1. Introduction
   a. Welcome and introduction

   Dr. Jeffery Auletta moderated the introduction of the working committee followed by which all the attending co-chairs and the statisticians were introduced.

   Dr. Auletta reviewed the goal of the working committee is to publish high impact studies in a timely manner. The expectations of the meeting are review of the current status of ongoing studies and timelines and for members to assess and select proposals that will have a high impact on the field. The working committee is limited by the complicated nature of infection data (Best before day 100) including data regarding infection prophylaxis.

   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 on the transplant community. Due to limited statistical hours and ongoing work in the INWC, only one proposal will be accepted this year.

   Dr. Auletta mentioned 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: 1. substantial and timely contributions to conception and design, acquisition of data, or analysis and interpretation of data; 2. drafting the article or revising it critically for important intellectual content; 3. final approval of the version to be published. All three
conditions must be met. The studies that are closest to submission will receive highest priority.

Last, Dr. Auletta introduced sources of HCT data in the CIBMTR. Dr. Marcie Riches emphasized infection information only available in CRF forms, which is a subset of reported patients based upon an internally reviewed selection algorithm.

b. Minutes and Overview Plan from February 2016 meeting
The minutes and overview plan from the 2016 Tandem meeting held in Honolulu, Hawaii were reviewed and approved by committee members.

2. Published papers
Dr. Jeffery Auletta reported that the infection working committee has published four papers in the past year.

a. **IN10-01** Karen Ballen, Kwang Ahn, Min Chen, Dr. Hisham Abdel-Azim, Ibrahim Ahmed, Dr. Mahmoud Aljurf, Dr. Joseph Antin, Ami Bhatt, Michael Boeckh, George Chen, Dr. Christopher Dandy, Dr. Biju George, Mary Laughlin, Dr. Hillard Lazarus, Dr. Margaret MacMillan, David Margolis, Prof. David Marks, Dr. Maxim Norkin, Dr. Joseph Rosenthal, Ayman Saad, Prof. Bipin Savani, Dr. Harry Schouten, Jan STOREK, Paul Szabolcs, Dr. Celalettin Ustun, Dr. Michael Verneris, Dr. Edmund K Waller, Dr. Daniel Weisdorf, Dr. Kirsten Williams, John Wingard, Baldeep Wirk, Tom Wolfs, Jo-Anne Young, Jeffery Auletta, Dr. Krishna Komanduri, Dr. Caroline Lindemans, Dr. Marcie Riches: Infection Rates among Acute Leukemia Patients receiving Alternative Donor Hematopoietic Cell Transplantation. *Biol Blood Marrow Transplant* 22(9):1036-1645

b. **IN09-01** Richard Maziarz, Dr. Ruta Brazauskas, Min Chen, Dr. Aleksandra McLeod, Dr. Rodrigo Martino, John Wingard, Dr. Mahmoud D Aljurf, Minnoo Battiwalla, Dr. Christopher Dvorak, Prof. Biju George, Dr. Eva Guinan, Dr. Gregory Hale, Dr. Hillard Lazarus, Prof. Jong Wook Lee, Dr. Jane Liesveld, Dr. Muthalagu Ramanathan, Dr. Vijay Reddy, Prof. Bipin Savani, Dr. Franklin Smith, Dr. Lynne Strasfeld, Dr. Randy Taplitz, Dr. Celalettin Ustun, Dr. Michael Boeckh, Dr. Juan Gea-Banacloche, Dr. Caroline Lindemans, Jeffery Auletta, Dr. Marcie Riches: Outcomes of allogeneic HSCT for patients with hematologic malignancies (AML, ALL, MDS, CML) with and without pre-existing fungal infections- pre-existing invasive fungal infection is not a contraindication for subsequent HSCT: a CIBMTR® study. *Bone Marrow Transplantation. doi:10.1038/bmt.2016.259. Epub 2016 Dec 19.*


d. **IN12-01b** Muthalagu Ramanathan, Pierre Teira, Minnoo Battiwalla, Dr. A. Barrett, Kwang Ahn, Min Chen, Carolyn Behrendt, Jaime Green, Mary Laughlin, Dr. Hillard Lazarus, Prof. David Marks, Ayman Saad, Dr. Matthew Seftel, Dr. Wael Saber, Prof. Bipin Savani, Dr. Edmund K Waller, John Wingard, Jeffery Auletta, Dr. Caroline Lindemans, Michael Boeckh, Dr. Marcie Riches: Impact of Early Cytomegalovirus Reactivation in Cord blood Stem Cell Recipients in the Current Era. *Bone Marrow Transplant 51(8):1113-1120*
3. Studies with Preliminary Results
Dr. Jeffery Auletta also introduced two studies with preliminary results.

a. **IN07-01/IN11-01** Early Bacterial infection in patients undergoing allogeneic HCT (M Robien/G Papanicolaou/Celalettin Ustun/ JA Young)
   Two manuscripts are under preparation based on this study. One of them has been accepted as a poster in this tandem meeting.

b. **IN13-01** Bacterial and fungal infections in patients undergoing allogeneic hematopoietic cell transplantation following non- myeloablative and myeloablative regimens (C Usten)
The final analysis has been circulated to the writing comment for comments and the manuscript is under preparation.

4. Studies in progress
Dr. Krishna Komanduri mentioned the ongoing studies.

a. **IN14-01** Post allogeneic hematopoietic transplant Epstein Barr Virus related Lymphoproliferative disorder following conditioning with Antithymocyte globulin or Alemtuzumab (S Naik, C Bachier, P Shaughnessy, P Hari, R Kamble) **Date file preparation**
   Dr. Jeffery Auletta updated the study on behalf of the PIs.

   The specific aims of this study are: to describe the characteristics of patients with post-transplant lymphoproliferative disorders (PTLD) following allogeneic hematopoietic cell transplantation (allo HCT); To determine morbidity and outcomes associated with Epstein Barr virus (EBV) positive and EBV negative PTLD. The current population has 236 EBV positive patients and 34 EBV negative patients. 190 path reports have been reviewed.

   Comments from Working Committee:
   - Campath may effect EBV. Dr. Riches mentioned few patients received Campath in the current population.
   - Assessment of prior use of Rituximab in the conditioning regimen. It was noted that since the patients included did not have B-cell lymphoma as the disease for transplant, it was unlikely that patients had received Rituximab during the conditioning regimen.

b. **IN16-01** Viral Encephalitis in Hematopoietic Stem cell Transplant Recipients, 2007-2013 (M Abidi, P Hari) **Protocol development**
   Dr Abidi Maheen updated the study.

   The objectives of the study are: to describe the frequency and significance of viral DNA detection in cerebrospinal fluid (CSF) in hematopoietic stem cell transplant (HCT) recipients screened for viral encephalitis; to determine the OS of patients with viral encephalitis after HCT. The primary endpoint will be overall survival of patients developing EBV positive and EBV negative PTLD. The secondary endpoints will be time to onset of PTLD. Factors at transplant impacting outcomes following diagnosis of EBV positive PTLD. There are 118 patients in the current population.

   Dr. Komanduri expressed surprise by how much HHV6 dominated the infections in this study. The lack of viremia may due to some centers do not test viremia routinely until recently. Dr.
Riches pointed out, during the time period, cord blood transplants were over selected and it may potentially skew the data.

Additional issues raised by the working committee:
1. Limitations include: no clear systematic evaluation of patients, unknown symptomatology triggering LP, inability to determine HHV6 latency in the study, inability to have a control cohort that also had an LP
   - These limitations may result in erroneous conclusions
2. Discussion of unpublished data from NIH suggesting a low level of HHV-6 in the CSF when tested in patients receiving intrathecal chemotherapy
3. Should we address the season of the year for the encephalitis?

**c. IN16-02** Determination of the burden of mucosal barrier injury-laboratory confirmed bloodstream infections (MBI-LCBI) in the first 100 days after stem cell transplant (C. Dandoy, P. Daniels) Protocol development

Dr. Christopher Dandoy updated the study.

This study hypothesizes that patients in the first 100 days after stem cell transplant who develop mucosal barrier injury laboratory confirmed bloodstream infections (MBI-LCBI) have increased transplant related mortality (TRM) and decreased overall survival (OS) compared to those with no infection or an infection not classified as an MBI-LCBI. The Specific Aims of the study are: compare TRM and OS post-SCT between patients who develop a MBI-LCBI versus those with no infection or a non-MBI-LCBI in the first 100 days; Determine the incidence of MBI-LCBIs in the first 100 days post SCT; Determine the risk factors for development of a MBI-LCBI in the first 100 days; and determine the timing of MBI-LCBI after SCT. The outcomes of the study are: overall survival; transplant related mortality (TRM); Incidence of MBI-LCBI within the first 100 days; and Incidence of bloodstream infections (bacterial and fungal) not meeting criteria for MBI-LCBI; and infection as primary or secondary cause of death by day 100 and by 1 year.

A bloodstream infection will be classified as a MBI-LCBIs if it meets both the organism criteria and the patient criteria from the NHSN.

Study strengths are: Large sample size, Contemporary, Reflects the global reality of HSCT by including all centers, Identify MBI-LCBI burden for public health reporting, Public health implications and should target major public health journal such as JAMA.

Comments:
- Important topic for hospital epidemiology/infection control
- Consider inclusion of autologous transplants

5. **Future/proposed studies**

Dr. Caroline Lindemans reported that 9 proposals were received this year and 4 will be presented. Since there is significant overlap of Prop 1611-02, Porp1611-117 and Prop1611-134, we propose to merge the three proposals into one study to maximize efficiency and statistical hours.

a. **PROP1605-01** Clinical outcomes for patients with invasive fungal infections undergoing hematopoietic stem cell transplant, (Myeloablative vs. Nonmyeloablative/Reduced intensity stem cell transplant) in the era of newer anti-fungals, 2009-2015 (Maheen Abidi/
Dr. Maheen Abidi presented the proposal.

The objectives of this proposal are: 1. Study period 2010-2015 in era of newer antifungals; compare results with outcomes of IFIs that underwent HSCT 1995-2009 (IN09-01); 2. Determine outcomes & mortality rates of patients with leukemia & other hematologic malignancies with & without IFIs that undergo HSCT; 3. Determine the relationship between IFIs and the incidence & severity of GVHD & on relapse rates.

Dr. Riches answered the question regarding why limited the patients with 2046 and 2146 form (fungal supplemental forms) only, since the requested information is available only in the 2046/2146 form. Dr. Komanduri suggested adding time from diagnosis to transplant, or time of remission. Since delay of transplant will increase the relapse mortality.

Committee Discussion:
- Inability to determine if the fungal infection is possible/probable/proven
- Lack of information of the status of the infection at the time of transplant

b. **PROP 1611-02** The Incidence of Cytomegalovirus Viremia and Disease following HLA-Haploidentical Hematopoietic Cell Transplantation Compared to HLA-Matched Related Donor, Matched Unrelated Donor, and Umbilical Cord Blood Transplantation (Rizwan Romee / Ephraim Fuchs / Asad Bashey / Stefan Ciurea)

Dr. Scott Goldsmith presented the proposal.

The hypotheses of the study are: Incidence of CMV reactivation and disease higher after haploHCT with PTCy compared to MUD/MRD/UCB; CMV reactivation does not promote decreased relapse, or longer DFS or OS in haploHCT. The Inclusion criteria are: Heme malignancy, age ≥ 18 years, and HCT between 2008-2015; HaploHCT w/ PTCy, UCB, 8/8 MUD, MRD. The exclusion criteria are: Ex-vivo T-cell depletion; HaploHCT for benign condition; Lack of donor/recipient CMV serostatus. The Primary Endpoint are: Compare incidence of CMV reactivation and disease between haploHCT w/ PTCy to MRD/MUD/UCB. Secondary Endpoints: Determine association of CMV donor/recipient serostatus with CMV disease; Compare DFS, relapse, NRM, GVHD and GRFS between the groups (Association with CMV reactivation; Association with CMV donor/recipient serostatus; Subset analysis for patients with AML).

c. **PROP 1611-117** Impact of CMV Reactivation on Relapse of Hematological Malignancies after Haploidentical HSCT: a CIBMTR Analysis (Anurag Singh / Siddhartha Ganguly) (Attachment 11)

Dr. Anurag Singh presented the proposal.

The specific aim of the study is to describe the effect of early CMV reactivation on relapse in the setting of haploidentical transplant. The Inclusion criteria are: patients receiving a first allogeneic transplantation for any AML, MDS, ALL and lymphomas from a haploidentical donor between 2000 and 2015 and reported to the CIBMTR. The exclusion criteria are: Second transplant or more; lack of day 100 follow-up forms capturing CMV reactivation data. The statistical methods are: Patient-, disease-, and transplant-related factors will be compared among groups using the Pearson $\chi^2$ test for discrete variables and the Kruskal-Wallis test for continuous variables.
d. **PROP 1611-134** Incidence and Outcomes of individuals with and without viral infections in recipients of haploidentical versus other allogeneic hematopoietic stem cell transplantation for patients with hematologic malignancies (Randy Allison Taplitz/ Carolyn Mulroney/ Richard Maziarz) (Attachment 12)

Dr. Randy Allison Taplitz presented the proposal.

This study hypothesizes that outcomes of treatment related mortality, overall survival, relapse rate, GVHD, diagnosis of bronchiolitis obliterans/COP, leukemia-free survival and presence of co-infection in patients with any viral infections after transplant will be inferior in those patients receiving haploidentical donors vs some other donor type transplant (compared separately – cord and mismatched unrelated, matched transplants; and as a group). Characteristics of patient who underwent first Allo transplant with AML, ALL, MDS, CML, CLL, NHL, HL, plasma cell disorders and severe aplastic anemia reported to the CIBMTR from 2010-2015

Dr. Marcie Riches mentioned, if we decide this combined proposal proceed forward, we have to redefine the population. Dr. Komanduri is concerned the testing methods change overtime, so some compromise has to be made.

**Committee Discussion (for proposals b – d)**

- Issues of Haploidentical with post-transplant cyclophosphamide vs without PTCy
- Issues of PTCy in donors other than Haploidentical
- Consideration of including an lymphocyte recovery data at day 100
- Limited data/events for viruses other than CMV
- Can we include information on duration of CMV reactivation (data not available) and treatment of CMV (data not available)

Chairs discussion: Is there a way to collaborate with the EBMT to increase the Haplo population?

**Dropped proposed studies**

a. **PROP 1611-72** CMV exposure of cord blood donor- Impact on CMV reactivation in the recipient. *Dropped due to feasibility-low number of patients.*

b. **PROP 1611-151** Immune Reconstitution and its relation with Infectious Morbidity Post Autologous Peripheral Blood Stem Cell Transplantation (PBSCT). *Dropped due to feasibility - the CIBMTR does not capture the data required to answer the hypothesis.*

c. **PROP 1611-122** Outcomes from progressive multifocal leukoencephalopathy in hematopoietic stem cell transplant patients

   *Dropped due to feasibility-low number of patients*

d. **PROP 1611-54** The Effect of Antibacterial Prophylaxis on Early Post-transplant Mortality in Patients with Multiple Myeloma and Lymphoma Undergoing High-dose Chemotherapy and Autologous Stem Cell Transplantation. *Dropped due to feasibility*

e. **PROP 1611-01** Infection Density per Donor Type and Conditioning Intensity and Their Association with NRM in 3 different time points (0-33, 34-66, and 67-100 days) within 100 days after alloHCT. *Dropped due to low scientific impact*
6. Other Business
Dr. Marcie Riches presented the infection form updates.
The following sections have/will be updated:
   1. Infection Prophylaxis data (activated Jan 2017)
   2. PostHCT infection data capture revisions (activated Jan 2017)
   3. Revised organism lists focusing on viral and fungal infections (activated Jan 2017)
   4. 2046/2016 form (fungal infection form) (anticipated July 2017)
   5. 2149 form (Respiratory Virus form) (anticipated July 2017)
   6. 2150 form (CMV/EBV/ADV/HHV-6 form) (anticipated July 2017)

Working Committee Overview Plan for 2017-2018

a. **IN07-01/IN11-01** Early bacterial infection in patients undergoing allogeneic HCT (C Ustun /J-A Young/M Robien/G Papanicolaou).
   i. **VEP vs LEP BSI**: Plan to submit to Blood by June 2017. We anticipate the paper is published by June 30, 2018. (Hour to completion: 60; Allocated by Jun 30, 2017: 60)
   ii. **VRE vs Other BSI**: Plan to submit to Blood by June 2017. We anticipate the paper is published by June 30, 2018. (Hour to completion: 60; Allocated by Jun 30, 2017: 60)

b. **IN 13-01** Bacterial and fungal infections in patients undergoing allogeneic hematopoietic cell transplantation following nonmyeloablative and myeloablative regimens (C Usten). Plan to submit to BBMT by July 2017. We anticipate paper is published by June 30, 2018. (Hour to completion: 70; Allocated by Jun 30, 2017: 70)

c. **IN 14-01** (PROP 1303-03/PROP1311-19): Post allogeneic hematopoietic transplant Epstein Barr Virus related lymphoproliferative disorder following conditioning with antithymocyte globulin or alemtuzumab (R Kamble/ P Hari/S Naik /C Bachier/P Shaughnessy). We anticipate paper is submitted by June 30, 2018 (Hour to completion: 150; Allocated by Jun 30, 2017: 150)

d. **IN16-01** Viral encephalitis in hematopoietic stem cell transplant recipients, 2007-2013 (Maheen Abidi/ Parameswaran Hari) (PROP1510-16). We anticipate paper is published by June 30 2018. (Hour to completion: 230; Allocated by Jun 30, 2018: 230)

e. **IN16-02** Determination of the burden of mucosal barrier injury-laboratory confirmed bloodstream infections in the first 100 days after stem cell transplant (Christopher Dandoy/ Paulina Daniels) (PROP 1511-85). We anticipate receiving the paper for submission by June 30, 2018. (Hour to completion: 300; Allocated by Jun 30, 2018: 300)

f. **IN17-01** Incidence and Outcomes of individuals with and without viral infections in recipients of haploididentical versus other allogeneic hematopoietic stem cell transplantation for patients with hematologic malignancies (Rizwan Romee/ Ephraim Fuchs/ Asad Bashey/ Stefan Ciurea/ Anurag Singh/ Siddhartha Ganguly/ Randy Allison Taplitz/ Carolyn Mulroney/ Richard Maziarz). We anticipate data file ready for analysis by June 30, 2018. (Hour to completion: 310; Allocated by Jun 30, 2018: 160)
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