Not for publication or presentation

2021 STATUS REPORT
INFECTION AND IMMUNE RECONSTITUTION WORKING COMMITTEE

Working Committee Leadership	
Co-Chair:	Miguel-Angel Perales; Memorial Sloan Kettering Cancer Center; peralesm@mskcc.org
Co-Chair:	Roy Chemaly; M.D. Anderson Cancer Center; rfchemaly@mdanderson.org
Co-Chair:	Christopher Dandoy; Cincinnati Children's Hospital Medical Center; christopher.dandoy@cchmc.org
Scientific Director:	Marcie Riches; University of North Carolina at Chapel Hill; marcie_riches@med.unc.edu
Statistical Director:	Soyoung Kim; CIBMTR Statistical Center; skim@mcw.edu
Statistician:	Naya He; CIBMTR Statistical Center; nhe@mcw.edu

INTRODUCTION

a. Minutes and overview plan from 2020 TCT meeting (Attachment 1)

PROPOSALS MOVING FORWARD FOR SCORING (click here to cast your score)

a. PROP 2010-159 Evaluating time from diagnosis to transplant as an important contributor for post-allogeneic stem cell transplant infections and infection/delayed immune reconstitution associated mortality/morbidity (Lohith Gowda/ Celalettin Ustun/ Marcos de Lima/ Jaap Boelens). (Attachment 2)

PROPOSALS DROPPED BECAUSE THEY OVERLAP WITH EXISTING STUDIES OR ARE NOT FEASIBLE DUE TO LIMITATIONS OF AVAILABLE PATIENTS OR DATA

a. PROP 2009-16 Outcomes of and toxicities after allogeneic and autologous hematopoietic cell transplantation and CAR T cells in patients who had COVID-19 pre cellular therapy (Gunjan L Shah/ Loannis Politikos/ Miguel-Angel Perales). *Overlap CV20-04.*

b. PROP 2009-17 Impact of COVID-19 in patients with aggressive B cell lymphoma and acute lymphoblastic leukemia treated with CD19 CAR T cell therapy (Nishi Shah/ Gunjan L Shah/ Miguel-Angel Perales). *Overlap CV20-04.*

c. PROP 2010-102 The impact of Covid19 on outcomes in patients undergoing chimeric antigen receptor T-cell therapy in patients with B-cell acute lymphoblastic leukemia and diffuse large B-cell lymphoma (Nasheed M. Hossain/ Patrick J. Stiff). *Overlap CV20-04.*

d. PROP 2010-105 Impact of donor stem cell graft composition on immune reconstitution in allogeneic hematopoietic cell transplantation (Hemant Murthy/ Nosha Farhadfar). *Consider adding sub-analysis to IN19-01.*

e. PROP 2010-107 Outcomes of HIV+ patients undergoing autologous HCT for multiple myeloma (Hemant Murthy/ Ricardo Parrondo/ Mohamed A. Kharfan-Dabaja). *Insufficient patients.*

f. PROP 2010-111 Infection related outcomes in allogeneic stem cell transplantation, what has changed in the past decade? A BMT CTN/ CIBMTR study (Hemant Murthy/ Zainab Shahid/ Jo-Anne Young).

g. PROP 2010-116 Skin and soft tissue infections in allogeneic hematopoietic cell transplantation recipients with and without acute and chronic graft versus host disease (Emily Lynde Baumrin/ Loren Wakoff Alison/ Rosenbach Misha). *Insufficiently granular data.*

h. PROP 2010-122 Determinants of the humoral immune response to neoantigens in alloHSCT recipients undergoing HBV vaccination (Myung Sun Kim/ Inhye Ahn). *Vaccination data not collected.*

i. PROP 2010-155 Determinants of hypogammaglobulinemia and impact of intravenous immune globulin replacement in patients receiving chimeric antigen T-cell receptor therapy (Ameet Patel/ Olalekan Oluwole/ Bhagirathbhai Dholaria). *Overlap IN20-01.*

j. PROP 2010-19 Incidence of hypogammaglobulinemia following CD-19 directed CAR T-cell therapy and its impact on outcomes (Muhammad Bilal Abid). *Overlap IN20-01.*

k. PROP 2010-201 Viral complications after post-transplantation cyclophosphamide based haploidentical stem cell transplantation: BM vs PB (Shatha Farhan). *Overlap IN17-01.*

l. PROP 2010-209 Letermovir prophylaxis in patients with allogeneic SCT starting before or after day +14 (Shatha Farhan). *Insufficient data for Letermovir based upon how data are collected.*

m. PROP 2010-21 Posttransplant cyclophosphamide and infection risk according to the donor types (Merve Pamukcuoglu). *Overlap IN17-01 and IN18-01.*

n. PROP 2010-220 Outcomes of hematopoietic cell transplantation (HCT) recipients acquiring COVID-19 infection within six months of HCT compared with a propensity score matched controls without COVID-19 infection (Guru Subramanian Guru Murthy/ Mehdi Hamadani). *Overlap CV20-04.*

o. PROP 2010-228 Impact of fluoroquinolone vs. beta-lactam antibiotic prophylaxis on pseudomonas aeruginosa bloodstream infection in allogeneic hematopoietic cell transplant recipients (Hannah N. Imlay/ Sagar S. Patel). *Overlap IN19-02.*

p. PROP 2010-230 Risk factors for breakthrough CMV viremia despite letermovir prophylaxis among allogeneic hematopoietic cell transplant recipients (Hannah N. Imlay/ Sarar S. Patel). *Insufficient data for Letermovir based upon how data are collected.*

q. PROP 2010-235 Impact of personal protective equipment, universal masking, and physical distancing on community respiratory viral infections in transplant and cellular therapy patients (Sagar S. Patel/ Hannah N. Imlay/ Daniel R. Couriel). *Requires supplemental data collection.*

r. PROP 2010-241 Infectious complications and outcomes of HIV-infected allogenic hematopoietic cell transplant recipients (Jana Kubrin Dickter/ Randy Allison Taplitz/ Sanjeet Singh Dadwal/ Joseph C. Alvarnas). *Insufficient patients.*

s. PROP 2010-88 Outcomes and safety of hematopoietic stem cell transplants from HTLV positive donors and HTLV positive recipients (Murali Janakiram/ Grigori Okov/ R. Alejandro Sica/ Astha Thakkar). *Overlap with an ASH 2020 presentation.*

t. PROP 2010-99 Clinical outcomes in acute leukemia patients with co-existing diagnosis of human immunodeficiency virus (HIV) after allogeneic hematopoietic cell transplantation (Allo-HCT) (Talha Badar/ Hemant Murthy/ Mohamed Kharfan Dabaja). *Insufficient patients.*

Two proposals addressing COVID-19 were submitted in March 2020. Due to the clinical importance and the CIBMTR response to COVID-19, these proposals merged [CV20-04] and proceeded. An initial analysis was completed and accepted in Lancet Haematology. A subsequent analysis will be circulated for review and comment. If possible, questions of interest in the above proposals will be incorporated and the proponents included in the writing committee.

PROPOSALS NOT ACCEPTED FOR CONSIDERATION AT THIS TIME DUE TO RELATIVE SCIENTIFIC IMPACT COMPARED TO ONGOING STUDIES AND/OR OTHER PROPOSALS

a. PROP 2009-02 Invasive fungal infections after autologous hematopoietic stem cell transplantation for the treatment of lymphoma and solid tumors (Jane Yoon Koo/ Christopher Eugene Dandoy).

b. PROP 2010-205 Posaconazole vs. voriconazole prophylaxis in patients with allogeneic SCT (Shatha Farhan).

c. PROP 2010-207 Antifungal prophylaxis after hematopoietic stem cell transplantation in children (Sarah M. Heston/ Matthew S. Kelly/ Kristin M. Page).

d. PROP 2010-22 Incidence and impact of late infectious complications (viral, bacterial, fungal) on outcomes between haploHCT recipients receiving PTCy-based versus other GVHD prophylaxis (Muhammad Bilal Abid).

e. PROP 2010-322 Impact of primary fungal prophylaxis choice on invasive mold Infection in patients undergoing allogeneic hematopoietic stem cell transplantation without graft versus host (Zeinab El Boghdadly/ Aliyah Baluch).

f. PROP 2010-71 Retrospective study of the impact of mammalian target of rapamycin inhibitors (mTORi) in the incidence of herpesvirus-associated complications after allogeneic hematopoietic cell transplantation (HCT) (Kamil Rechache/ Jennifer Kanakry).

Due to the virtual nature of the 2021 Transplant and Cell Therapy (TCT) Meetings, the CIBMTR leadership changed the Working Committee process for this year. The details were sent previously in a broadcast email to WC members. In summary, each WC could select a maximum of 2 proposals to put forward for voting and only 10 – 15 proposals total from all WC will be presented with only 5 – 10 accepted for this coming year. Within the INWC, we received 27 proposals in addition to a COVID proposal received in March 2020 that was approved and work ongoing. Consequently, we had a very difficult time selecting and several excellent proposals cannot move forward this year.

STUDIES IN PROGRESS

a. **IN17-01b** Incidence and impact of non-cytomegalovirus herpes viral infection in haploidentical and matched sibling donors receiving post-transplant cyclophosphamide: A CIBMTR analysis. Status: Manuscript Preparation. Goal for June 2021: Submitted.

b. **IN18-01** Comparison of early (by day+100) infections between post transplantation cyclophosphamide and other graft-vs-host disease prophylaxis. Status: This study is under analysis. Goal for June 2021: Manuscript Preparation.

c. **IN18-02** Study the incidence, and impact of C difficile infection within 100 days on transplant outcomes after allogeneic stem cell transplant. Status: This study is under analysis. Goal for June 2021: Manuscript Preparation.

d. **IN19-01** Immune recovery predicts post-transplant outcomes. Status: Protocol Development. Goal for June 2021: Analysis.

e. **IN19-02** Impact of antibacterial prophylaxis on outcomes after allogeneic hematopoietic stem cell transplant. Status: Protocol Development. Goal for June 2021: Present the protocol at CIBMTR stats meeting and start preparing the dataset.

f. **IN20-01** Infectious complications in patients with B-Lymphoid hematologic malignancy treated with CD19 chimeric antigen receptor T cell therapy. Status: Protocol Development. Goal for June 2021: Present the protocol at CIBMTR stats meeting and start preparing the dataset.

PUBLICATIONS, SUBMITTED PAPERS, PRESENTATIONS

a. **IN16-02** Dandoy CE, Kim S, Chen M, Ahn K-W, Ardura MI, Brown V, Chhabra S, Diaz MA, Dvorak C, Farhadfar N, Flagg A, Ganguly S, Hale GA, Hashmi SK, Hematti P, Martino R, Nishihori T, Nusrat R, Olsson RF, Rotz SJ, Sung AD, Perales M-A, Lindemans CA, Komanduri KV, Riches ML. Incidence, risk factors, and outcomes of patients who develop mucosal barrier injury-laboratory confirmed bloodstream infections in the first 100 days after allogeneic hematopoietic stem cell transplant. JAMA Network Open. 2020 Jan 3; 3(1):e1918668. doi:10.1001/jamanetworkopen.2019.18668. Epub 2020 Jan 8. PMC6991246.

b. **CV20-04** Sharma A[*], Bhatt NS[*], St. Martin A, Abid MB, Bloomquist J, Chemaly RF, Dandoy CE, Gauthier, Gowda L, Perales MA, Seropian S, Shaw BE, Tuschi EE, Zeidan AM, Riches ML[†], Shah GL[†]. Clinical Characteristics and Outcomes of COVID-19 in Hematopoietic Cell Transplant Recipients: A Cohort Study. Lancet Haematology (*in press).* Oral Abstract, TCT 2020, Best Abstracts Session.

c. **IN17-01a** Incidence and impact of cytomegalovirus infection in haploidentical and matched-related donors receiving post-transplant cyclophosphamide: A CIBMTR analysis. *Submitted.*

d. **IN17-01c** Incidence and impact of community respiratory viral infection in haploidentical and matched sibling donors receiving post-transplant cyclophosphamide: A CIBMTR analysis. *Submitted.*

e. **CV20-04** COVID-19 in Hematopoietic Cell Transplant Recipients: A CIBMTR Study. *Oral presentation at the TCT 2021 Annual Meeting.*

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A G E N D A
CIBMTR WORKING COMMITTEE FOR INFECTION AND IMMUNE RECONSTITUTION
Orlando, FL
Saturday, February 22, 2020, 12:15 – 2:15 PM

Co-Chair:	**Krishna Komanduri, MD, University of Miami; Miami, FL;** **Telephone: 305-243-5302; E-mail: kkomanduri@med.miami.edu;**
Co-Chair:	**Miguel-Angel Perales, MD, Memorial Sloan Kettering Cancer Center, New York, NY;** **Telephone: 212-639-8682; E-mail: peralesm@mskcc.org;**
Co-Chair:	**Roy Chemaly, MD, UT MD Anderson Cancer Center, Houston, TX;** **Telephone: 713-792-0007; E-mail: rfchemaly@mdanderson.org;**
Scientific Director:	**Marcie Riches, MD, MS, The University of North Carolina at Chapel Hill, Chapel Hill, NC;** **Telephone: 919-966-3048; E-mail: marcie_riches@med.unc.edu**
Statistical Directors:	**Soyoung Kim, PhD, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-955-8271; E-mail: skim@mcw.edu**
Statistician:	**Naya He, MS, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-805-0685; E-mail: nhe@mcw.edu**

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1. **Introduction**
   a. Welcome and introduction

   Dr. Miguel-Angel Perales moderated the introduction of the working committee followed by which all the attending co-chairs and the statisticians were introduced. He welcomed Dr. Christopher Dandoy, M.D. Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio as the new chair for INWC starting March 1st, 2020, and thanked Dr. Krishna Komanduri for his excellent service to the INWC in the past 5 years.

   The expectations of the meeting are to review the status of ongoing studies and timelines, and for members to assess and select proposals that will have a high impact on the field. Each proposal presentation was limited to 5 minutes to allow 10 minutes for adequate discussion. The working committee members were asked to vote on a level of scientific impact score, 1 is the highest impact and 9 is the lowest impact score for the new proposals based on the feasibility and impact to the transplant community. Due to limited statistical hours and on-going work in the INWC, one proposal will be accepted this year. The studies that are closest to submission will receive highest priority.

   Dr. Perales reviewed that the working committee's membership is open to any individual willing to take an active role in study development and completion. He emphasized the rules of authorship which define the for an individual to be an author, the individual should engage and commit to substantial contributions to study concept, analysis, data interpretation, and manuscript preparation for the life cycle of the study. These include:

   1. Revising the study draft critically for important intellectual content
   2. Critical review of the analysis and data interpretation
   3. Final approval of the manuscript to be published

4. Agreement to be accountable for all aspects of the project in ensuring that questions related to the accuracy of any part of the study.

The number of authors could be limited by the journal.

He reminded the working committee members that the infection data are collected only on CRF level forms and also reviewed the sources of cellular therapy data.

c. Minutes and Overview Plan from February 2019 meeting
The minutes and overview plan from the 2019 Tandem meeting were reviewed and approved by committee members.

2. Accrual summary

Due to the full agenda, the accrual summary of registration and research cases between 1995 and 2019 were not presented to the committee but were available as part of the Working Committee attachments. The working committee was notified of this attachment

3. Studies published/submitted/Preliminary results

Dr. Miguel-Angel Perales noted 3 papers have been published this year from INWC and 3 draft manuscripts are under preparation.

a. **IN13-01** Ustun C, Kim S, Chen M, Beitinjaneh AM, Brown VI, Dahi PB, Daly A, Diaz MA, Freytes CO, Ganguly S, Hashmi S, Hildebrandt GC, Lazarus HM, Nishihori T, Olsson RF, Page KM, Papanicolaou G, Saad A, Seo S, William BM, Wingard JR, Wirk B, Yared JA, Perales M-A, Auletta JJ, Komanduri KV, Lindemans CA, Riches ML. **Increased overall and bacterial infections following myeloablative allogeneic HCT for patients with AML in CR1.**
Blood Advances 3(17):2525-2536, 2019. **Published.**

b. **IN14-01** Naik S, Riches M, Soyoung K, Chen M, Bachier C, Shaughnessy P, Hill J, Ljungman P, Battiwalla M, Chhabra S, Daly A, Storek J, Ustun C, Diaz MA, Cerny J, Beitinjaneh A, Yared J, Brown V, Page K, Dahi PB, Ganguly S, Seo S, Chao N, Freytes CO, Saad A, Savani BN, Ahn KW, Boeckh M, Heslop HE, Lazarus HM, Auletta JJ, Kamble RT. **Survival Outcomes of Allogeneic Hematopoietic Cell Transplants with EBV positive or EBV negative Post Transplant Lymphoproliferative Disorder (PTLD), A CIBMTR Study.Submitted.** *Transpl Infect Dis. 2019 Oct;21(5):e13145. doi: 10.1111/tid.13145. Epub 2019 Jul 31.* **Published.**

c. **IN16-02** Christopher E. Dandoy, MD, MS; Soyoung Kim, PhD; Min Chen, MS; Kwang Woo Ahn, PhD; Monica I. Ardura, DO, MSCS; Valerie Brown, MD, PhD; Saurabh Chhabra, MD; Miguel Angel Diaz, MD, PhD; Christopher Dvorak, MD; Nosha Farhadfar, MD; Aron Flagg, MD; Siddartha Ganguly, MD; Gregory A. Hale, MD; Shahrukh K. Hashmi, MD; Peiman Hematti, MD; Rodrigo Martino, MD; Taiga Nishihori, MD; Roomi Nusrat, MD; Richard F. Olsson, MD; Seth J. Rotz, MD; Anthony D. Sung, MD; Miguel-Angel Perales, MD; Caroline A. Lindemans, MD, PhD; Krishna V. Komanduri, MD; Marcie L. Riches, MD, MS. **Incidence, Risk Factors, and Outcomes of Patients Who Develop Mucosal Barrier Injury–Laboratory Confirmed Bloodstream Infections in the First 100 Days After Allogeneic Hematopoietic Stem Cell Transplant,** *JAMA Netw Open. 2020;3(1):e1918668. doi:10.1001/jamanetworkopen.2019.18668.* **Published.**

d. **IN17-01 (a)** Incidence and Impact of Cytomegalovirus Infection in Haploidentical and Matched-Related Donors Receiving Post-Transplant Cyclophosphamide (PTCy): A CIBMTR Analysis (S Goldsmith/E Fuchs/A Bashey/S Ciurea/A Singh/ S Ganguly/R Taplitz/C Mulroney/R Maziarz/ R Romee) **2020 TCT Abstract (Oral); Manuscript preparation**

e. **IN17-01 (b)** Incidence and impact of Non-CMV herpes viral infection in Haploidentical and Matched Sibling Donors receiving Post-transplant Cyclophosphamide (PTCy): A CIBMTR Analysis. (A Singh/E Fuchs/A Bashey/S Ciurea/S Goldsmith/S Ganguly/Randy A Taplitz/C Mulroney/R Maziarz/R Romee)**2020 TCT Abstract (Poster); Manuscript preparation**

f. **IN17-01 (c)** Incidence and Impact of Community Respiratory Viral Infection (CRV) in Haploidentical and Matched Sibling Donors receiving post-transplant Cyclophosphamide (PTCy): A CIBMTR analysis (R Taplitz/R Maziarz/C Mulroney/R Romee, S Goldsmith/E Fuchs/A Bashey/S Ciurea/A Singh/S Ganguly) **2020 TCT Abstract (Oral); Manuscript preparation**

4. Studies in progress

Dr. Krishna Komanduri introduced the ongoing studies.

a. **IN18-01** Comparison of early (by day 100) infections after haploidentical HSCT between patients receiving cyclophosphamide-based or other GVHD prophylaxis (Celalettin Ustun/Genovefa Papanicolaou) **Data file preparation**

Dr. Marcie Riches updated the study.

Allogeneic hematopoietic cell transplant (HCT) outcomes differ between fully matched related donor transplants (MRD) and Haploidentical (HaploHCT) transplant with further differences associated with the use of post-transplant cyclophosphamide (PTCy). The study aims are: Determine the incidence and infection density of bacterial infections and fungal infections occurring within 100 days after HCT; Assess the impact of bacterial and fungal infections by day 100 on 1 year transplant outcomes(relapse, non-relapse mortality (NRM), disease free survival (DFS), overall Survival (OS) and Chronic GVHD). The committee was reminded that this will utilize the same dataset as IN 1701.

The study is going to be presented at the CIBMTR statistical meeting soon.

There is no comment/question from the audience.

b. **IN18-02** The Incidence, and impact of Clostridium difficile infection within 100 days on Transplant outcomes after allogeneic stem cell transplant (Muthalagu Ramanathan/ Bipin Savani/ Celalettin Ustun) **Data file preparation**

Dr. Muthalagu Ramanathan updated the study.

The study aims are: Determine Incidence of CDI (Clostridium Difficile infection) following Allogeneic HCT; Determine Impact of CDI on transplant outcomes (Acute GVHD, Chronic GVHD, TRM, Overall Survival); Identify pre-transplant risk factors for development of CDI after allogeneic HCT.

Eligible population: All patients age 2 years and older receiving first allogeneic HCT for AML, ALL, or MDS in 2013 to 2018. Fully HLA matched 8/8 related or unrelated donor. Cases will be patients reported with CDI by day 100 and controls will be all patients from the same centers with cases. There are (826+77) cases and 6725 controls identified in 127 transplant Centers. 77 cases were identified pre HCT: during conditioning day -7 to -1. Patient, donor and disease related characteristics seem comparable between cases and controls. Transplant related characteristics seem comparable in terms of time to transplant, HLA matching, GVHD prophylaxis, year of transplant, systemic antibacterial use etc.

Dr. Ramanathan pointed out the limitations of the study: Prophylactic antibiotic use is not captured in CIBMTR database prior to March 2017; CIBMTR does not capture any diagnostic information for CDI, hence all data is based on Center's reporting; Not all CDI causes clinical symptoms and definition of CDI is center specific; Above center specific effects has been partially

overcome by using controls from only centers that have cases; History of CDI prior to HCT, severity of CDI or the treatment that was given is not captured in the CIBMTR database.
The study has been sent to Infection Working Committee for comments. The study will be revised and analyzed based on the comments.
Comments: report # of patients with recurrent CDI

c. **IN19-01** Immune recovery predicts post-transplant outcomes (Miguel-Angel Perales/ Paul Szabolcs) **Protocol development**
Dr. Miguel-Angel Perales updated this study.
The study aims are: Assess transplant outcomes in adult and pediatric patients who undergo allo-HCT based on day 100 CD4 count (Survival, GVHD, Relapse/progression, Infections);
Assess transplant outcomes in adult and pediatric patients who undergo allo-HCT based on day 180 immune recovery of CD4 count and attaining IgA levels within normal range. (Survival, GVHD, Relapse/progression, Infections); Descriptive analysis of immune recovery post HCT including T, B and NK cells, as well as Ig levels; Risk factors for poor immune recovery by day 100.
Dr. Perales mentioned, this is the first multicenter immune reconstitution study at the CIBMTR. It is largest dataset to date. This study will confirm and expand single center studies results.
Dr. Marcie Riches mentioned all of the 2236 eligible patients in this study have immune reconstitution data at day100 and day180. This study will be presented at the CIBMTR statistical meeting soon.

d. **IN19-02** Impact of Antibiotic Prophylaxis in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation in the Current Era (Zeinab El Boghdadly/ Christopher Eugene Dandoy/ Priscila Badia Alonso) **Protocol development**
Dr. Zeinab El Boghdadly presented this study.
The study objectives are: Compare clinical outcomes between patients (adults and pediatrics) undergoing first allo-HSCT who received and did not receive pre-engraftment antibiotic prophylaxis. The primary outcomes are: Incidence of pre-engraftment blood stream infections (BSIs); Incidence of acute GVHD II-IV; OS and NRM by day100 and 1 year. The secondary outcomes are: Acute lower GI GVHD III-IV by day100; Infection episodes (BSIs, CDI, septic shock, fungal, viral) by day100; Cause of Death (infection vs non-infectious).
The study will be presented in the CIBMTR statistical meeting in about 2 months.
One suggestion from the audience is to have a separate analysis for the pediatric population.

5. Future/proposed studies

Dr. Roy Chemaly moderated the future/proposed studies.

a. **PROP 1911-49** Risk for early post-transplant bacterial, viral and fungal infection in Hodgkin's lymphoma patients that receive pre-transplant therapy with checkpoint inhibitors (M McGhee/ D P. Melendez/ J Holter-Chakrabarty/ S K. Vesely)
Dr. Miranda McGhee presented the proposal. The scientific justification of the study are Infections and infectious complications cause significant morbidity and mortality in patients undergoing HCT. No study has been performed studying the effect that check-point inhibitors (CPIs) have on the risk of infectious complications in patients with Hodgkin lymphoma who are undergoing HCT. One study suggest a 13.5% infection risk when managing Immune related adverse events (IRAEs) and a 2% infection risk with CPIs independent of the management of IRAEs. ; There are no data to investigate the need for antimicrobial prophylaxis when using CPIs or managing associated IRAEs. The hypothesis of the proposal is those who received CPIs prior to HCT are higher risk for infection and have worse outcomes including disease-free survival and mortality. The primary Aims are to

compare the occurrence of bacterial, viral and fungal infection in patients with HL that received CPI prior to HCT compared to those that did not receive CPI prior to HCT. The secondary aims are to identify risk factors besides prior CPI use for development of infection in patients that undergo HCT;

Compare outcomes between those who did and did not receive CPI in each group. The study population is all patients that received HCT (both allogeneic and autologous) for the treatment of HL and were reported to CIBMTR from 2013 to 2019.

Suggestions from the committee are:

- Select patients from 2008 to increase the population
- Limit to allogeneic HCT due to the small number of cases in auto population
- Look "other specified field" to find more cases
- The statistical designed will be refined by the statistical center at the CIBMTR if the proposal going forward. One suggestion was to consider matched control design versus a case-cohort design
- Dr. Perales noted that a study examining transplant outcomes for HL patients with prior CPI use was presented in the Lymphoma WC with plans to collaborate with EBMT.

b. **PROP 1911-90** Changing epidemiology and outcomes of invasive candida infections in the current era of stem cell transplantation (J S. Green/ C Ustun)

Dr. Jaime Green presented this proposal.

The specific aims are: Characterize the epidemiology of breakthrough yeast infections in the modern era of antifungal prophylaxisexamining Candida spp and other less common yeasts; timing after transplant (early, before neutrophil engraftment; late onset, after neutrophil engraftment); Identification of risk factors for breakthrough invasive yeast infections (Expanded SCT platforms, donor sources); Mortality impact and incidence of Candida albicans versus Candida non-albicans spp.

The hypothesis of the proposal are: Incidence of Non-albicans candida and other breakthrough yeast infections has been increasing with fluconazole prophylaxis; Non-albicans candida and other breakthrough yeast infections have a higher mortality compared to C. albicans infections;
Early invasive Candida (IC) (before neutrophil engraftment) has a higher mortality compared to late IC (after neutrophil engraftment).

Dr. Marcie Riches mentioned the infections listed in the table are not mutually exclusive. The collection of infection prophylaxis prior to 2017 is a limitation.

c. **PROP 1911-197** Evaluating time from diagnosis to transplant as an important contributor for post-allogeneic stem cell transplant infections and infection/delayed immune reconstitution associated mortality/morbidity (L Gowda/ C Ustin/ M de Lima/ J Boelens)

Dr. Lohith Gowda presented this proposal.

The Scientific rationale of this proposal are that Chemo or RT peri-transplant affects thymic output (lymphomagenesis). A delay in transplant generally leads to more treatment to maintain remission. ; Post-transplant T cell quantitative deficiency linked with increased infections, relapse and second malignancy. Conversely,prior studies demonstrate that early T cell recovery is assoiciated with better PFS, OS and prevention of CMV reactivation. Therefore, protecting the thymus, minimizing infections, and expediting immune-reconstitution by better understanding associated risk factors is an unmet need.

The hypothesis is that thetime (delay) to transplant from diagnosis is an important contributor for post-transplant infections, delayed immune-reconstitution and contributes to non-relapse mortality (NRM).
The aims are: To describe incidence and patterns of post-transplant infections at different timepoints based on time from diagnosis to transplant; To explore association between infectious complications and clinical outcomes based on timeline; To longitudinally evaluate T cell recovery (including CD4/CD8 ratio) and quantitative immunoglobulin levels post-transplant based on time to transplant from the time of diagnosis.
The outcomes are: Relate early and late infections (bacterial, viral and fungal) to the time to transplant and donor source. (stratified for CR status); Relate T cell lymphocyte absolute numbers and CD4/CD8 ratio at days +100 and +180 to donor source; Infection specific survival and Infectious mortality/morbidity (OS, EFS, GVHD and GRFS based on donor/graft source); Evaluate quantitative immunoglobulin levels at D+ 100 and +180.
The working committee noted that many factors affect the time to HCT, may not be representative of the treatment but could reflect disease risk such that higher risk may move to HCT more quickly or relative disease refractoriness may result in longer time due to requirement for additional treatments. There are also other confounders such as the conditioning intensity used or development of GVHD post-transplant impact infections and immune recovery.
Dr. Miguel-Angel Perales suggested to use IN1901 dataset to improve the efficiency.
Dr. Marcie Riches suggested to limit the population to CR1.

d. **PROP 1911-34** Infectious disease patterns, clinical impacts and treatment in aggressive B cell non-Hodgkin lymphoma and precursor B acute lymphoblastic leukemia patients treated with CD19 CAR T cell therapy (K Wudhikarn/ M-A Perales)
PROP 1911-50 Impact of early infection in chimeric antigen receptor T cell therapy outcomes in the first 100 days post-therapy (M McGhee/ D P. Melendez/ J Holter-Chakrabarty/ S K. Vesely)
PROP 1911-76 Infectious complications after CAR-T cell immunotherapy in patients with B-cell malignancies (J Maalouf/ J A. Hill/ C J. Turtle)
PROP 1911-155 Infections after CD19-targeted chimeric antigen receptor–modified T-cell therapy for non-Hodgkin lymphoma(M Herr/ T Hahn)
PROP 1911-158 Observational study of infectious complications among patients treated with anti-CD19 chimeric antigen receptor T cells (H Rangarajan/ P Satwani)
PROP 1911-209 Infectious complications and immune reconstitution following CD19-directed CAR-T cell therapy (J H. Baird/ S Sidana/ J Y. Spiegel/ D Epstein/ D B. Miklos)
PROP 1911-235 The role of intravenous immune globulins in patients after CAR-T therapy (E McGehee/ A Kansagra/ P Ramakrishnan/ F Awan)
PROP 1911-254 Patterns of infections post CD 19 directed CAR-T cells infusions (L Gowda)
PROP 1911-266 Risk factors for clinically significant infections following CD-19 CD19-targeted CAR-T cells therapy for hematological malignancies (A C Cordeiro/ G Fatobene/ M Bar/ V Rocha)

Dr. Miguel-Angel Perales presented this combined proposal.

Background/hypothesis: Infections after CD19 CAR T cells are common but vary based on time after CAR T cell therapy. Infections after CD19 CAR T cells may be mild and not associated with inferior survival outcomes. Antimicrobial prophylaxis and IVIG replacement may provide benefit on infection prevention in patients treated with CD19 CAR T cells

The proposal aims: To report incidence of infection stratified by pathogens & time after CAR T cell therapy; To explore association between infection & outcomes in patients treated with CAR T cells; To describe benefit of antimicrobial prophylaxis & IVIG on infectious complications in patients treated with CAR T cells.

Patients population is B-ALL and B-NHL with commercial CD19 CAR T cell. Patients receiving immunotherapy to augment CAR T action, or clinical Trial CAR T cell or Primary CNS lymphoma patients will be excluded.

Dr. Perales also pointed out the potential issuers: No infection prophylaxis data are available; No pre-treatment IDMs and No info on baseline infection (unless cell therapy given for an infection); IVIG – No IgG levels in cellular therapy registry but instructions to report if <600 (<500 for peds); No Immunoglobulin levels on 4100 form; All infections reported on 4100 form just as reported on CIBMTR 2100 form; Info re: GM-CSF on 4006 form (no G-CSF except other specify); No lymphocyte subset analyses on f/u forms.

Comments/suggestions:

- Plan for two analyses: ALL and NHL. This is due to the variability in prior treatments as well as very different age groups.
- If a patient had a HCT before a CAR T, we may have baseline infection data including IDMs
- It is a hot topic and could be a rapid publication
- The authorship for this paper follows the same CIBMTR rule of authorship. Because this is a merged protocol with 27 proponents, the goal will be to provide junior investigators as the PIs.
- The CIDR steering committee and the Chairs of the Cellular Therapy Working Committee must be involved in this study.

Dropped proposed studies

Dr. Marcie Riches explained the reasons for dropping proposals.

a. **PROP 1907-02** The effect of antibacterial prophylaxis on early post-transplant mortality in patients with multiple myeloma and lymphoma undergoing high-dose chemotherapy and autologous hematopoietic cell transplantation: A retrospective study on behalf of the infection and immune reconstitution working committee. *Dropped due to small sample size.*
b. **PROP 1911-86** Impact of Letermovir on rates of CMV reactivation and transplant outcomes. *Dropped due to supplemental /additional data needed.*
c. **PROP 1911-109** The impact of CMV serostatus on outcomes after haploidentical stem cell transplant. *Dropped due to overlap with current study/publication.*
d. **PROP 1911-226** Outcomes of allogeneic hematopoietic cell transplant recipients with serious viral infections including EBV, CMV, HHV6, BK and adenovirus post haploidentical transplants compared to cord transplants and matched donor allogeneic hematopoietic cell transplants (allo HCT). *Dropped due to low scientific impact.*

6. **Other Business**

Dr. Marcie Riches moderated this section:

- There is an immune recovery data collection issue with significant missing data
- Reminded the working committee that if a patient never had a HCT, we would not have infection information before a cellular therapy
- Encourage PIs to submit ideas for proposals early to the Scientific Director and/or Chairs to allow a pre-assessment of feasibility as well as to facilitate strengthening of the proposal.
- The INWC is working on the Dynamic Landmark analysis paper.
- Encouraged audience to attend 2 oral presentations and 1 poster presentation of study IN1701 on Sunday.

Working Committee Overview Plan for 2020-2021							
Study number and title	**Current status**	**Goal with date**	**Total hours to complete**	**Total hours to goal**	**Hours allocated to 06/30/20**	**Hours allocated 7/1/2020-6/30/2021**	**Total Hours allocated**
IN 17-01(a): Incidence and Impact of Cytomegalovirus Infection in Haploidentical and Matched-Related Donors Receiving Post-Transplant Cyclophosphamide (PTCy): A CIBMTR Analysis	Manuscript Preparation	Published– June 2021	50	**60**	50	10	**60**
IN17-01(b): Incidence and impact of Non-CMV herpes viral infection in Haploidentical and Matched Sibling Donors receiving Post-transplant Cyclophosphamide (PTCy): A CIBMTR Analysis.	Manuscript Preparation	Published - June 2021	50	**60**	50	10	**60**
IN17-01(c): Incidence and Impact of Community Respiratory Viral Infection (CRV) in Haploidentical and Matched Sibling Donors receiving post-transplant Cyclophosphamide (PTCy): A CIBMTR analysis	Manuscript Preparation	Published - June 2021	50	**60**	50	10	**60**
IN18-01: Comparison of Early (d100) Infections after Haplo HCT between patients receiving Cy-based vs other GVHD prophylaxis	Data file Preparation	Submitted June 2021	170	**170**	100	70	**170**
IN18-02: Study the Incidence, and impact of C diff infection within 100 days on Transplant outcomes after allogeneic stem cell transplant	Protocol development	Submitted- June 2021	250	**250**	180	70	**250**
IN19-01: Immune recovery predicts post-transplant outcomes	Protocol development	Manuscript Preparation- June 2021	280	**210**	50	160	**210**
IN19-02: Impact of antibacterial prophylaxis on outcomes after allogeneic hematopoietic stem cell transplant	Protocol development	Data file Preparation- June 2021	280	**50**	50	0	**50**
IN20-01: Infectious complications after CAR.T Cell therapy	Protocol Pending	Manuscript Preparation- June 2021	330	**260**	0	260	**260**

Work Assignments for Working Committee Leadership (March 2020)	
Krishna Komanduri	**IN17-01(a):** Incidence and Impact of Cytomegalovirus Infection in Haploidentical and Matched-Related Donors Receiving Post-Transplant Cyclophosphamide (PTCy): A CIBMTR Analysis (S Goldsmith/E Fuchs/A Bashey/S Ciurea/A Singh/ S Ganguly/R Taplitz/C Mulroney/R Maziarz/ R) (PROP 1611-02/1611-117/1611-134) **IN17-01(b):** Incidence and impact of Non-CMV herpes viral infection in Haploidentical and Matched Sibling Donors receiving Post-transplant Cyclophosphamide (PTCy): A CIBMTR Analysis. (A Singh/E Fuchs/A Bashey/S Ciurea/S Goldsmith/S Ganguly/Randy A Taplitz/C)(PROP 1611-02/1611-117/1611-134) **IN17-01(c):** Incidence and Impact of Community Respiratory Viral Infection (CRV) in Haploidentical and Matched Sibling Donors receiving post-transplant Cyclophosphamide (PTCy): A CIBMTR analysis (R Taplitz/R Maziarz/C Mulroney/R Romee, S Goldsmith/E Fuchs/A Bashey/S Ciurea/A Singh/S Ganguly) (PROP 1611-02/1611-117/1611-134)
Miguel-Angel Perales	**IN18-01:** Comparison of Early (d100) Infections after Haplo HCT between patients receiving Cy-based vs other GVHD prophylaxis (Genovefa Papanicolaou/Celalettin Ustun) **IN19-01:** Immune recovery predicts post-transplant outcomes (Miguel-Angel Perales) **IN20-01:** Infectious complications after CAR.T Cell therapy (TBD)
Roy Chemaly	**IN18-02:** Study the Incidence, and impact of C diff infection within 100 days on Transplant outcomes after allogeneic stem cell transplant (Muthalagu Ramanathan/ Bipin Savani)
Chris Dandoy	**IN19-02:** Impact of antibacterial prophylaxis on outcomes after allogeneic hematopoietic stem cell transplant (C Dandoy/ P Alonso/ Z El Boghdadly)

Proposal: 2010-159

Title:
Evaluating time from diagnosis to transplant as an important contributor for post-allogeneic stem cell transplant infections and infection/delayed immune reconstitution associated mortality/morbidity.

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Hypothesis:
We hypothesize that delay in transplant (or time to transplant) from the time of diagnosis is an important contributor for post-transplant infections and delayed immune reconstitution, which contributes to non-relapse mortality (NRM).

Aims:
- Identify density and types of early and late infections (bacterial, viral and fungal) in patients that went to transplant a) <6 months b) Between 6- 12 months and c) > 12 months from diagnosis
- Identify T cell lymphocyte absolute numbers at days 100 and 180 and CD4/CD8 ratio for different timeline transplant recipients with individual donor types.
- Evaluate the impact of bacterial, viral or fungal infections by D 100 and day 180 on 1-year post-transplant outcomes- a) relapse b) Non-relapse Mortality (NRM) c) disease free survival (DFS) and d) acute and chronic graft versus host disease (GVHD).
- Evaluate quantitative immunoglobulin levels at D+ 100 and + 180 if available.

Rationale:
As a post remission strategy consolidation with allogenic stem cell transplant (ASCT) prolongs remission duration and is potentially curative in many cases. Of the different non-relapse mortality causes, infections are a major source of unmet need to improve overall success rates with ASCT(1). Appropriately, prior studies have identified the impact of conditioning regimens, graft versus host disease prophylaxis etc: on post-transplant risks. Continually, the field in general has understudied the impact of pre-transplant maneuvers on post-transplant infection risk. Irrespective of the reason for delay, in most cases patients with delayed transplants are likely exposed to higher burden of cytotoxic agents to maintain remission till they get to transplant(2). Repeat cytotoxic agents' exposure are well known to injure thymic epithelial compartment, an important reservoir for early lymphoneogenesis and immune reconstitution(2, 3). In addition, repeat chemo or radiation worsens mucosal injury, and helps microbes cross the barrier easily. So, it is foreseeable that delay in transplant will likely lead to higher probability of post-transplant infections, a confirmation of which is not yet known. A few pediatric studies have confirmed a possible relation between time to transplant and post-transplant adverse events(4). To answer this question, we propose a pilot study using donor sources, GVHD prophylaxis and conditioning regimens that are commonly used in contemporary era.

Significance:
In an era of increased drug approval to prolong remissions, addressing NRM is a priority for the field of HSCT. 1) If our study shows that time is an important variable and reduced time to transplant is associated with lower rates of infections and infection related mortality, then programs will have to make a commitment to work on expediting this process and set new benchmarks. With the introduction

of haplos, which has now consistently shown equal efficacy to MSD/MUD, future studies can exploit this donor source judiciously to increase access to transplant expediently. Hopefully, this will lead to better overall transplant outcomes. Prior to that we need to characterize infections patterns and subtypes and their mortality risk, based on pre-transplant timelines 2) Pre-emptively design tailored anti-microbial prophylaxis strategies to mitigate infection risk for different cohorts based on types of infections. 3) Propel Immune-reconstitution pre-clinical work to expedite drugs that can be tested in trials or find appropriate drugs in induction phase that are less toxic to thymus and minimize mucosal breach.

Inclusion criteria:

- (Will include bulk of population used in IN1901)
- AML/ALL/MDS limiting to CR1
- Age ≥ 2 to ≤ 75 years
- first ASCT between 2012 - 2019
- Any donor
- GVHD prophylaxis (CNI/MTX, CNI/MMF, PTCY/CNI/MMF)
- Myeloablative or Reduced intensity/Non-myeloablative conditioning
- In vivo or Ex vivo T cell depletion allowed
- MDS, AML, ALL,

Exclusion criteria:

- Multiple donors (except cord)
- Syngeneic transplant
- If no 2100 form available
- If no lymphocyte subset analysis performed at day 100 and day 180
- If no values for CD4, CD8, CD19/20, or CD56 at day 100 and day 180
- No consent

Outcomes:

Incidence, frequency and type of bacterial/viral and fungal infections- cumulative incidence with death as competing risk. If any systemic or visceral involvement will also be characterized.

Infection associated mortality for different cohorts:

Cumulative incidence of infection attributable to infection with death from non-infectious cause and relapse as competing events. Dynamic landmark analysis at days 30, 60 and 100 will be examined. Description of causes of death from different infections will also be given. Incidence of aGVHD (landmark analysis D 30) and cGVHD (landmark analysis D 100), with death as competing risk. Traditional definition of DFS, OS will be used.

Study variables:

Patient Related: Age at diagnosis (18-30 years and every decade till 70), Gender, Race, KPS < 70 or 70, HCTCI, Donor age (in decades), Donor/recipient ABO and CMV pairing, CD3, CD4 and CD 8 counts at 100 days and 6 months post-transplant. Quantitative B cell markers and immunoglobulin levels if available by D100 and D 180 post-transplant. CD3, CD34 and CD 19 quantitation in the graft if available.
Disease: AML, ALL, MDS. Time from diagnosis to transplant (<3 months, between 3-6 months, between 6- 12 months and > 12 months), DRI (low vs high vs intermediate).
Treatment: Pre-transplant treatment (Number of lines, chemo vs hypomethylating agents), conditioning intensity (MAC vs RIC- Chemo vs RT), GVHD prophylaxis (Tacro/sirolimus, tacro/cellcept,

Tacro/methotrexate, PTCY based, Cyclosporine based), growth factors peri-transplant (Y/N). If available data on bacterial, viral and fungal prophylaxis used.
Complication: Timing and types of infections (bacterial, viral and fungal) for different timelines for respective donor types. CMV reactivation by D180 (Y/N). GVHD- acute and chronic -Y/N- need for systemic immunosuppression -Y/N.
CIBMTR statistical team will be used for support. Patient, disease and transplant- related metrics will be compared between groups using the Chi-square test for categorical variables and the Wilcox on two sample test for continuous variables. The probabilities of progression-free and overall survival will be calculated using the Kaplan Meier method. Cumulative incidence estimates to account for competing risks will be calculated. Cox proportional hazards regression will be used for outcome of interest. The variables to be considered in the multivariable regression models are listed above. The assumption of proportional hazards for each factor in the Cox model will be evaluated. When the proportional hazards assumption is violated, time-dependent variable will be added in the model. Interactions between main effect and significant covariates will be tested. Description of infections, B and T cell recovery will be presented.

References:

1. Yilmaz M, Chemaly RF, Han XY, Thall PF, Fox PS, Tarrand JJ, et al. Adenoviral infections in adult allogeneic hematopoietic SCT recipients: a single center experience. Bone Marrow Transplant. 2013;48(9):1218-23.
2. Perry GA, Jackson JD, Talmadge JE. Effects of a multidrug chemotherapy regimen on the thymus. Thymus. 1994;23(1):39-51.
3. Bejanyan N, Brunstein CG, Cao Q, Lazaryan A, Luo X, Curtsinger J, et al. Delayed immune reconstitution after allogeneic transplantation increases the risks of mortality and chronic GVHD. Blood Adv. 2018;2(8):909-22.
4. Boelens JJ, Rocha V, Aldenhoven M, Wynn R, O'Meara A, Michel G, et al. Risk factor analysis of outcomes after unrelated cord blood transplantation in patients with hurler syndrome. Biol Blood Marrow Transplant. 2009;15(5):618-25.

Characteristics of patients who underwent first allogeneic transplants for AML in CR1, ALL in CR1 or MDS in US from 2012 to 2019 reported to the CIBMTR

Characteristic	<3 months	3-6 months	6-12 months	>12 months
No. of patients	522	3171	2008	1176
No. of centers	96	151	144	113
Age of recipient - no. (%)				
Median (min-max)	57.5 (2.1-74.5)	56.8 (2-75)	61.7 (2.5-74.9)	65.8 (2.7-75)
0 - 9	13 (2.5)	97 (3.1)	40 (2)	6 (0.5)
10 - 19	27 (5.2)	168 (5.3)	64 (3.2)	10 (0.9)
20 - 29	33 (6.3)	229 (7.2)	103 (5.1)	30 (2.6)
30 - 39	48 (9.2)	258 (8.1)	122 (6.1)	28 (2.4)
40 - 49	61 (11.7)	389 (12.3)	171 (8.5)	52 (4.4)
50 - 59	125 (23.9)	732 (23.1)	398 (19.8)	166 (14.1)
60 - 69	175 (33.5)	1068 (33.7)	875 (43.6)	657 (55.9)
70+	40 (7.7)	230 (7.3)	235 (11.7)	227 (19.3)
Disease - no. (%)				
AML	343 (66)	1729 (55)	563 (28)	46 (4)
ALL	44 (8)	544 (17)	388 (19)	66 (6)
MDS	135 (26)	898 (28)	1057 (53)	1064 (90)
MDS pre-HCT disease stage - no. (%)				
Early	17 (13)	139 (15)	200 (19)	87 (8)
Advanced	110 (81)	745 (83)	843 (80)	965 (91)
Missing	8 (6)	14 (2)	14 (1)	12 (1)
Donor type - no. (%)				
HLA-identical sibling	218 (42)	814 (26)	435 (22)	287 (24)
1 Ag/allele	5 (1)	30 (1)	6 (0)	9 (1)
≥2 Ag/allele	78 (15)	517 (16)	346 (17)	202 (17)
Other related(matching TBD)	22 (4)	130 (4)	78 (4)	27 (2)
Well-matched unrelated (8/8)	105 (20)	1105 (35)	753 (38)	500 (43)
Partially-matched unrelated (7/8)	14 (3)	134 (4)	113 (6)	82 (7)
Mis-matched unrelated (≤6/8)	0	13 (0)	14 (1)	4 (0)
Unrelated (matching TBD)	3 (1)	21 (1)	19 (1)	2 (0)
Cord blood	77 (15)	407 (13)	244 (12)	63 (5)
Stem cell source - no. (%)				
Bone Marrow	93 (18)	639 (20)	349 (17)	176 (15)
Peripheral Blood	352 (67)	2124 (67)	1415 (70)	937 (80)
Cord Blood	77 (15)	407 (13)	244 (12)	63 (5)
Missing or Other	0	1 (0)	0	0
Conditioning intensity - no. (%)				
MAC	298 (57)	1712 (54)	859 (43)	351 (30)
RIC/NMA	224 (43)	1459 (46)	1149 (57)	825 (70)

Characteristic	<3 months	3-6 months	6-12 months	>12 months
GVHD prophylaxis - no. (%)				
CD34 selection	5 (1)	34 (1)	18 (1)	12 (1)
Post-CY + other(s)	105 (20)	740 (23)	503 (25)	292 (25)
Post-CY alone	7 (1)	33 (1)	8 (0)	4 (0)
CNI (TAC/CSA) + MMF +/- Other(except post-CY)	125 (24)	720 (23)	499 (25)	258 (22)
CNI (TAC/CSA) + MTX +/- Other(except MMF, post-CY)	248 (48)	1370 (43)	780 (39)	484 (41)
CNI (TAC/CSA) +/- Other (except MMF, MTX, post-CY)	23 (4)	189 (6)	159 (8)	107 (9)
TAC alone	6 (1)	29 (1)	20 (1)	4 (0)
CSA alone	1 (0)	6 (0)	1 (0)	0
Others	2 (0)	45 (1)	15 (1)	12 (1)
Missing	0	5 (0)	5 (0)	3 (0)
Year of transplant - no. (%)				
2012	29 (6)	213 (7)	126 (6)	95 (8)
2013	77 (15)	381 (12)	227 (11)	136 (12)
2014	94 (18)	496 (16)	280 (14)	148 (13)
2015	78 (15)	509 (16)	304 (15)	156 (13)
2016	83 (16)	491 (15)	280 (14)	156 (13)
2017	71 (14)	392 (12)	290 (14)	193 (16)
2018	52 (10)	390 (12)	269 (13)	174 (15)
2019	38 (7)	299 (9)	232 (12)	118 (10)
Infection by day 100				
Bacterial - no. (%)				
No	317 (61)	1918 (60)	1219 (61)	718 (61)
Yes	204 (39)	1253 (40)	789 (39)	458 (39)
Missing	1 (0)	0	0	0
Viral - no. (%)				
No	354 (68)	1953 (62)	1219 (61)	741 (63)
Yes	167 (32)	1218 (38)	789 (39)	435 (37)
Missing	1 (0)	0	0	0
Fungal - no. (%)				
No	495 (95)	3010 (95)	1889 (94)	1082 (92)
Yes	26 (5)	161 (5)	119 (6)	94 (8)
Missing	1 (0)	0	0	0
Follow-up – median (min-max)	47.6 (1.28-97.11)	46.68 (2.34-98.78)	37.04 (2.86-100.33)	36.81 (3.09-97.99)