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A G E N D A For conference call and TCT meeting
CIBMTR WORKING COMMITTEE FOR AUTOIMMUNE DISEASES AND CELLULAR THERAPIES
Houston, Texas
Friday, February 22, 2019, 12:15 pm – 2:15 pm

Co-Chair:	**Sarah Nikiforow, MD, PhD, Dana Farber Cancer Institute Boston, Massachusetts; Telephone: 6176323470; E-mail: snikiforow@partners.org**
Co-Chair:	**Peiman Hematti, MD, University of Wisconsin Hospital and Clinics, Madison, WI; Telephone: 608-265-0106; E-mail: pxh@medicine.wisc.edu**
Co-Chair:	**Stefanie Sarantopoulos, MD, PhD, Duke University Medical Center, Durham, NC; Telephone: 919-668-4383; E-mail: stefanie.sarantopoulos@duke.edu**
Scientific Director:	**Marcelo C. Pasquini, MD, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0700; E-mail: mpasquini@mcw.edu**
Statistical Director:	**Ruta Brazauskas, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-456-8687; E-mail: ruta@mcw.edu**
Statistician:	**Khalid Bo-Subait, MPH, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0711; E-mail: Kbosubait@mcw.edu**

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1. **Introduction**
   a. Minutes and Overview Plan from February 2018 meeting (Attachment 1)
   b. Introduction of incoming Co-Chair: **George Georges, MD;** Fred Hutchinson Cancer Research Center. Thank you to **Stephanie Sarantopoulos MD, PhD** for all the input to this committee

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

3. **Cellular Therapy Registry Update** (M Pasquini)

4. **Studies in progress**
   a. **CT10-01** Donor Leukocyte Infusion versus Second Allogeneic Hematopoietic Stem Cell Transplantation for Disease Relapse after First Allogeneic Stem Cell Transplantation (N Frey/A Loren/D Porter) **Manuscript Preparation**
   b. **CT13-01** Utility of Unmanipulated Donor Lymphocyte Infusion (DLI) for the Treatment of Infections in Allogeneic Hematopoietic Cell Transplantation Recipients (G Akpek, B Omar) **Analysis**
   c. **AC14-01** Long Term Outcomes after Autologous Hematopoietic Cell Transplantation for Rapidly Progressive Systemic Scleroderma (D Farge) **Data Collection – deferred**
   d. **AC16-01** Pattern of use and outcomes with donor lymphocyte infusion (DLI) after HLA-haploidentical allogeneic hematopoietic stem cell transplant (V Roy) **Data File Preparation**
   e. **AC17-01** CD-19 chimeric antigen receptor T Cells with or without hematopoietic cell transplantation for treatment of refractory ALL (S Nikiforow/J Park/M Perales) **Protocol Development**
   f. **AC18-01** Effect of stem cell boost and donor lymphocyte infusion on the incidence of GVHD (James Yoon/ Edmund Waller) **Deferred**
   g. **AC18-02** Prospective Cohort study of Recipients of Autologous Hematopoietic cell Transplant for Systemic Sclerosis (George Georges) **Deferred**

5. Future/proposed studies

Autoimmune:

a. **PROP 1811-11** To evaluate the outcomes of hematopoietic stem cell transplant with cyclophosphamide and ATG vs total body irradiation conditioning in the treatment of systemic sclerosis (Gul,Khan,Abuali) (Attachment 3)

Cellular Therapy:

b. **PROP 1809-03** Allogeneic hematopoietic cell transplantation vs chimeric antigen receptor t-cell therapy for dlbcl patients with prior autologous transplant failure or refractory disease (Hamadani, Pasquini, Locke, Gopal) (Attachment 4)

c. **PROP 1811-66** Clinical predictors of response and toxicity following CD-19 directed chimeric antigen receptor t-cell therapy in patients with diffuse large b-cell lymphoma (Hossain, Stiff) (Attachment 5)

d. **PROP 1811-88** Impact of DLI dose on outcomes of relapsed MDS and AML patients who have had an allogeneic transplant from matched related and unrelated donors (Varadarajan) (Attachment 6)

e. **PROP 1811-141** Prolonged cytopenia following CD-19 targeted CAR-T therapy for diffuse large b-cell lymphoma (Shadman) (Attachment 7)

f. **PROP 1811-109** CAR-T therapy vs autologous transplant in early rituximab failure in patients with diffuse large b cell lymphoma (Shah, Hamadani) (Attachment 8)

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR AUTOIMMUNE DISEASES AND CELLULAR THERAPIES
Salt Lake City, Utah
Thursday, February 22, 2018, 2:45 – 4:45 pm

Co-Chair:	**Sarah Nikiforow, MD, PhD, Dana Farber Cancer Institute Boston, Massachusetts; Telephone: 6176323470; E-mail: snikiforow@partners.org**
Co-Chair:	**David McKenna, MD, University of Minnesota Medical Center, Minneapolis, MN; Telephone: 612-624-5736; E-mail: mcken020@umn.edu**
Co-Chair:	**Stefanie Sarantopoulos, MD, PhD, Duke University Medical Center, Durham, NC; Telephone: 919-668-4383; E-mail: stefanie.sarantopoulos@duke.edu**
Scientific Director:	**Marcelo C. Pasquini, MD, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0700; E-mail: mpasquini@mcw.edu**
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1. Introduction

The Committee chairs (David McKenna, MD, Sarah Nikiforow MD, and Stefanie Sarantopoulos, MD) and the Scientific Director (Marcelo Pasquini, MD) welcomed the committee and started the meeting. After the brief introduction, Dr. Pasquini acknowledged the contributions by the outgoing chair David McKenna, MD. Dr. Pasquini then introduced the new incoming working committee co-chair Peiman Hematti, MD from University of Wisconsin Hospital and Clinics. The minutes from the 2017 meeting in Orlando were then approved by the committee.

2. Accrual Summary (attachment 2)

Dr. Pasquini briefly discussed the status of data that is available for cellular therapy and autoimmune related diseases. Dr. Pasquini encouraged all members of the working committee to participate in all stages of studies weather in study development or completion.

3. Cellular Therapy Registry Update:

Dr. Pasquini presented the major updates to the cellular therapy registry. The NCI Pilot study was completed in July 2017 and to date we have collected around 900 CT infusions through the new Cellular Therapy Essential Data (CTED). Most of these cases were transplant related CT, as donor cellular infusions and 300 of these CT recipients were treated for lymphoid malignancies and neurologic diseases as a regenerative medicine approach. 87 were identified as CAR-T cell therapies for cancer. Dr. Pasquini discussed about utilizing this mechanism to capture long term follow up on recipients of genetically modified commercial cellular products. The cellular therapy

registry data flow with all the forms developed under the CTED series was shown demonstrating how all cellular therapy data elements are currently collected. Dr. Pasquini then explained that all the data collection so far is voluntary unless the infusion was transplant related which is required submitted according to the SCTOD framework.
Dr. Pasquini then introduced the Cellular Immunotherapy Data Resource (CIDR) project, outlined by a NCI RFA released late in 2017, focused on CT for treatment of cancer. The CIBMTR applied to this funding opportunity which if funded would provide funding for forms reimbursement, IT infrastructure and allow the CIBMTR to participate in activities related to the Moonshot Initiative.
Dr. Pasquini then discussed the CT for regenerative medicine registry initiative. The current CTED is adapted to capture CT for any indication and it is currently in operation. This initiative will reach out to different subject matter experts to develop data elements for different indications for forms development and implementation.
Lastly, Dr. Pasquini announced the upcoming CT registry forum October 25-26th 2018 in Minneapolis.

4. Studies In progress (attachment 3)

Dr. Pasquini briefly discussed the studies in progress before we started presenting the proposals.

a) **CT10-01** Donor Leukocyte Infusion versus Second Allogeneic Hematopoietic Stem Cell Transplantation for Disease Relapse after First Allogeneic Stem Cell Transplantation (N Frey/A Loren/D Porter) **Manuscript Preparation.**
b) **CT13-01** Utility of Unmanipulated Donor Lymphocyte Infusion (DLI) for the Treatment of Infections in Allogeneic Hematopoietic Cell Transplantation Recipients (G Akpek, B Omar) **Analysis**
c) **AC14-01** Long Term Outcomes after Autologous Hematopoietic Cell Transplantation for Rapidly Progressive Systemic Scleroderma (D Farge, A Oliveira, G Georges) **Data Collection**
d) **AC16-01** Pattern of use and outcomes with donor lymphocyte infusion (DLI) after HLA-haploidentical allogeneic hematopoietic stem cell transplant(V Roy) **Data collection**
e) **AC17-01** CD-19 chimeric antigen receptor T Cells with or without hematopoietic cell transplantation for treatment of refractory ALL (S Nikiforow/J Park/M Perales) **Protocol development**

5. Future/proposed studies

a) PROP 1711-157 Effect of Stem Cell Boost and Donor Lymphocyte Infusion on the Incidence of Graft-versus-Host Disease (J Yoon, M. Graiser, E. Waller)
James Yoon presented the proposal. There are 4075 patients who received SCB/DLI for graft failure or relapse with any hematological malignancy between 2003-2016. One major comment that came up was regarding how many of the cases who received a DLI actually received it for relapse or disease progression as a large number of the population list that as primary indication for DLI. Dr. Pasquini responded to this comment by pointing out that sometimes centers will list other types of cells that they infused. Any undetermined cell types that were not relevant to this study were excluded. Additionally any DCI for hematopoietic recovery, centers are supposed to record that as a second transplant. So the data is not perfect and will need to be cleaned more thoroughly if this study is accepted as a study into the working committee. This study was accepted into the ACWC.

b) PROP 1711-166 Mesenchymal Stromal Cell treatments in allogeneic hematopoietic cell transplantation (K.Hashmi, O Ringden, S.Kendarian, P.Kebriaei, H. Lazarus)

Dr. Hashmi presented the proposal there were 136 patients who received Mesenchymal stromal cell treatments in allogeneic hematopoietic cell transplantation for GVHD. Dr. Hashmi mentioned that they may be able to secure funding from industry as well as collect supplemental data from clinical trials that did not report to the CIBMTR. One comment was regarding why the presenter believes he can secure over 800 cases despite only 136 records being available using CIBMTR data. Dr. Hashmi response was that he can get most of the cases using supplemental data forms for clinical trial data that wasn't reported to the CIBMTR and that he has interest from industry to fund the data collection as well. This study was not accepted based on the voting priorities by the committee members. We suggest that the best method for this study to move forward would be for them to meet with the industry representatives that showed interest in providing data and funding and have them pursuit this as a funded study.

c) PROP 1711-167 Prospective Cohort study of Recipients of Autologous Hematopoietic cell Transplant for Systemic Sclerosis (G. Georges)

George Georges presented. His proposal suggested conducting a prospective cohort study of recipients of autologous hematopoietic cell transplant for systemic sclerosis. 3 standard treatment plans are proposed to be used for this proposal. The goal of this proposal would be to start a SSc registry with the CIBMTR. This would require updating the SSc form that the CIBMTR uses which hasn't been updated in many years. Furthermore this would require a more hands on approach for data collection from centers as it would require input from rheumatologist. Follow up forms would be administered at 3 months, 6 months and then annually after that. Outcomes of interest include overall survival, progression free survival. Dr. Pasquini had a comment regarding the importance of having a resource for the community to create a registry. As to date most of these transplants have been clinical trial cases and we don't have access to them in the CIBMTR database. This study will be accepted as it does not require a lot of statistical hours to start working on this study to determine its feasibility in creating a SSc registry.

The meeting adjourned at 4:24 PM.

Working Committee Overview Plan for 2018-2019

a. **CT10-01** Donor Leukocyte Infusion versus Second Allogeneic Hematopoietic Stem Cell Transplantation for Disease Relapse after First Allogeneic Stem Cell Transplantation. We expect to finalize manuscript and submit for peer-review by June 2019. (Total hours to completion: 10; Allocated for the next fiscal year: 0)

b. **CT13-01** Utility of Donor Leukocyte Infusion (DLI) for the Treatment of Drug-resistant Viral or Fungal Infections in Allogeneic HCT Recipients: A CIBMTR Analysis. The supplemental data forms are finalized. We expect to in manuscript preparation by June 2019. (Total hours: 220; Allocated for the next fiscal year: 70)

c. **AC14-01** Long Term Outcomes after Autologous Hematopoietic Cell Transplantation for Rapidly Progressive Systemic Scleroderma (D Farge, A Oliveira, G Georges) – This study is in data collection for 18 months with little response from US sites. A total of 34 cases were collected, including 26 from a single center. There was consideration in dropping the study in order not to delay the activities at EBMT given the delay to capture data by CIBMTR centers. Further discussions during the 2018 BMT Tandem meetings, mainly with recent publication of the SCOT trial, interest in having a long term outcome analysis was rekindled. The approach is to complete data collection by June 2018 and to share with EBMT for analysis. This is a collaborative work and the CIBMTR will collect and collate the data, share with EBMT and review analysis results.

c. **AC16-01** Pattern of use and outcomes with donor lymphocyte infusion after HLA-haploidentical allogeneic hematopoietic stem cell transplant. The goal of this study is to be starting analysis by June 2019. (Total hours: 240; Allocated for the next fiscal year: 140)

d. **AC17-01** CD-19 Chimeric Antigen Receptor T Cells with or without Hematopoietic Cell Transplantation for Treatment of Refractory Acute Lymphocytic Leukemia. Goal is to have protocol development complete by June 2018. (Total hours: 310; Allocated for the next fiscal year: 60)

e. **AC18-01** Effect of Stem Cell Boost and Donor Lymphocyte Infusion on the Incidence of Graft-versus-Host Disease. Goal is to have the study in analysis by June 2019. (Total hours:310; Allocated for next fiscal year:160)

f. **AC18-02** Prospective Cohort study of Recipients of Autologous Hematopoietic cell Transplant for Systemic Sclerosis. Goal for this study is to have a protocol by June 2019. (Total hours:310; Allocated for next fiscal year:30 as most of the work will be in forms development and implementation)

Oversight Assignments for Working Committee Leadership (March 2018)

Sarah Nikiforow	**CT10-01**	DLI vs Second Allo HCT for relapse
	AC17-01	CD19 CAR T cells without HCT for ALL
Peiman Hematti	**CT13-01**	DLI for viral or fungal Infections in Allo HCT
	AC18-01	Effect of SCB and DLI on GVHD incidence
Stephanie Sarantopoulos	**AC18-02**	Prospective Cohort study of Auto HCT for SSC
	AC16-01	DLI After HLA-haploidentical allogeneic transplant
Marcelo Pasquini	**AC14-01**	Long term outcomes of recipients of Auto HCT for SSC

Accrual Summary for the Autoimmune Disorders and Cellular Therapy Working Committee

Recipients of first transplant for Autoimmune Disorders *registered* to the CIBMTR, 2007-2018

Characteristic	Allogeneic	Autologous
Number of patients	68	317
Number of centers	40	54
Age at transplant		
Median age (range)	15 (<1-62)	43 (4-74)
0-18	42 (62)	19 (6)
18-30	13 (19)	39 (12)
30-40	2 (3)	78 (25)
40-50	5 (7)	94 (30)
50-60	4 (6)	63 (20)
>60	2 (3)	24 (8)
Gender		
Male	40 (59)	128 (40)
Female	28 (41)	189 (60)
Karnofsky Score, %		
>=90	23 (34)	65 (21)
<90	41 (60)	233 (74)
Missing	4 (6)	19 (6)
Graft type		
BM	33 (49)	1 (<1)
PB	24 (35)	313 (99)
UCB	11 (16)	1 (<1)
Not Reported	0	2 (<1)
Donor type		
Autologous HSCT	0	176 (56)
HLA-identical sibling(may include non-monozygotic twin)	16 (24)	1 (<1)
Syngeneic (monozygotic twin)	1 (1)	0
Unrelated donor	46 (68)	0
HLA-matched other relative	1 (1)	0
HLA-mismatched relative	4 (6)	0
Not Reported	0	140 (44)
Disease		
Myasthenia gravis	0	3 (<1)
Multiple sclerosis	1 (1)	148 (47)
Rheumatoid arthritis	0	1 (<1)
Psoriatic arthritis or psoriasis	0	1 (<1)
Systemic lupus erythematosis (SLE)	4 (6)	10 (3)

Characteristic	Allogeneic	Autologous
Polymyositis-dermatomyositis	0	1 (<1)
System Scleroderma	10 (15)	100 (32)
Antiphospholipid syndrome	1 (1)	3 (<1)
Other Connective tissue disease[1]	2 (3)	1 (<1)
Churg-Strauss	0	1 (<1)
JIA systemic	1 (1)	0
JIA Oligoarticular	1 (1)	0
Other neurological disorder[2]	3 (4)	25 (8)
ITP- Idiopathic thrombocytopenic purpura	2 (3)	0
Hemolytic anemia	7 (10)	0
Evan syndrome	6 (9)	0
Other autoimmune cytopenia[3]	8 (12)	0
Crohns disease	7 (10)	22 (7)
Other bowel disorder, spec	15 (22)	1 (<1)
Conditioning regimen		
TBI + FLUD ± others	15 (22)	0
TBI + CY ± others	1 (1)	33 (10)
TBI+ ATG ± others	0	1 (<1)
BU+ CY ± others	7 (10)	5 (2)
BU + FLUD ± others	14 (21)	0
CY + FLUD ± others	5 (7)	16 (5)
CY + ATG± others	2 (3)	112 (35)
TLI ± others	3 (4)	0
CY ± others	0	73 (23)
LPAM ± others	18 (26)	52 (16)
FLUD ± others	3 (4)	1 (<1)
ATG ± others	0	1 (<1)
Others	0	23 (7)
GVHD prophylaxis		
TDEPLETION +- other	3 (4)	0
CD34 select alone	2 (3)	0
Cyclophosphamide +- others	8 (12)	0
FK506 + MMF +- others	12 (18)	0
FK506 + MTX +- others(not MMF)	6 (9)	0
FK506 +- others(not MMF,MTX)	5 (7)	0
FK506 alone	1 (1)	0
CSA + MMF +- others(not FK506)	14 (21)	0
CSA + MTX +- others(not MMF,FK506)	5 (7)	0
CSA +- others(not FK506,MMF,MTX)	6 (9)	0
CSA alone	1 (1)	0
Other GVHD Prophylaxis	3 (4)	0

Characteristic	Allogeneic	Autologous
Identical twin donor	1 (1)	0
Not reported	1 (1)	0
Not Applicable for autologous	0	317
Time from diagnosis to transplant, months		
Median (range)	33 (2-565)	55 (<1-443)
<12 months	21 (31)	48 (15)
12-24 months	8 (12)	50 (16)
24-36 months	9 (13)	26 (8)
>36 months	30 (44)	193 (61)
Country		
USA	58 (85)	139 (44)
Australia	1 (1)	5 (2)
Belgium	2 (3)	0
Brazil	1 (1)	31 (10)
Canada	3 (4)	25 (8)
France	0	1 (<1)
Germany	0	4 (1)
India	0	1 (<1)
Israel	0	3 (<1)
Italy	0	1 (<1)
Netherlands	2 (3)	3 (<1)
Poland	0	4 (1)
Saudi Arabia	0	2 (<1)
Spain	0	6 (2)
Sweden	1 (1)	0
Switzerland	0	1 (<1)
Russia	0	2 (<1)
Mexico	0	72 (23)
Iran	0	1 (<1)
Singapore	0	13 (4)
Columbia	0	1 (<1)
Czech Republic	0	2 (<1)
CRF or TED track		
TED	50 (73)	277 (87)
CRF	18 (26)	40 (13)
Year of transplant		
2007-2008	5 (7)	38 (12)
2009-2010	12 (18)	63 (20)
2011-2012	11 (16)	33 (10)
2013-2014	18 (26)	45 (14)
2015-2016	14 (21)	76 (24)

Characteristic	Allogeneic	Autologous
2017-2018	8 (12)	62 (20)
Median follow-up of survivors (range), months	25 (3-127)	24 (<1-138)

[1] CREST (n=1); Mixed Connective Tissue Disease (n=1); Relapsing Polychodritis (n=1) ;

[2] Neuromyelitis optica (n=6); Stiff person syndrome (n=9); Chronic inflammatory demyelinating polyneuropathy (n=2; Immune mediated encephalopathy (n=2); Adrenomyeloneuropathy (n=1); ADULT-ONSET LEUKODYSTROPHY WITH AXONAL SPHEROIDS AND PIGMENTED GLIA (SF1R MUTATION) (n=1); Chronic Inflamatory polyradiculoneuropathy (n=1); Chronic-Recurring Myelitis (n=1); CIDP (n=1); Demyelinisation Neuropathy (n=1); Limbic Encephalitis (n=1); Rasmussen Encephalitis (n=1); Progressive motor neuropathy (n=1).
Mediated Encephalopathy (n=2); Limbic Encephalitis (n=1); Rasmussens Encephalitis (n=1);
Stiff Person Syndrome (n=5)

[3] Autoimmune Neutropenia (n=2); Autoimmune Lymphoproliferative Syndrome (n=2); Autoimmune Neutropenia (n=1); Congenital neutropenia VPS45 Mutation (n=1); Erythropoetic Protoporphyria (n=1); Unidentified autoimmune disorder (n=1)

[5] Ipex Syndrome (n=7); Autoimmune Enteropathy (n=2); IPEX syndrome (n=3); IL-10 Receptor Mutation (n=1); IL-10 Receptor Defect; Inflammatory Bowel Disease (n=1); Inflamatory bowel disease-gene mutation XIAP (n=1).

Accrual Summary of patients who received Cellular therapy after 2016 reported to the CIBMTR through CTED

Characteristic	N (%)
Number of patients	2484
Number of centers	204
Age, median (range), years	47 (0-81)
Age	
< 10	514 (21)
10-19	251 (10)
20-29	174 (7)
30-39	139 (6)
40-49	256 (10)
50-59	440 (18)
60-69	519 (21)
>= 70	182 (7)
Missing	9 (<1)
Gender	
Male	1529 (62)
Female	952 (38)
Missing	3 (<1)
Disease/indication	
GVHD treatment	41 (2)
Promote stem cell engraftment	9 (<1)
Suboptimal donor chimerism	301 (12)
Immune reconstitution	58 (2)
GVHD prophylaxis	22 (<1)
Prevent disease relapse	265 (11)
Infection prophylaxis	17 (<1)
Infection treatment	65 (3)
Cardiovascular disease	5 (<1)
Neurologic disease	261 (11)
Solid tumor	18 (<1)
Malignant hematologic disorder	1354 (55)
Non-malignant disorder	14 (<1)
Other indication	54 (2)
Type of CT	
CAR-T	651 (26)
DLI	1266 (51)
Regenerative medicine	269 (11)
Other CT, genetic modified	6 (<1)
Other CT, not genetic modified	177 (7)

Characteristic	N (%)
Genetic modified DLI	33 (1)
TBD	82 (3)
Genetically modified	
No	1694 (68)
Yes	790 (32)
Prior HCT type	
No prior HCT	709 (29)
Prior allo-HCT	1493 (60)
Prior auto-HCT	250 (10)
Missing	32 (1)
Year of CT	
2016	587 (24)
2017	1072 (43)
2018	815 (33)
2019	10 (<1)

Proposal: 1811-11

Title:
To evaluate the outcomes of hematopoietic stem cell transplant with Cyclophosphamide and ATG vs Total Body Irradiation (TBI) conditioning in the treatment of Systemic Sclerosis.

Zartash Gul, MD, gulzh@ucmail.uc.edu, University of Cincinnati Medical Center
Rafiullah Khan, MD, KhanRL@ucmail.uc.edu, University of Cincinnati Medical Center.
Inas Abuali, MD, abualiis@ucmail.uc.edu, University of Cincinnati Medical Center

Specific aims:

- Evaluate outcome data (PFS, EFS and OS) for patients with systemic sclerosis who underwent hematopoietic stem cell transplant (HSCT), comparing Cyclophosphamide and ATG vs Total Body Irradiation (TBI) conditioning in the treatment of Systemic Sclerosis.
- To look for immediate and long-term post-transplant complications of adults receiving HSCT, comparing Cyclophosphamide and ATG vs Total Body Irradiation (TBI) conditioning in the treatment of Systemic Sclerosis.
- To evaluate length of response with Cyclophosphamide and ATG conditioning regimen vs TBI based regimen.

Scientific justification:
Systemic sclerosis (SSc) is an autoimmune disease which is associated with vasculopathy, internal organs damage and significant inflammation and fibrosis of the skin and soft tissues. HSCT is not widely used for the management of SSc at this point. However, in the setting of improvement in HSCT at multiple levels now, there is an effort to expand its indications and increase its utilization in the management of autoimmune diseases such as SSc.
In 1997, Tyndall et al reported a case of early response of systemic sclerosis who underwent HSCT after immune ablation. (1) From there-on, phase I and II studies have been encouraging. Immune ablation (with cyclophosphamide and ATG) followed by HSCT has demonstrated improvement in quality of life, EFS and OS. (2)
Based on the limited data we have so far from the SCOT trial and the ASTIS trial, we noted that TBI conditioning is related to an increased risk of malignancies when transplanted systemic sclerosis patients are followed long term. 9 % of the patients in the SCOT trial (two cases of myelodysplastic syndrome and a case of medullary thyroid cancer vs 2.5% in the ASTIS trial (2 cases of EBV positive lymphoproliferative disorder). (2, 3)
Furthermore, it was noted by Farge in 2004 that TBI was associated with exacerbation of pulmonary hypoxia and renal crises in this patient population. (4)
Interestingly, data from a meta-analysis in 2013 confirmed that patients with SSc have a higher incidence of cancer as compared to the general population. (5) Therefore a closer look at how we can minimize further malignancy risk is imperative in SSc patients who undergo transplantation.
The CIBMTR database is highly suitable for more definitive characterization of both the burden of comorbidities among HSCT survivors, as well as the patient and treatment characteristics associated with short-term and long-term morbidity and mortality post-transplant for SSc who receive Cyclophosphamide and ATG vs Total Body Irradiation (TBI) conditioning in the treatment of Systemic Sclerosis.
In the process of using the CIBMTR database to assess outcome in survivors of HSCT, we propose also to evaluate and improve upon the data collection forms with respect to post-transplant infections and quality of life. Such work could be performed through establishing a sub-committee of the Working Committee for Late Effects. Ultimately, our results can help support HSCT use with the appropriate

conditioning regimen for this otherwise debilitating autoimmune disease. There is a need to look into it in a larger data base.

Patient eligibility population:
All recipients age 18 or older at time of either autologous or allogeneic HCT for systemic sclerosis.

Data requirements:
All data is already available in the CIBMTR database using established forms.
Subject-related variables:

- Age at transplant
- KPS
- Gender
- Race
- HST-CI (when available)

Disease–related variables:

- Diagnosis
- Stage
- Remission state at transplant (CR, PR, SD, POD)
- Prior lines of therapy for SSc

Infections risk factors and co-morbidities pre-transplant:

- Infections
- Obesity
- Concomitant immune suppressive therapies for other comorbidities
- Extent of skin fibrosis and inflammation
- Neurological conditions
- HTN, DM, HLD
- Tobacco use
- Renal insufficiency
- CVAs
- Pulmonary disease

Transplant-related variables:

- Conditioning regimen (comparing Cyclophosphamide and ATG vs Total Body Irradiation (TBI) conditioning in the treatment of Systemic Sclerosis).
- Dose of TBI
- Stem cell dose
- Pre- and post- transplant immune suppression
- Post-Transplant Polyoma virus infections and titer
- Other complications (CMV, ARF, etc)

Outcomes considered at 100 days, 6 months, and annually:

- Improvement in Fatigue Impact Scale (FIS)
- Improvement in Quality of Life (QOL) as measured by improved ADLs and reduced hospitalizations
- Mortality and causes of mortality

- Neurological complications

Study design:
This is a retrospective study of patients age 18 or older who have undergone HSCT for systemic sclerosis. We will evaluate for short term and long term complications of patients who received Cyclophosphamide and ATG vs non-TBI conditioning regimens. This will include, but is not limited to, infections, respiratory, neurological, renal and cardiovascular complications.
Standard statistical analyses with a t-test will be performed for continuous variables, chi-square for discrete variables comparing groups with and without pre-existing cardiac conditions and short- and long-term outcomes with HSCT. In addition, transplant-related mortality, neurologic event-free survival, improvements in FIS and quality of life and overall survival will be evaluated using Kaplan-Meier survival curves when comparing groups (for example, Cyclophosphamide and ATG vs TBI) and Cox proportional hazard model will be used to analyze the effect of multiple variables (pre-transplant, conditioning and post-transplant) on disease event free survival, PFS and as well as overall survival.

References:
1. Tyndall A, Black C, Finke J, et al. Treatment of systemic sclerosis with autologous haemopoietic stem cell transplantation. *Lancet (London, England).* 1997;349(9047):254.
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Selection Criterial:	Excluded #	Remaining #
Inclusion		
First auto for Systemic sclerosis		164
Age > 18	Age < 18 (n=8)	156
Exclusion		
No follow up	No follow up reported (n=20)	136
Consent	No consent (n=1)	135
Embargoed centers	(n=1)	147
Additional Exclusions		
Conditioning	Cy/Flu (n=7) Beam like (n=2) Mel alone (n=2) Other (n=4) Missing (n=8)	112

Table 1. Characteristics of patients

Characteristic	TBI	CY
Number of patients	52	60
Number of centers	12	24
Patient age at HCT		
Median (range)	44 (24-65)	46 (20-71)
18-29	8 (15)	5 (8)
30-39	12 (23)	17 (28)
40-49	21 (40)	15 (25)
50-59	8 (15)	18 (30)
60-69	3 (6)	4 (7)
70+	0	1 (2)
Gender		
Male	21 (40)	19 (32)
Female	30 (58)	41 (68)
9	1 (2)	0
Karnofsky score at HCT		
<90	21 (40)	41 (68)
>=90	7 (13)	8 (13)
Missing	24 (46)	11 (18)
Conditioning regimen		
TBI/Cy	51 (98)	0
TBI/other(s)	1 (2)	0
Cy alone	0	60

Characteristic	**TBI**	**CY**
Country		
USA	51 (98)	43 (72)
Australia	0	4 (7)
Canada	1 (2)	7 (12)
Spain	0	2 (3)
Iran	0	1 (2)
Singapore	0	2 (3)
Columbia	0	1 (2)
Year of transplant		
1998	0	2 (3)
1999	3 (6)	1 (2)
2000	3 (6)	2 (3)
2001	5 (10)	1 (2)
2002	3 (6)	0
2003	3 (6)	0
2004	0	1 (2)
2005	1 (2)	1 (2)
2006	2 (4)	3 (5)
2007	11 (21)	2 (3)
2008	4 (8)	2 (3)
2009	6 (12)	2 (3)
2010	6 (12)	1 (2)
2011	3 (6)	2 (3)
2012	0	5 (8)
2013	0	7 (12)
2014	0	4 (7)
2015	0	10 (17)
2016	0	6 (10)
2017	1 (2)	6 (10)
2018	1 (2)	2 (3)
Median follow-up of survivors (range), months	89 (3-217)	25 (2-216)

*ALLO: TBI (n=5) Cy (n=3)

Proposal: 1809-03

Title:
Allogeneic Hematopoietic Cell Transplantation vs. Chimeric Antigen Receptor T-cell Therapy for DLBCL patients with prior autologous transplant failure or refractory disease.

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Hypothesis:
We hypothesize that overall survival in DLBCL patients with a prior autologous HCT failure or refractory disease following CAR-T therapy will be comparable to patients undergoing allogeneic HCT.

Objectives:
To compare the following outcomes for DLBCL patients undergoing allogeneic HCT vs. immunotherapy with CAR T-cells:

- Neutrophil and platelet recovery
- Cumulative incidence of acute and chronic graft-versus-host disease (GVHD) [allogeneic cohort only]
- Cumulative incidence of grade 2-4 CRS and CRES [CART cohort only]
- Cumulative incidence of Non-relapse mortality (NRM)
- Disease relapse and/or progression
- Progression-free survival (PFS)
- Overall survival (OS)
- Cause of death

Scientific justification:
Although rituximab-based first line chemoimmunotherapy is highly effective in diffuse large B cell lymphoma (DLBCL), 20%-40% of patients with DLBCL do not respond to standard first-line treatment or experience disease recurrence. Only a minority of these early failures can be durably rescued by high-dose chemotherapy with autologous hematopoietic cell transplantation (auto-HCT), whilst the majority will be chemotherapy-resistant. The prognosis of DLBCL patients relapsing after a prior auto-HCT or those with refractory disease is poor, and represent an ultra-high-risk (UHR) group of patients. Standard salvage strategy in this UHR setting in eligible patients is cellular immunotherapy, namely allogeneic hematopoietic cell transplantation (allo-HCT) (1, 2) and, more recently, chimeric antigen receptor-engineered T cells (CART) (3, 4).
Using the Center for International Blood and Marrow Transplant Research (CIBMTR) database, we reported on 503 patients who underwent alloHCT after disease progression/relapse following a prior autoHCT. The 3-year probabilities of non-relapse mortality, progression/relapse, progression-free survival (PFS) and overall survival (OS) were 30, 38, 31 and 37% respectively. Factors associated with worse OS on multivariate analysis included KPS<80, chemoresistance and myeloablative conditioning (5). Before the advent of CAR T cell like therapies, CIBMTR data have also evaluated role of alloHCT in refractory DLBCL (n=533) (6) undergoing either myeloablative (MA; n = 307) or reduced-intensity/nonmyeloablative conditioning (RIC/NST; n = 226). At 3 years, MA allo-HCT was associated with a higher NRM compared with RIC/NST (53% versus 42%; P = .03), similar PFS (19% versus 23%; P =

.40), and lower OS (19% versus 28%; P = .02), respectively. This analysis clearly showed that despite a refractory state, a small subset of DLBCL patients can attain durable remissions after allo-HCT. Conditioning regimen intensity was not associated with PFS and OS (6).
In the current era, for this subset of UHR DLBCL (with either failed prior autoHCT or refractory disease), CAR T cell is an additional therapeutic option. Recently published results of the pivotal phase II clinical trial ZUMA-1 (4) using axicabtagene ciloleucel, an anti-CD19 CAR T cell construct, have demonstrated an objective response rate of 82% with a complete remission (CR) rate of 54%. With a median follow-up of 15.4 months, 42% of the patients continued to have a response, with 40% continuing to have a CR. In the same direction, the phase II Juliet Trial (3) using tisagenlecleucel (CTL019) in a population of 147 patients with multiply relapsed / refractory aggressive B cell lymphoma, gave an overall response rate of 53% with a CR rate of 40%.
Cost, graft-versus-host disease (GVHD), NRM and patients with excellent performance status at HCT have been the Achilles heel of alloHCT. However, treatment-related-toxicity mainly comprises neurological effects and cytokine release syndrome, financial considerations and patients fitness are also not negligible with CAR T cell therapies. Durability of CAR T responses in DLBCL with mature follow up is also not known. Hence in otherwise fit patients, with UHR DLBCL (auto-HCT failure or active disease), arguably both allo-HCT and CART cells are viable options, with no comparative data available to show benefit of one approach over another. Hence using the CIBMTR database we propose a registry comparing alloHCT vs. CART cell therapy in UHR DLBCL patients.

Feasibility:
If the number of CAR T treated patients in the CIBMTR registry is low or registry contractual obligations precludes using those data then study team will obtain data regarding DLBCL receiving CAR T therapy from following potential collaborating centers:

- Fred Hutchinson Cancer Center
- Medical College of Wisconsin
- Moffitt Cancer Center
- Vanderbilt University
- Ohio State University
- Levine Cancer Institute
- Cleveland Clinic Foundation
- University of Kansas Medical Center
- University of Wisconsin
- (additional site can be involved)

Study population:
Inclusion criteria:

- Adult DLBCL patients (age ≥18) undergoing a first allo-HCT or CAR T cell therapy between Jan 2012 to July 2018
- For allogeneic HCT cohort any conditioning intensity, donor source, graft source and GVHD prophylaxis will be permitted
- For the CAR T cell cohort any lymphodepletion approach or any commercially approved or investigational second generation or later CAR T cell platforms will be eligible
- Study will be limited to DLBCL patients either failing a prior autologous HCT or those without a CR at the time of alloHCT or CAR T administration

Exclusion criteria:

- Patients undergoing a second allogeneic HCT
- Transformed DLBCL from indolent histologies

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. This will have both multivariate and univariate analyses.

Secondary outcomes:

- Hematopoietic recovery: The primary measures for hematopoietic recovery will be (univariate analyses only):
    - Time to neutrophils (ANC) > 0.5 $x10^9$/L sustained for three consecutive days within 28 and 100 days post-transplant. This endpoint does not specify whether recovery is engraftment of donor cells or autologous reconstitution.
    - Time to achieve a platelet count of (a) >20 x 10^9/L independent of platelet transfusions for 3 consecutive days within 28 and 100 days post-transplant.
- Incidence of acute and chronic GVHD (alloHCT cohort only): Cumulative incidence of grade II-IV acute GVHD per consensus criteria, with death as competing risk. Cumulative incidence of chronic GVHD, with death as competing risk.
- Incidence of CRS and CRES (CAR T cohort only): Cumulative incidence of grade II-IV CRS and CRES per consensus TBD criteria, 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 (variables to be included in multivariate model ***TBD):

Main Effect:

- Allogeneic HCT vs. CAR T cells

Patient related:

- **Age at HCT or CAR-T therapy**: continuous to find the appropriate cut point for the survival model
- **Patient sex:** male vs. female
- **Karnofsky performance score** at HCT or CAR-T: ≥90 vs. <90 vs. missing
- **HCT comorbidity index** HCT or CAR-T: 0 vs. 1-2 vs. ≥3 vs. missing
- Race: Caucasians vs. African Americans vs. Hispanics vs. Asians vs. others vs. missing

Disease related:

- **Time from diagnosis to HCT or CAR-T**: >12 months vs. ≤12 months vs. missing
- **History of autologous transplant:** No vs. Yes
- **Disease status at the time of HCT or CAR-T:** CR vs. PR vs. chemorefractory vs. untreated/unknown
- **Lines of prior therapy (**won't be available at TED)

Immunotherapy related:

- **Reporting registry:** CIBMTR vs. EBMT
- **Conditioning**: MAC vs. RIC
- **Lymhodepletion**: Flu/CY vs. CY alone vs. Other
- **Graft type:** bone marrow vs. PB vs. cord
- **CAR T platform:** Axicabtagene ciloleucel vs. tisagenlecleucel vs. lisocabtagene maraleucel (JCAR017) vs. others (specify)
- **Donor type:** Matched related vs. matched unrelated vs. cord blood vs. haploidentical
- **Year of transplant:** Continuous
- GVHD prophylaxis: calcineurin inhibitors + MTX vs calcineurin inhibitor + MMF vs others Vs. PT-CY based

Study design:

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, time to GVHD (or CRS/CRES) or last FU are measured from the date of transplantation or CAR therapy. 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. Cumulative incidence curves for GVHD/CRS/CRES 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. Multivariable Cox regression analysis will be performed to estimate the risk factors for survival, GVHDs, relapse, NRM, and PFS. The proportional hazards assumption will be examined. If violated, it will be added as time-dependent covariates. The interaction between the main effect and significant variables will be checked. Because of severe confounding between the main effect and some covariates, the propensity score adjustment may be conducted.

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Selection criteria for PROP 1809-03:

CAR-T Cohort

The below selection criteria was applied	# excluded	N
Patients with DLBCL		257
Patients who received first CAR-T	37	220
Include only patients with a prior auto HCT (*excluding no prior HCT = 159, prior allo-HCT = 4, unknown = 4*)	167	53
Exclude patients under 18 years old	0	53
Exclude no consent	1	52

Allo-HCT Cohort (using CRF data)

The below selection criteria was applied	# excluded	N
Patients with DLBCL		1653
Patients with a prior auto-HCT who received first allo-HCT between 1/1/2012 and 7/31/2018	1534	119
Include only patients where HCT used to treat relapse or persistent disease (*excluding planned 2nd tx, per protocol = 8, second malignancy = 1, other = 1, unknown = 10*)	20	99
Exclude patients under 18 years old	1	98
Exclude no consent	2	96

Allo-HCT Cohort (using TED data)

The below selection criteria was applied	# excluded	N
Patients with DLBCL		34501
Patients with a prior auto-HCT who received first allo-HCT between 1/1/2012 and 7/31/2018	33736	765
Include only patients where HCT used to treat relapse or persistent disease (*excluding no engraftment = 1, partial engraftment = 1, graft failure-rejection = 3, planned 2nd tx, per protocol = 39, second malignancy = 3, other = 8, unknown = 240*)	295	470
Exclude patients under 18 years old	1	469
Exclude no consent	23	446

Table 1. Characteristics of adult patients with DLBCL who received an allo-HCT (CRF data) or CAR-T cellular therapy

Characteristic	CAR-T N (%)	Allo-HCT N (%)
Number of patients	52	96
Age, median (range), yrs	64 (22-75)	56 (23-75)
Age		
20-29	2 (4)	2 (2)
30-39	2 (4)	8 (8)
40-49	7 (13)	14 (15)
50-59	7 (13)	38 (40)
60-69	22 (42)	30 (31)
>= 70	12 (23)	4 (4)
Gender		
Male	38 (73)	50 (52)
Female	14 (27)	46 (48)
KPS prior to CT/Transplant		
90-100	18 (35)	53 (55)
80-90	15 (29)	27 (28)
< 80	12 (23)	13 (14)
Missing	7 (13)	3 (3)
Disease classification		
Diffuse, large B-cell lymphoma - NOS	20 (38)	90 (94)
T-cell / histiocytic rich large B-cell lymphoma	1 (2)	2 (2)
Primary mediastinal (thymic) large B-cell lymphoma	1 (2)	2 (2)
Diffuse, large B-cell lymphoma - germinal center B-cell type	18 (35)	0
Diffuse, large B-cell lymphoma - activated B-cell type	11 (21)	0
High-grade B-cell lymphoma, NOS	1 (2)	1 (1)
High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements	0	1 (1)
Time from diagnosis to HCT/CT, median (range)	3 (1-22)	5 (<1-21)
Time from diagnosis to HCT/CT		
0-3 years	28 (54)	27 (28)
3-5 years	13 (25)	24 (25)
> 5 years	11 (21)	45 (47)
Time from prior HCT to CT, median (range)	14 (3-165)	Not applicable
Time from prior HCT to CT		
0-6 months	8 (15)	0
6-12 months	11 (21)	0
>= 12 months	31 (60)	0

Characteristic	CAR-T N (%)	Allo-HCT N (%)
Missing	2 (4)	96
Time from prior auto-HCT to allo-HCT, median (range)	Not applicable	21 (2-197)
Time from prior auto-HCT to allo-HCT		
0-3 years	0	2 (2)
3-5 years	0	19 (20)
> 5 years	0	75 (78)
Missing	52	0
Graft type		
Bone marrow	0	10 (10)
Peripheral blood	0	61 (64)
Umbilical cord blood	0	25 (26)
Missing	52	0
Year of HCT/CT		
2012	0	9 (9)
2013	0	18 (19)
2014	0	27 (28)
2015	0	18 (19)
2016	1 (2)	10 (10)
2017	6 (12)	11 (11)
2018	45 (87)	3 (3)
Disease status at HCT/CT		
CR	2 (4)	44 (46)
PR	10 (19)	25 (26)
Resistant	11 (21)	10 (10)
Missing	29 (56)	17 (18)
Prior lines of treatment		
No	16 (31)	16 (17)
Yes	29 (56)	65 (68)
Missing	7 (13)	15 (16)
N of prior lines of treatment		
No treatment	16 (31)	16 (17)
1	0	42 (44)
2	0	5 (5)
3	0	4 (4)
4+	0	14 (15)
Missing	36 (69)	15 (16)
Clinical trial		
No	45 (87)	0
Yes	7 (13)	0

Characteristic	CAR-T N (%)	Allo-HCT N (%)
Missing	0	96
Median follow-up of survivors (range), months	0 (<1-16)	37 (6-76)

Proposal: 1811-66

Title:
Clinical predictors of response and toxicity following CD-19 directed Chimeric Antigen Receptor T-cell therapy in patients with Diffuse Large B-cell Lymphoma

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Hypothesis:
Baseline clinical characteristics of patients may predict likelihood of response to CD19 directed CAR-T cell therapy and the risk of associated toxicities, including cytokine release syndrome, neurotoxicity and prolonged cytopenias, in patients with DLBCL.

Specific aims:
- Identify which clinical characteristics of a patient are most predictive of a response to CD19 directed CAR-T therapy
- Identify which clinical characteristics are predictive of long-term duration of response to CD19 directed CAR-T therapy
- Identify which clinical characteristics are associated with CD19 CAR-T toxicity; specifically looking at Cytokine Release Syndrome, Neurotoxicity and prolonged cytopenias

Scientific impact:
Provide clinicians with an objective approach to determining which patients are suitable for CAR-T therapy by helping to determine who has the highest chance of a response. At the same time this may help to identify more accurately who is at greatest risk of toxicity following CAR-T therapy.

Scientific justification:
Standard DLBCL induction therapy provides approximately 60%o f DLBCL patients long-term remissions.[1] Unfortunately, 10-15% of DLBCL patients have primary refractory disease (and an additional 20-25% have relapsed disease after initial response to therapy.[2] A recent meta-analysis of over 600 patients (SCHOLAR-1) demonstrated that patients refractory to chemotherapy have a CR rate of only 7%, median OS of 6.3 months and 1 year OS of 23%.[3] The North American retrospective study (REFINE) of over 300 patients also highlighted dismal outcomes in patients with relapsed or refractory disease and that patients with MYC rearranged DLBCL are prone to primary treatment failure and less success with salvage therapies; including ASCT and allogeneic stem cell transplantation.[4] Taken together, SCHOLAR-1 and REFINE established that chemotherapy refractory DLBCL represents a critical unmet medical need, with approximately 5,400 patients seeking improved therapeutic options annually. Chimeric Antigen Receptor (CAR) therapy targeting CD19 has recently emerged as a potential treatment option for lymphoid malignancies, specifically ALL and NHL. Multiple groups have reported complete remission (CR) rates ≥70% in patients with B-cell ALL and 75% in NHL.[5, 6] Durable response (lasting >6months) seen primarily in patients with an initial CR but not those who achieve a PR following CAR therapy. Furthermore, initial insights into CAR dynamics indicate that effective therapy is characterized by initial robust CAR T-cell expansion and persistence of the CARs beyond the 6-month mark.

A review of the current ongoing clinical trials highlights that though initial responses are greater 50% in patients after CAR-T therapy, a much smaller group have had any type of durable response lasting beyond 6 months. The ZUMA1 trial has recently reported on their experience with 42% of patients in complete remission at 12 months and overall survival at 18 months of 52%.[6] Similarly, the JULIET reported a 30% CR rate at 6 months and an overall survival rate at 12 months of 49%.[7] In both trials over 75% of patients experienced some type of grade 3 or 4 adverse event. The observations from these large multi-institutional trials highlight the need to improve our ability to predict who has the greatest chance of achieving a durable response to CAR-T therapy and which patients are at greatest risk of encountering significant toxicities after CAR- T therapy. Such objective tools would greatly enhance the approach to deciding on and managing patients after treatment with CAR-T therapy.

Patient eligibility population:
Any patient with a history of DLBCL who is undergoing their first treatment with a CD19 directed CAR-T therapy.

Data requirements:

- Diagnosis (r/r DLBCL, transformed DLBCL, PMLBCL)
- Age
- Gender
- Stage at Diagnosis
- IPI score at diagnosis
- Presence of bulky disease (at diagnosis and at time of CAR-T)
- Disease status at CAR-T treatment
- Prior History of Auto or AlloSCT
- CART product received
- Type of CART product (CD28 co-stim versus 4-1bb costim)
- LDH,Ferritin, CRP at time of CAR-T treatment at each follow up date
- Blood counts at treatment (WBC, Platelets, Hemoglobin, ANA, ALC) and at each subsequent follow up date when response assessed
- D28 Response
- D90 Response
- D120 Response
- Month 6 Response
- Month 9 Response
- Month 12 Response
- Maximum grade of CRS
- Maximum grade of Neurotoxity
- Duration of cytopenias
- Proceed to Auto or AlloSCT?
- Timing of disease relapse

Sample requirements:
Sample size will be all patients for whom CIBMTR has adequate information to allow for at least 6 months of follow-up. Biologic samples are required.

Study design:
This retrospective study will compile the above mentioned clinical parameters for each DLBCL patient who has undergoneCD19 directed CAR-T therapy. The study will aim to identify variables which may predict efficacy and risk of toxicity from CAR-T therapy in DLBLC patients. The pre-treatment clinical parameters will be compiled and multivariate and univariate analysis will be carried out related to each patient's initial response at D28 to determine which ones appear to have high likelihood of predicting a favorable response. Based on data availability this analysis will be extended to disease at status at 3 months, 6 months, 9 months and 12 months after CAR-T infusion.
A similar analysis will be carried out for each of the clinical variables at each response assessment time-point. One question to be tested will whether changes in these clinical measures over time has any ability to predict improvement of response (PR→ CR, SD→PR/CR) or risk of relapsed disease.
We will also compile the toxicity profile for all patients and carry our multivariate and univariate analysis of collected clinical measurements to determine which pre CAR-T infusion factors might predict risk of severe CRS, severe Neurotoxicity and prolonged cytopenias.

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Conflicts of interest:
None

Selection criteria for PROP 1811-66:

The below selection criteria was applied	# excluded	N
Patients with DLBCL that received first CAR-T therapy		259
Patients that received CD19 directed CAR-T therapy	14	245
Exclude no consent	31	214

Table 1. Characteristics of patients with DLBCL who received a CD19 directed CAR-T therapy

Characteristic	N (%)
Number of patients	214
Age, median (range), yrs	61 (18-81)
Age	
10-19	1 (<1)
20-29	7 (3)
30-39	11 (5)
40-49	28 (13)
50-59	54 (25)
60-69	72 (34)
>= 70	41 (19)
Gender	
Male	150 (70)
Female	64 (30)
KPS	
90-100	83 (39)
80-90	67 (31)
< 80	53 (25)
Missing	11 (5)
Disease classification	
Diffuse, large B-cell lymphoma - NOS	72 (34)
T-cell / histiocytic rich large B-cell lymphoma	4 (2)
Primary mediastinal (thymic) large B-cell lymphoma	6 (3)
Diffuse, large B-cell lymphoma - germinal center B-cell type	68 (32)
Diffuse, large B-cell lymphoma - activated B-cell type	48 (22)
EBC+ DLBCL, NOS	2 (<1)
High-grade B-cell lymphoma, NOS	1 (<1)
High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements	13 (6)
Time from diagnosis to CT, median (range)	18 (2-274)
Time from diagnosis to CT	
0-6 months	11 (5)
6-12 months	59 (28)
>= 12 months	144 (67)
Prior HCT type	
No prior HCT	142 (66)

Characteristic	N (%)
Prior allo-HCT	4 (2)
Prior auto-HCT	64 (30)
Missing	4 (2)
Year of CT	
2016	3 (1)
2017	9 (4)
2018	202 (94)
Disease status at CT	
CR	17 (8)
PR	82 (38)
Resistant	31 (14)
Missing	84 (39)
Prior lines of treatment	
No	49 (23)
Yes	131 (61)
Missing	34 (16)
N of prior lines of treatment	
No treatment	49 (23)
1	24 (11)
2	25 (12)
3	23 (11)
4+	59 (28)
Missing	34 (16)
Clinical trial	
No	190 (89)
Yes	24 (11)
Median follow-up of survivors (range), months	3 (<1-16)

Proposal: 1811-88

Title:
Impact of DLI dose on outcomes of relapsed MDS and AML patients who have had an allogeneic transplant from matched related and unrelated donors.

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Hypothesis:
The dose of DLI from 0.5x10^7 to 1x 10^7 CD3+ cells correlates with an improved overall survival (OS)and relapse free survival(RFS), in patients who have had relapsed MDS and AML after allogeneic transplants.

Specific aims:
Primary aim:

- To determine if dose of 0.5x10^7 to 1 x10^7 CD3+ cells/kg for initial DLI correlates with improved Relapse free and overall survival (1yrs) in patients with relapsed myeloid malignancies -AML and MDS. DLI from matched unrelated donors and matched related donors patients will be analyzed from 2005-2015. The doses of DLI will be classified <1x10^6 cells/kg, 1x10^6 - 0.5x 10^7, 0.5x10^7- 1.0 x10^7 and >1x10^7 cells/kg. OS and RFS will determined in for these groups.
- Correlating grade of GVHD and degree of pancytopenia to the dose of DLI.

Secondary aim:

- To see if timing of DLI has an impact on overall survival and relapse free survival.

Primary end point:

- Overall survival at 1 yr post DLI

Secondary end point:

- To see if the timing of DLI administration i.e. <6 months, 6 months to 2yr,>2 yrs. correlates with OS and RFS.
- Incidence of pancytopenia after DLI administration.

Scientific impact:
This is observational study on DLI will help determine the optimal dose and timing of administration that might influence outcomes in patients who have relapsed MDS and AML post-transplant. As far as we know there is no set strategy that can be universally applied to all patients who need DLI. Timing and strategies of dose escalation have considerable inter-institutional variability. A bigger cohort could validate these characteristics potentially lead to standardization, which would help guide many centers around the world. It could also lead to potential studies to determine doses for DLI in alternative donors like haplo-identical and MMUD and also dose correlation for prophylactic DLI for mixed chimerism and minimal residual disease.

Scientific justification:
Allogeneic transplants are one of the few therapies that could offer a chance of cure in MDS and AML. There has been a decrease in non-relapse mortality, due to reduced intensity conditioning regimens, improvements in control of GVHD. However relapse remains a major cause of treatment failure, predicting poor prognosis. [1-3]Donor Lymphocyte infusion (DLI) is an important immunotherapeutic modality, which

could reinforce graft versus leukemia effect. However there is no set consensus on the dose and timing of DLI that would produce the best outcome. Optimal dose range in DLI would improve outcomes by striking the balance between graft versus Leukemia effect (GVL) and graft versus host disease (GVHD).
Reduction of tumor burden and enhancement of GVL are common strategies used to improve the grim prognosis associated with relapsed MDS and AML post-transplant. DLI was introduced in 1990s and was extremely effective in Chronic Myelogenous leukemia. However studies in AML have been less successful, but it continues to benefit some patients[4]. There have been very few studies that have studies the dosing and timing in DLI. Study by Karl et al suggested that CD3+ doses > 1x 10^6 /kg were needed to obtain an optimal response from DLI. This study had 46 patients and included all hematological malignancies[5]. Bar et al reported that an initial CD3+ dose >10x10^7 or higher increased the risk of GVHD, without an improvement in overall survival. This was a cohort consisting of 225 pts of which a total of 93 pts AML (71), and MDS (22) received DLI[6]. Hence the suggested starting dose of DLI is in between 1x10^6 to 1x10^7 CD 3+ cells /kg. The dose and timing of DLI may have to be specific for the disease as nature of relapse is very different for AML as opposed to lymphomas. The conditioning therapy at the time of relapse may also have an adjunctive role to DLI[7]. There have been many variations reported in the median CD3+ dose in other studies involving AML, much higher than the given range[4, 8]. Hence a retrospective study from a large centralized database would provide credible information due to increased number of patients. There have been very few studies that has reported the effect of timing of DLI. Timing between the DLIs are usually 8 weeks and protocols are often institution based[9]. A time interval between Allo-HCT and DLI of 2yrs has been reported to be relevant for development of GVHD[10].
Overall there have been very few studies, many of them reporting single center experiences. Due to the dearth of occurrences of DLI and vast interinstitutional variability, this question can be answered only if it is analyzed at the CIBMTR as it maintains one of the world's largest database of clinical information on Hematopoietic stem cell transplantation.

Patient eligibility:
Inclusion criteria:

- Patients with MDS and AML relapsed after Allogeneic SCT from 8/8 MUD or MRD.
- Relapse post first allogeneic transplant.
- Source of stem cell -MUD and MRD from bone marrow or peripheral blood stem cell
- Age ≥18 yrs.
- Received donor lymphocyte infusion any time after Allogeneic SCT.
- Years of transplant 2005 – 2015.
- Patient consented to participate in research

Exclusion criteria:

- Patients receiving an allogeneic transplant from alternate donors such as Cords, Haplo-identical and MMUD donors.
- Patients received more than 1 allogeneic transplant
- Patients receiving post-transplant Cytoxan or ATG for GVHD prophylaxis.

Data requirements:
Data collection forms:

- Hematopoietic Stem cell infusion
- Pre-Transplant Essential Data
- Disease Classification
- Post-Transplant Essential Data
- Acute Myelogenous Leukemia Pre-HCT data

- Acute Myelogenous Leukemia – Post HCT data
- MDS/MPN post HSCT data form
- Myelodysplastic/ Myeloproliferative disorders Pre HCT-HCT Data
- 6 months to 2 years POST HSCT data
- Yearly Follow up for greater that 2 years post HSCT data.
- Recipient Death Data

Variables needed:

Patient related variables:

- age
- race
- sex
- performance status
- HCT-CI score

Disease-related variables:

- AML -disease status prior to transplant, risk classification, cytogenetics, molecular markers, pre-HCT treatment.
- MDS –disease status prior to transplant, IPI risk classification, cytogenetics, pre-HCT treatment.
- Induction chemotherapy and median number of cycles.
- Time from diagnosis to transplant

Transplant related variables:

- Conditioning regimen – Reduced Intensity Conditioning vs Myeloablative conditioning
- Graft Source – Bone marrow versus Peripheral blood.
- Dose of CD34 during transplant
- GVHD prophylaxis

Post-Transplant related variables:

- Time of relapse
- Time from transplant to relapse
- Therapy given at time of relapse
- Time of administration of DLI (Time between Transplant and DLI administration)
- Dose of Initial DLI
- Dose of Total DLI
- Number of DLI infusions administered
- Therapy given prior to DLI
- Maintenance therapy used post-transplant
- Median follow up
- Transplant related mortality

Study design:

This is an observational study that intends to study relationship between the dose of DLI and Overall survival. The doses of DLI will be classified <1x10^6 cells/kg, 1x10^6 - 0.5x 10^7, 0.5x10^7- 1.0 x10^7 and doses >1x10^7 cells/kg. This classification of the dose will apply for both the initial DLI and the total DLI. We will collect variables as mentioned above. Some of the variables would include, time from transplant

to relapse, time from relapse to DLI administration. Type of treatment received prior to DLI, dose of Initial DLI, and total dose of DLI. We would like to analyze the period of 2005-2015, and determine a 2 year OS and PFS. We would also like analyze the occurrence of GVDH after DLI. All information will be obtained in the above mentioned Data Collection Forms.

Data sources:
CIBMTR Research Database. No non- CIBMTR resources are needed.

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Conflicts of interest:
None

Selection Criterial: Ted Nov 18	**Excluded #**	**Remaining #**
Inclusion		
DLI reported to CT extract		1,477
CT indication: Relapse	Promote stem cell engraftment (n=8) Suboptimal donor chimerism (n=376) Immune Reconstitutuion (n=52) GVHD prophy (n=15) Prevent disease relapse (n=232) Infection prophy (n=7) Infection Treatment (n=60) Other indication (n=2)	725
AML/ MDS	Not AML/MDS (n=243)	482
Age > 18	Age < 18 (n=42)	440
Exclusion		
Post tx-Cy or ATG	Post-CY (n=84) ATG, in conditioning regimen (n=106) ATG, in GVHD prophylaxis (n=2)	248
Consent	No consent (n=12)	236
Embargoed centers	(n=0)	236
Additional Exclusions		
Auto tx	Auto tx (n=1)	235

Table 1. Characteristics of patients

Characteristic	N (%)
Number of patients	235
Number of centers	73
Patient age at HCT	
Median (range)	55 (19-75)
18-29	24 (10)
30-39	27 (11)
40-49	30 (13)
50-59	64 (27)
60-69	75 (32)
70+	15 (6)
Sex	
Male	116 (49)
Female	119 (51)
Disease	
Acute myelogenous leukemia	179 (76)
Myelodysplastic/myeloprolifterative disorders (please classify all preleukemias)	55 (23)
Non-Hodgkin lymphoma	1 (<1)
Donor HCT	
HLA-identical sibling(may include non-monozygotic twin)	120 (51)
Unrelated donor	94 (40)
HLA-mat. oth relative	5 (2)
HLA-mis. relative	16 (7)
Country	
USA	193 (82)
Australia	4 (2)
Brazil	3 (1)
Canada	6 (3)
Denmark	16 (7)
India	1 (<1)
New Zealand	1 (<1)
Norway	1 (<1)
Saudi Arabia	10 (4)
Year of transplant	
2005	1 (<1)
2006	1 (<1)
2007	1 (<1)

Characteristic	N (%)
2009	1 (<1)
2010	3 (1)
2011	6 (3)
2012	27 (11)
2013	15 (6)
2014	25 (11)
2015	36 (15)
2016	69 (29)
2017	46 (20)
2018	4 (2)
Year of DLI	
2011	1 (<1)
2012	2 (<1)
2013	5 (2)
2014	1 (<1)
2015	11 (5)
2016	74 (31)
2017	114 (49)
2018	27 (11)
Number of infusions	
1	150 (64)
2	18 (8)
3	13 (6)
4	1 (<1)
5	1 (<1)
Missing	52 (22)
Interval HCT to CT, months (range)	11 (<1-135)
CD3+ dose X10^7 (IQR)	77 (24-601)
Median follow-up of survivors (range), months	49 (3-144)

Proposal: 1811-141

Title:
Prolonged Cytopenia Following CD-19 Targeted CAR-T Therapy for Diffuse Large B-Cell Lymphoma (DLBCL)

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Hypothesis:
We hypothesize that at least 50% of patients who receive one of the FDA-approved CD-19 targeted CAR-T products for DLBCL have at least grade 2 thrombocytopenia (platelet < 75,000/mm3) or grade 2 neutropenia (1,500/mm3) 6 months after treatment.

Specific aims:
- To determine the rate and grade of thrombocytopenia at 6 and 12 months after CAR-T therapy
- To determine the rate and grade of neutropenia at 6 and 12 months after CAR-T therapy
- To determine pre and post treatment factors that may be associated with prolonged cytopenia after CAR-T therapy

Scientific impact:
- Prolonged cytopenia is a common clinical finding in DLBCL patients treated with Axicabtagene Ciloleucel (axi-cel; Yescarta) or Tisagenlecleucel (tisa-cel; Kymriah). However, there is no published data from the clinical trials on incidence and severity of cytopenia beyond day 30 after treatment.
- This study will establish a benchmark for cytopenia (thrombocytopenia and neutropenia) at 6 and 12 months after treatment with FDA approved CD19 targeted CAR-T products.

Scientific justification:
- Prolonged cytopenia limit treatment options for patients with relapsed or refractory disease after CAR-T. Understanding the incidence, severity and associated factors with prolonged cytopenia can lead to interventional studies to address the problem.

Patient eligibility population:
- Adult patient with a diagnosis of DLBCL (or other aggressive lymphomas) who received Axicabtagene Ciloleucel (axi-cel; Yescarta) or Tisagenlecleucel (tisa-cel; Kymriah) commercially.
- Patients with at least 6 months follow-up information .
- Patients treated on clinical trials are excluded.

Data requirements:
<u>Forms</u>:
- 4000
- 4100

<u>Baseline:</u>
- Age
- Sex
- Prior lines of treatment (n and type)

- Time from last chemotherapy to lymphodepletion (weeks)
- Bridging therapy between lymphodepletion and cell infusion (type)

Post CAR-T

- Cytokine-release syndrome (CRS) (yes/no, grade)
- Neurotoxicity (NT) (yes/no, grade)
- Response at first assessment (1 month) (CR,PR,SD,PD)
- Relapse (yes/no)
- Date of relapse
- Died (yes/no)
- Date of death
- Date of last contact

Follow-up

- Blood counts at 1,3,6,9 and 12 months
- Time to neutrophil to 500, 100 and 1500
- Time to platelet to 25,000, 50,000, 75,000 and 100,000
- Number of platelet transfusion in the first 1, 6 and 12 months
- Number of pRBC transfusion in the first 1, 6 and 12 months
- Use of growth factor for platelet (yes/no, type and number)
- Use of growth factors for neutrophil (yes/no, type and number)

Study design:
Retrospective analysis

Conflicts of interest:
None

Selection criterial PROP 1811-141:

The below selection criteria was applied	# excluded	N
Patients receiving Yescarta or Kymriah cellular therapy after FDA approval		314
Patients with DLBCL	101	213
Exclude patients under 18 years old	0	213
Exclude patients in a clinical trial	11	202
Exclude no consent	13	189

Table 1. Characteristics of adult patients with DLBCL who received Kymriah or Yescarta after FDA Approval

Characteristic	N (%)
Number of patients	189
Age, median (range), yrs	61 (22-81)
Age	
20-29	6 (3)
30-39	10 (5)
40-49	25 (13)
50-59	50 (26)
60-69	61 (32)
>= 70	37 (20)
Gender	
Male	133 (70)
Female	56 (30)
KPS	
90-100	68 (36)
80-90	63 (33)
< 80	49 (26)
Missing	9 (5)
Disease classification	
Diffuse, large B-cell lymphoma - NOS	62 (33)
T-cell / histiocytic rich large B-cell lymphoma	3 (2)
Primary mediastinal (thymic) large B-cell lymphoma	6 (3)
Diffuse, large B-cell lymphoma - germinal center B-cell type	59 (31)
Diffuse, large B-cell lymphoma - activated B-cell type	44 (23)
EBC+ DLBCL, NOS	2 (1)
High-grade B-cell lymphoma, NOS	1 (<1)
High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements	12 (6)
Time from diagnosis to CT, median (range)	18 (2-274)
Time from diagnosis to CT	
0-6 months	8 (4)
6-12 months	51 (27)
>= 12 months	130 (69)
Prior HCT type	

Characteristic	**N (%)**
No prior HCT	125 (66)
Prior allo-HCT	4 (2)
Prior auto-HCT	56 (30)
Missing	4 (2)
Year of CT	
2017	4 (2)
2018	185 (98)
Disease status at CT	
CR	17 (9)
PR	70 (37)
Resistant	29 (15)
Missing	73 (39)
Prior lines of treatment	
No	44 (23)
Yes	117 (62)
Missing	28 (15)
N of prior lines of treatment	
No treatment	44 (23)
1	18 (10)
2	23 (12)
3	21 (11)
4+	55 (29)
Missing	28 (15)
Median follow-up of survivors (range), months	3 (<1-7)

Proposal: 1811-109

Title:
CAR-T cell Therapy versus Autologous Transplant in Early Rituximab Failure Patients with Diffuse Large B-cell Lymphoma

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Hypothesis:
CAR-T cell therapy improves OS in patients with early Rituximab failure (<12 months) compared to autologous transplant

Specific aims:
To evaluate clinical outcomes in terms of progression free and overall survival

- Primary outcome will be to compare overall survival among patients who relapse within 1 year of initial diagnosis after first-line rituximab-based chemo-immunotherapy who undergo autologous transplant versus those who receive CAR-T cell therapy against CD19.
- Secondary outcomes will include overall survival, relapse rates, and rates of non-relapse mortality.

Scientific justification:
Diffuse large B-cell lymphoma (DLBCL) is the most common form of aggressive non-Hodgkin lymphoma (NHL) accounting for approximately 30-40% of cases[1]. The standard frontline treatment option generally includes combination chemo-immunotherapy given for 6-8 cycles of which R-CHOP (Rituximab, Cyclophosphamide, Adriamycin, and Prednisone) is considered standard of care for most patients[1, 2]. Despite long-term remissions achieved in approximately 60% of patients, for those with high risk features such as single or double hit lymphoma, primary refractory disease, or early relapse within <12 months, outcomes remain poor [3, 4].
For patients with early Rituximab failure (ERF) defined as relapse within <12 months of receiving a rituximab containing chemo-immunotherapy regimen, the standard approach had been salvage chemotherapy followed by consideration of autologous transplant in chemosensitive patients. The CIBMTR evaluated outcomes specifically in ERF patients with DLBCL and compared them to patients with late Rituximab failure (>1 year) and found that while ERF patients had a higher risk of treatment failure, the 3-year progression free survival was still an impressive 44% in this high-risk population. They concluded that even in this high-risk population that autologous transplant was an appropriate consideration in any chemosensitive patients[5].
Over the last few years, the development of novel cell-based therapies has challenged the existing algorithms for relapsed DLBCL. Chimeric Antigen Receptor modified T (CAR-T) cells redirected against the CD19 antigen on B-cells has produced remarkable outcomes in patients with relapsed, refractory large cell lymphoma[6, 7]. With CAR-T cell therapy, patients with resistant disease following 2 lines of chemotherapy or for those who relapse after autologous transplant, studies have demonstrated a 1-year PFS of 30-40% in this highly refractory population[7-9]. With two recent FDA approvals[10], CAR-T cell therapy is quickly challenging the role of autologous transplant in relapsed DLBCL.
In this study we aim to compare outcomes among patients with DLBCL and ERF who undergo autologous transplant versus CAR-T cell therapy.

Patient eligibility population:
Inclusion/exclusion criteria
Autologous Transplant Patients:

- Adults>18 years of age at the time of transplant from 2010-2016
- First line therapy with rituximab plus an anthracycline based regimen
- Early Rituximab Failure cohort (patients with primary refractory disease or those with first relapse within 1 year of initial diagnosis)

CAR-T cell patients

- Adults>18 years who received anti-CD19 CAR-T cell therapy reported to CIMBTR
- First line therapy with rituximab plus an anthracycline based regimen
- Early Rituximab Failure cohort (patients with primary refractory disease or those with first relapse within 1 year of initial diagnosis)

Data requirements:
Data will be captured through CIBMTR collection forms

Demographic/Patient Level Variables to be analyzed:
Main effect:

- CAR-T cell cohort vs Auto-HCT cohort

Patient-related:

- Age at time of transplant or CAR-T treatment, Continuous & decades
- Gender: male or female
- Karnofsky performance status at transplant: < 90% vs. ≥ 90%
- HCT comorbidity index at transplant 0, 1, 2, and ≥ 3

Disease-related:

- Disease stage at diagnosis: I/II vs III/IV
- Chemo-resistant vs Chemo-sensitive disease

Treatment related:

- Year of transplant: 2010-2013 vs 2014-2016

Study outcomes

- Progression-free survival (PFS): Survival without recurrence or tumor progression. 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. Death from any cause will be considered an event. Surviving patients will be censored at the time of last follow up.
- 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.
- Relapse/progression: Progressive disease or recurrences of disease would be counted as events. Treatment related death, 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.

Study design:

A retrospective multicenter study will be conducted utilizing CIBMTR dataset involving patients with a diagnosis of early rituximab failure DLBCL (as defined in inclusion criteria) who subsequently underwent either auto-HCT versus CAR-T cell therapy. Patients will be eligible if they satisfied the criteria detailed in the patient eligibility section above. The objective of this analysis is report outcomes, survival, and NRM with the two approaches.

PFS and OS will be calculated using the Kaplan-Meier estimator. For NRM, relapse/progression will be the competing event. For relapse rate, NRM will be the competing event. Data on patients without an event will be censored at last follow up. For univariate analysis, the log-rank test will be used to identify factors influencing survival and to compare survival among patients receiving auto-HCT versus CAR-T for relapsed DLBCL. The association between treatment groups and outcomes will be studied with multivariate Cox regression models. P values are 2 sided and values < 0.05 will be considered significant. The other variables tested will be retained in the final multivariate model if the variable will attain the level of significance set for these analyses. Results will be expressed as hazard ratio (HR) with 95% confidence intervals (CI). Possible interactions within the treatment groups and other variables will be tested. All models will be tested regarding proportional hazard of assumptions (PHA). If the assumption will be violated, time dependent covariates will be constructed.

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Selection criteria for PROP 1811-109:

CAR-T Cohort

The below selection criteria was applied	# excluded	N
Patients who received CAR-T therapy		444
Include patients with DLBCL	197	247
Exclude patients with prior HCT	74	173
Exclude patients under 18 years old	1	172
Exclude no consent	30	142

Auto-HCT Cohort (CRF data)

The below selection criteria was applied	# excluded	N
Patients with auto-HCT after 1/1/2010		9586
Include patients with DLBCL	8619	967
Include patients with first relapse within year of diagnosis date	787	180
Exclude patients under 18 years old	0	180
Exclude no consent	1	179

Table 1. Characteristics of adult patients with DLBCL who received an auto-HCT or anti-CD19 CAR-T cellular therapy

Characteristic	CAR-T N (%)	HCT N (%)
Number of patients	142	179
Age, median (range), yrs	60 (22-81)	56 (18-80)
Age		
10-19	0	3 (2)
20-29	5 (4)	13 (7)
30-39	8 (6)	15 (8)
40-49	17 (12)	28 (16)
50-59	39 (27)	50 (28)
60-69	45 (32)	54 (30)
>= 70	28 (20)	16 (9)
Gender		
Male	97 (68)	105 (59)
Female	45 (32)	74 (41)
KPS prior to CT/HCT		
90-100	59 (42)	106 (59)
80-90	45 (32)	49 (27)
< 80	35 (25)	23 (13)
Missing	3 (2)	1 (<1)
Disease classification		
Diffuse, large B-cell lymphoma - NOS	46 (32)	163 (91)
T-cell / histiocytic rich large B-cell lymphoma	1 (<1)	6 (3)
Primary mediastinal (thymic) large B-cell lymphoma	4 (3)	10 (6)
Diffuse, large B-cell lymphoma - germinal center B-cell type	46 (32)	0
Diffuse, large B-cell lymphoma - activated B-cell type	31 (22)	0
EBC+ DLBCL, NOS	2 (1)	0
High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements	12 (8)	0
Time from diagnosis to HCT/CT, median (range)	12 (2-274)	13 (4-141)
Time from diagnosis to HCT/CT		
0-6 months	11 (8)	6 (3)
6-12 months	57 (40)	66 (37)
>= 12 months	74 (52)	106 (59)
Missing	0	1 (<1)
Year of HCT/CT		
2010	0	10 (6)
2011	0	10 (6)
2012	0	10 (6)

Characteristic	CAR-T N (%)	HCT N (%)
2013	0	38 (21)
2014	0	30 (17)
2015	0	37 (21)
2016	3 (2)	24 (13)
2017	3 (2)	18 (10)
2018	136 (96)	2 (1)
Disease status at CT		
CR	14 (10)	82 (46)
PR	67 (47)	81 (45)
Resistant	18 (13)	14 (8)
Missing	43 (30)	2 (1)
Prior lines of treatment		
No	30 (21)	2 (1)
Yes	88 (62)	177 (99)
Missing	24 (17)	0
N of prior lines of treatment		
No treatment	30 (21)	2 (1)
1	13 (9)	22 (12)
2	19 (13)	82 (46)
3	18 (13)	51 (28)
4+	38 (27)	22 (12)
Missing	24 (17)	0
Clinical trial		
No	126 (89)	0
Yes	16 (11)	0
Missing	0	179
Median follow-up of survivors (range), months	4 (1-7)	36 (4-99)