients as some could have died before receiving a transplant.

c. **PROP 1511-37** Alternative donor source stem cell transplant vs matched donor stem cell transplant for Hodgkin lymphoma (S Ahmed/Y Nieto) (Attachment 6)
This study was presented by Dr. Ahmed. This study aims to compare four different donor types in Hodgkin's Lymphoma: HLA identical siblings, 8/8 matched related donors, haploidentical donors, and cord blood donors. The hypothesis is that alternative donor sources will be comparable to matched related and unrelated donors. There are 104 cord blood, 54 haploidentical, 508 HLA identical siblings, and 510 8/8 unrelated donors. One member of the Working Committee pointed out that knowing if a patient has a CR is very important to this study.

d. **PROP 1511-51** Outcome differences with maintenance rituximab post-allogeneic transplantation in patients with B-cell lymphoma (N Wagner-Johnston/J Bolanos-Meade/R Jones) (Attachment 7)
Dr. Bolanos-Meade presented this study. This study aims to look at the use of post-transplant maintenance rituximab in haploidentical transplants. The hypothesis is that the use of post-transplant rituximab is better than no maintenance post haploHCT. There were 99 patients not receiving maintenance and 50 patients who did. The Working Committee was concerned over a center effect as only 2 centers were performing maintenance rituximab. Dr. Hamadani said that this could actually help the study as the centers who do maintenance rituximab always do it, and those who do not always do not regardless of patient characteristics. This would eliminate the 'picking and choosing' of who gets the treatment. The Committee was also concerned with the dose and length of maintenance rituximab. Dr. Hamadani said that we could potentially contact the centers to find this information out.

e. **PROP 1511-60** Allografts in Non-Hodgkin lymphoma following reduced intensity conditioning (N Ghosh) (Attachment 8)
Dr. Ghosh presented this study. This study aims to look to see which reduced intensity conditioning regimen has the best outcomes in Non-Hodgkin Lymphoma. There were five major conditioning regimens that are being tested: Flu/Bu (n=531), Flu/Mel (n=645), Flu/Cy (n=679), Flu/Cy/2 GyTBI (n=75), 2Gy TBI +/- Flu (n=334). The committee commented that the Flu/Cy/TBI group could either be dropped or combined with the TBI +/- Flu category. Another member was concerned as to how to handle the differences between histologies. Some suggestions were to either look at these regimens within the different histologies or to use the DRI as a compound variable between disease subtype and disease status. Dr. Fenske recommended to look at Rituxan use in the conditioning as well.

f. **PROP 1509-07** Assessing the significance of conditioning regimen intensity (myeloablative vs reduced intensity/non-myeloablative) in haploidentical donor transplantation for lymphoid malignancies when using post-transplant cyclophosphamide (M Kharfan-Dabaja) (Attachment 9)
Dr. Hamadani presented this proposal on behalf of Dr. Kharfan-Dabaja. This study hypothesizes that there is no benefit of myeloablative conditioning vs reduced intensity conditioning in

haploidentical transplants in lymphoma patients. There were 33 patients with MAC haploHCT and 225 with RIC haploHCT. The committee was very worried about the number of patients in the MAC group being so low; they did not believe we would be able to get much information out of the analysis as there would be low power.

g. **PROP 1511-41** Conditioning regimen intensity in allogeneic hematopoietic cell transplantation outcomes for mantle cell lymphoma (T Nishihori) (Attachment 10)
Dr. Hamadani presented this proposal on behalf of Dr. Nishihori. This study looks to compare conditioning intensity in mantle cell lymphomas. It is hypothesized that myeloablative conditioning will have better outcomes than reduced intensity conditioning. There are 143 patients receiving MAC and 410 receiving RIC. The Working Committee mentioned that there was a study looking at chemoresistant patients and found no difference between myeloablative and reduced intensity, so they were concerned that this may not show us anything new.

h. **PROP 1511-102** Refined disease risk index-directed selection of conditioning intensity for allogeneic hematopoietic cell transplantation in adults with relapsed/refractory lymphoma (A Lazaryan/V Bachanova/N Bejanyan) (Attachment 11)
Dr. Lazaryan presented this study. This study aims to look to see whether DRI can predict conditioning intensity. There are 4617 patients in the study of which 3965 have DRI information. This study plans to also look at TRM and GVHD, which the original DRI paper did not look at. A member of the Working Committee was concerned as to how you would tease out whether it was the disease or the disease status that was driving the change in conditioning intensity, but they were reminded that the DRI has been validated to make sure that all groups of diseases/ disease status behave similarly, so the underlying cause does not matter. Another member suggested having a validation cohort to validate the study.

i. **PROP 1511-119** The use of hematopoietic cell transplantation comorbidity index to predict outcomes in older patients undergoing autologous hematopoietic cell transplantation for lymphoma (H Murthy/E Ayala) (Attachment 12)
Dr. Murthy presented this study. This study aims to look at the role of HCT-CI in elderly autologous transplants. The study suggests that it will be predictive of OS and TRM. There are 7139 patients in the cohort to be analyzed for this proposal. A member of the Working Committee pointed out that overall survival may not be the best primary endpoint to look at as patients with a higher comorbidity index will automatically have a lower survival rate even in patients not receiving transplants. TRM was decided to be a better primary endpoint. Another member of the committee suggested looking at the individual components of the HCT-CI as the weights used in the original score were based on alloHCT and might not hold true for autoHCT. Dr. Hamadani also mentioned that we need CRF level data for this, which will bring the patient count down to 417 patients, and only 5% of these will experience a TRM so there may be low power in this study.

j. **PROP 1512-03** Outcome of patients who have undergone a haplo-identical stem cell transplantation for diffuse large B-cell lymphoma: A retrospective study of the CIBMTR WC and EBMT WP (A Sureda/P Dreger) (Attachment 13)
Dr. Sureda presented this study. This study aims to combine EBMT data with CIBMTR data for a haploidentical vs matched sibling vs matched unrelated donor transplant in DLBCL patients. There are 77 haploHCT from the CIBMTR and an additional 70 from the EBMT. One committee member suggested doing a matched analysis, but Dr. Hamadani said that there are publications

showing that if you have a good multivariate analysis there is no benefit of doing a matched analysis.

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

a. **PROP 1507-01** Outcome study of Castleman Disease patients who have received hematopoietic stem cell transplant. *Dropped due to feasibility-low number of patients (n=16)*
b. **PROP 1509-04** Comparing outcomes between haploidentical donor transplantation using post-transplant cyclophosphamide against HLA-matched unrelated donor (8/8) when using myeloablative preparative regimens in lymphoid malignancies. *Dropped due to feasibility-low number of patients (n=33 haplos)*
c. **PROP 1509-10** Outcomes of low CD34+ cell dose autologous hematopoietic stem cell transplantation. *Dropped due to feasibility*
d. **PROP 1510-17** Allogeneic hematopoietic stem cell transplantation in HTLV-1 associated adult T-cell lymphoma/leukemia. *Dropped due to feasibility*
e. **PROP 1510-23** The impact of pre-allogeneic transplantation salvage cisplatin-containing chemotherapeutic regimens on the incidence of acute GVHD for patients with relapsed/refractory lymphoma. *Dropped due to feasibility*
f. **PROP 1511-14** Hematopoietic cell transplantation outcomes for relapsed or refractory marginal zone lymphomas. *Dropped due to feasibility*
g. **PROP 1511-26** Using IPS-3 in prediction of outcomes of autologous stem cell transplant for adults with Hodgkin lymphoma between Jan 2000-Dec2013. *Dropped due to feasibility*
h. **PROP 1511-42** Hematopoietic cell transplantation outcomes in marginal zone lymphoma. *Dropped due to feasibility*
i. **PROP 1511-46** Comparison of autologous vs allogeneic stem cell transplantation for relapsed/refractory primary mediastinal B cell lymphoma. *Dropped due to feasibility—low numbers (n=26)*
j. **PROP 1511-47** Trends in allograft use and survival after reduced intensity conditioning allogeneic hematopoietic cell transplantation for Hodgkin lymphoma: 1999-2014. *Dropped due to feasibility*
k. **PROP 1511-63** Myeloablative or reduced intensity conditioning for allogeneic transplantation in Hodgkin's disease in the modern era. *Dropped due to feasibility*
l. **PROP 1511-66** Study of the outcomes among high risk relapse/refractory Hodgkin and non-Hodgkin lymphoma patients receiving autologous hematopoietic cell transplant vs allogeneic hematopoietic cell transplant vs autologous hematopoietic cell transplant followed by a reduced intensity allogeneic hematopoietic cell transplant. *Dropped due to feasibility—low numbers (n=23 auto/RIC allo planned)*
m. **PROP 1511-73** Impact of pre-transplant salvage chemotherapy on survival in autologous transplantation of Hodgkin lymphoma. *Dropped due to feasibility—low numbers (n=31)*
n. **PROP 1511-74** The role of autologous transplantation on the treatment of primary CNS lymphoma. *Dropped due to feasibility—low numbers (n=17)*
o. **PROP 1511-83** Stem cell transplantation outcomes in the treatment of diffuse large B-cell lymphoma. *Dropped due to feasibility*
p. **PROP 1511-84** What is the correct timing of stem cell transplantation for double hit lymphoma? *Dropped due to feasibility—supplemental data*
q. **PROP 1511-91** Successive prognostic estimation for allograft recipients with lymphoma surviving beyond one year from transplantation: A landmark CIBMTR analysis. *Dropped due to feasibility*

r. **PROP 1511-117** Benefit of upfront autologous stem cell transplant in double hit lymphoma or double expressors following first complete remission. *Dropped due to feasibility-supplemental data)*
s. **PROP 1511-121** Outcomes of hematopoietic cell transplantation in patients with primary CNS lymphoma. *Dropped due to feasibility—low numbers (n=17)*

6. **Other Business**

After the new 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 4:39 pm.

Working Committee Overview Plan for 2016-2017

a. **LY06-03** Sib vs MUD for follicular NHL/EBMT with CIBMTR. We anticipate the final analysis to be done by July 1, 2015. We anticipate that the manuscript will be submitted by July 1, 2016 and published by July 1, 2017.

b. **LY14-03** Multi-center retrospective study of outcomes of autologous hematopoietic cell transplantation for patients with EBER-ISH/LMP positive relapsed/refractory Hodgkin lymphoma. This study is currently deferred and will be deferred until July 1, 2017.

c. **LY15-03** Does autologous stem cell transplant overcome the increased risk of death in patients with follicular lymphoma relapsing early after first line chemoimmunotherapy? We anticipate having this study in data file preparation by July 1, 2016, and having it published by July 1, 2017.

d. **LY16-01 (Prop 1511-16)** Role of allogeneic hematopoietic cell transplantation in NK/T cell lymphoma. We anticipate having this study in data file preparation by July 1, 2016 and submitted by July 1, 2017.

e. **LY16-02 (Prop 1511-37)** Alternative donor source stem cell transplant vs matched donor stem cell transplant for Hodgkin lymphoma. We anticipate having this study in data file preparation by July 1, 2016, and submitted by July 1, 2017.

f. **LY16-03 (Prop 1512-03)** Outcomes of patients who have undergone a haploHCT for DLBCL. We anticipate having this study in data file preparation by July 1, 2017.

g. **LY16-04 (Prop 1511-33)** Utility of autologous vs. allogeneic transplant as first transplantation approach in follicular lymphoma patients with early chemoimmunotherapy failure. We anticipate having this study in analysis by July 1, 2017.

h. **LY16-05 (CIBMTR Trainee-Fellow Research Program)** Impact of rituximab in reduced intensity conditioning allogeneic hematopoietic cell transplantation for B-cell lymphomas. We anticipate having this study in analysis by July 1, 2016, and submitted by July 1, 2017.

Work Assignments for Working Committee Leadership (March 2016)

Tim Fenske	**LY15-03** Does autologous stem cell transplant overcome the increased risk of death in patients with follicular lymphoma relapsing early after first line chemoimmunotherapy?
	LY16-01 Role of allogeneic hematopoietic cell transplantation in NK/T cell lymphoma
	LY16-02 Alternative donor source stem cell transplant vs matched donor stem cell transplant in Hodgkin lymphoma
Anna Sureda	**LY16-03** Outcomes of patients who have undergone haploHCT for DLBCL
Sonali Smith	**LY16-04** Utility of autologous vs allogeneic transplant as first transplantation approach in follicular lymphoma patients with early chemoimmunotherapy failure