1. Introduction
The CIBMTR Acute Leukemia Working Committee was called to order at 2:45 pm on Saturday, February 16, 2013, by Dr. Daniel Weisdorf. The chairs, scientific director and statisticians were presented. Attendees were asked to have their name badges scanned for attendance purposes and to maintain the committee membership roster, and to fill out the Working Committee evaluations and voting sheets for proposals. The CIBMTR guidelines for voting on proposals were discussed. The guidelines are based on a scale from 1 to 9; 1= high scientific impact, 9= low scientific impact. The meeting was limited to presentation and discussion of proposals. Dr. Donald Bunjes introduced the accrual summary, committee’s accomplishments for the past year and progress of ongoing studies. Each proposal presentation was limited to 5 minutes (maximum 3-4 slides) to allow for adequate time for discussion (5-7 minutes). The minutes of the February 2012 meeting were approved without modifications.

Dr. Donald Bunjes welcomed Dr. Marcos de Lima as newly appointed ALWC chair starting from March 2013 and presented a souvenir to departing chair Dr. John DiPersio.

Dr. Daniel Weisdorf announced the principles established by advisory committee to improve the quality and efficiency of working committees: 1) peer-reviewed publications of high scientific impact as target 2) work product to be finished within a reasonable time period 3) ensuring inclusiveness and fairness of the process.

2. Accrual summary
Due to the full agenda, the accrual summary of registration and research cases between 1995 and 2012 were not presented to the committee but were available as part of the Working Committee attachments:

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<th>Registration only</th>
<th>Research</th>
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<tbody>
<tr>
<td>AML allogeneic</td>
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<td>19854</td>
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<tr>
<td>ALL allogeneic</td>
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<td>1304</td>
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<tr>
<td>ALL autologous</td>
<td>730</td>
<td>218</td>
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3. **Published/submitted papers and presentations**

Due to the full agenda, the 2012 presentations and published papers were mentioned, but not presented. Three papers were published; one submitted and two ASBMT tandem presentations were given during the past year. These include:


g. LK10-03 Bachanova V, Marks DI, Zhang MJ, Wang HL, Weisdorf DJ. Older patients with Ph+ acute lymphoblastic leukemia (ALL) in first remission (CR1) have prolonged survival with either myeloablative or reduced intensity conditioning allogeneic transplantation: Impact of imatinib and minimal residual disease (MRD) on outcomes: a CIBMTR matched-pair study (V Bachanova). Presentation at the ASBMT Tandem Meetings in Salt Lake City, Utah, February 2013. Manuscript in preparation.

4. Studies in progress
The studies which made progress during the past year were not presented in order to provide reasonable time to the new proposals for presentation and discussion. A summary of the progress was provided as an attachment to the committee members. These were:

a. R02-09 Evaluation of donor leukocyte infusions to treat relapsed hematologic malignancies after related and unrelated donor myeloablative allogeneic hematopoietic stem cell transplantation (A Loren)
The value of related and unrelated donor DLI in treatment of acute leukemia relapsed after allografting will be examined, including the impact of disease status, timing, dose response, and comparative efficacy of the two donor sources. Secondary data collection is required and is underway. The supplemental data collection is finished and data file preparation is underway.

b. LK04-01 Comparison of autologous and allogeneic hematopoietic stem cell transplantation for patients with acute promyelocytic leukemia (APL) in second complete remission (M Rubinger/M Tallman)
This project analyzes outcome of APL in second CR including details of molecular remission prior to transplant. The analysis is finished and currently under manuscript preparation.

c. LK07-03 Reduced intensity or non-ablative hematopoietic cell transplantation in older patients with Non-Hodgkin Lymphoma: encouraging survival for patients ≥55 years (B McClune)
This study proposes to analyze outcome of NHL in older patients who received NMA/RIC conditioning. The draft manuscript has been circulated within writing committee and the PI is currently revising the manuscript for submission.

d. LK09-02 Impact of monosomal karyotype in the outcome of hematopoietic cell transplantation for Acute Myeloid Leukemia and Myelodysplasia (M Pasquini/ M Battiwala)
The purpose of this study is to identify the impact of high risk cytogenetic subsets: specifically chromosome 7 abnormalities (either monosomy7 or del(7q)) and monosomal karyotype in outcomes for AML and MDS after allogeneic HCT and to evaluate the impact of conditioning intensity in the outcome of patients with AML and monosomal karyotype. The draft protocol is currently being reviewed by PI.

e. LK10-02 Effect of pre-transplant consolidation chemotherapy on outcomes of RIC Allogeneic transplant for adults with AML in CR1 (E Warlick)
The purpose of this study is to (1) compare the outcomes of adults with AML in first remission who have received no consolidation, standard-dose cytarabine consolidation, or high-dose...
cytarabine consolidation followed by reduced intensity conditioning related or unrelated donor allogeneic stem cell transplantation (HCT) and (2) to determine if there is an exposure threshold (number of cycles of consolidation) that impacts post-transplant outcomes. The draft manuscript has been circulated within the WrC and is currently being revised by PI for submission.

f. **LK10-03** The outcome of adults with Philadelphia positive acute lymphoblastic leukemia comparing reduced intensity conditioning and myeloablative conditioning allogeneic stem cell transplantation (V Bachanova)
The purpose of this study is to (1) to compare outcomes of adults with Ph+ ALL who received reduced intensity versus myeloablative conditioning followed by sibling or matched unrelated donor HCT; (2) to examine the effect of pre-transplant treatment with tyrosine kinase inhibitors (TKI) on transplant outcomes using RIC and MA conditioning and (3) to examine the prognostic significance of patient, disease and transplant related characteristics on transplant outcomes. Supplemental data collection regarding TKI use was required and supported by external funding. The draft manuscript has been circulated and is currently being revised by PI for submission.

g. **LK11-01** Impact of extramedullary disease on the outcome of allogeneic HCT in AML (S Goyal/ G Uy)
The purpose of this proposal is (1) to describe the outcome of patients undergoing alloHSCT for AML with extramedullary involvement and (2) to assess patient, disease and transplant related factors which influence the outcome of alloHSCT in AML. There are 935 AML patients ≥18 years of age with extramedullary disease prior to HCT reported to the CIBMTR between 1995 and 2010. Protocol development and data file review is underway.

The following studies were previously proposed, but not initiated:

a. **LK12-01** Chemotherapy versus Allogeneic Hematopoietic Cell Transplantation in Philadelphia negative chromosome negative adult ALL (M Seftel)
The purpose of the study is to compare HSCT outcomes of younger adults with Philadelphia chromosome negative (Ph-) Acute Lymphoblastic Leukemia (ALL) in first complete remission (CR1) treated with either allogeneic hematopoietic cell transplantation (alloHCT) or with a pediatric style chemotherapy regimen.

b. **LK12-02** FLT3/ITD mutation in AML remains a poor prognostic factor compared to conventional cytogenetics with increased risk of relapse and decreased overall survival after allogeneic stem cell transplantation in first complete remission (S Sengsayadeth)
The purpose of this study is to (1) To study the prognostic significance of FLT3/ITD mutation in AML in patients receiving allo-HSCT in CR1 and (2) To study the impact of FLT3/ITD mutation on incidence of relapse, disease-free survival (DFS), overall survival (OS) after allo-SCT in CR1.

5. **Future/ Proposed studies**

Drs. Devine and DiPersio led this section. The proposals were the following:

a. **PROP 1012-02** To Determine whether In-vivo T Cell Depletion with Alemtuzumab Affects Outcome after Myeloablative TBI-based Conditioning in Children and Young Adults who Received Unrelated Donor Transplants for AML (S Samarasinghe/ P Veys/ M Eapen)
Dr. Veys presented the proposal. The purpose of this study is to compare transplant outcomes including aGVHD/ cGVHD/ OS/ LFS/ 1 year TRM/ viral infection in children and AYA who have undergone a myeloablative HSCT for AML, the incidence of acute GVHD and chronic GVHD between regimens with in vivo T cell depletion using Alemtuzumab/ATG or T cell replete. There are 2225 patients who are under age of 40 and underwent 1st allo unrelated donor T-cell replete myeloablative conditioning HSCT between 1997 and 2010. Drs. Weisdorf and Eapen
commented that CIBMTR forms do not capture the administration dates or specific doses of Alemtuzumab/ATG but only the product name and total dose. The proposal was not approved because concerns raised about the arbitrary age limit of 40 years old and also lack of novelty.

b. PROP 1112-06 Comparing Autologous to Allogeneic Transplant in APL Patients with Extramedullary Disease who Achieve a Second or Subsequent Complete Remission (CR) (C Ganzel/ M Tallman/ D Douer)
Dr. Douer presented the proposal. The purpose of this study is to compare the OS, DFS and toxicity between auto HSCT and ATO-based treatment in relapsed APL patients, using large databases. There are 129 patients (allo n=106; auto n=23) in the CIBMTR dataset who had 1st HSCT for APL with extramedullary involvement. Comparatively there are 46 patients treated with ATO in an available Indian cohort. The issue of high percentage of earlier patients (year<=1995, 62%) with different HSCT therapy approaches was commented. The proposal was not approved because 1) small number (n=23) in extramedullary group 2) overlap with ongoing study LK04-01

c. PROP 1112-10 Comparing Autologous Transplant to Arsenic Trioxide (ATO) for Patients with Acute Promyelocytic Leukemia (APL) in First and Subsequent Relapse (C Ganzel/ M Tallman/ D Douer)
Dr. Douer presented the proposal. The purpose of this study is to compare the OS, DFS, TRM, hematological toxicity, infectious disease, cardiovascular events, arrhythmias, neurologic events and APL differentiation syndrome between auto HSCT and ATO-based treatment in relapsed APL patients and 2) identify predictive patient characteristics for favorable outcome. There are 125 patients who relapsed before 1st auto HSCT for APL. This proposal was not approved because concerns were raised about the potential selection bias of patients who received transplant vs. ATO treatment. Also the ATO group likely had a high proportion of transplanted patients with no further available information thus confounding the comparisons.

d. PROP 1112-38 Allogeneic Transplantation For Older Patients with Acute Lymphoblastic Leukemia: Impact of Age on Transplant Outcomes (V Bachanova)
Dr. Bachanova presented the proposal. The purpose of this study is to 1) analyze outcomes of allogeneic donor transplantation for older patients with acute lymphoblastic leukemia comparing 3 age groups: 40-50, 51-60 and ≥61 years of age; 2) define the prognostic factors (patient, disease and transplant related (including graft choice and conditioning regimen intensity)) impacting on mortality, relapse and survival. There are 1216 patients older than 40 years of age who had 1st allo HSCT for ALL between 01/01/2000 and 06/30/2011.

e. PROP 1112-35 Prognostic Significance of Cytogenetic Abnormalities in Patients with Philadelphia-negative Acute Lymphoblastic Leukemia undergoing Allogeneic Hematopoietic Stem Cell Transplantation in Complete Remission: A CIBMTR Study (A Lazaryan)
Dr. Lazaryan presented the proposal. The purpose of this study is to 1) develop a novel HCT-specific cytogenetic classification scheme for prognostication of relapse and survival outcomes following allo-HCT in patients with Philadelphia-negative ALL; 2) validate major existing cytogenetic groupings of Ph-ALL among the recipients of allo-HCT from multicenter cohort of CIBMTR patients; 3) compare the performance of novel and existing classification schemes in an independent cohort of HCT patients from CIBMTR patient database. There are 3062 adult patients who had 1st allo BM/PB graft HSCT for Ph-negative and non-L3 ALL in remission. EBMT cytogenetic data was suggested to be used as validation set. PI will need to review cytogenetic report to determine proper category for analysis.
f. PROP 1112-41 Outcomes of Allogeneic Stem Cell Transplantation in T cell Acute Lymphoblastic Leukemia (W Rasheed)
Dr. Rasheed presented the protocol. The purpose of this study is to analyze outcomes of allo HSCT in adult patients with T-Cell ALL including OS, DFS and NRM. There are 821 adult patients who received 1st allo BM/PB graft HLA-id sibling or unrelated donor HSCT for T-ALL between 1990 and 2010. The proposal was not approved due to lack of novelty compared with the recently published EBMT study (Cahu et al). Also there was concern about correlation between years of HSCT, conditioning intensity and disease status prior to HSCT.

g. PROP 0712-04 Allogeneic Transplantation for Acute Biphenotypic Leukemia (ABiL): Disease Characteristics, Complications and Outcomes (R Munker)
Dr. Munker presented the proposal. The purpose of this study is to describe frequency of allogeneic transplant for ABiL, demographics and disease characteristics before transplant, describe outcomes of transplant for ABiL. There are 278 patients younger than 70 years of age who had 1st allo HSCT for biphenotypic leukemia (per CIBMTR disease category) since 1996. It was suggested that detailed diagnostic reports need to be reviewed for every patient to determine the specifics and diagnostic subsets of biphenotypic leukemia. It was considered as an interesting and unique study since no similar publication is available.

h. PROP 1112-26 The Impact of Peripheral Blood Chimerism on Transplant Outcomes in Patients with Acute Leukemia and Myelodysplastic Syndrome (P Kebriaei)
Dr. Kebriaei presented the proposal. The purpose of the study is to 1) assess the impact of persistent mixed chimerism at 3 months following allogeneic HSCT on the rate of relapse post HSCT; 2) assess the impact of persistent mixed chimerism on the rate of GVHD; 3) describe the kinetics of donor chimerism in the first year following transplant. There are 6262 patients who had 1st allo T-cell replete BM/PB graft HCT for AML/ALL/MDS. This study was not approved because chimerism data is not readily available in CIBMTR database, although there is potential interest in chimerism studies.

Three additional proposals were submitted to the committee, but not presented as stated below:

a. PROP 1012-06 Evaluation of Outcomes in Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) / Leukemia after Transplantation (S Ahmed/ P Kebriaei/ R Champlin): Hard to define cases/ insufficient number of cases.

b. PROP 1112-54 Outcomes of Hematopoietic Cell Transplantation for Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (Nishihori T): similar proposal as p1012-06 and dropped for same reason.

c. PROP 1112-57 Comparative outcome of nonmyeloablative allogeneic hematopoietic stem cell transplantation combined with pre-emptive donor lymphocyte infusion and myeloablative allogeneic hematopoietic stem cell transplantation in older patients with high-risk leukemia (Huang H): Hard to define post-tx DLI cases/ insufficient detail available and insufficient number of cases.

6. Other business
After the new proposals were presented, each participant in the meeting had the opportunity to rate each proposal using paper ballots. Based on the voting results, current scientific merit and the impact of the study on the field, the following studies will move forward as the committee’s research portfolio for the upcoming year:
PROP 1112-35 Prognostic Significance of Cytogenetic Abnormalities in Patients with Philadelphia-negative Acute Lymphoblastic Leukemia undergoing Allogeneic Hematopoietic Stem Cell Transplantation in Complete Remission: A CIBMTR Study

PROP1112-38 Allogeneic Transplantation for Acute Biphenotypic Leukemia (ABiL): Disease Characteristics, Complications and Outcomes

PROP 0712-04 Allogeneic Transplantation For Older Patients with Acute Lymphoblastic Leukemia: Impact of Age on Transplant Outcomes

Dr. Bunjes expressed gratitude to the Committee members for their active role and valuable support to the Committee.

Without additional comments, the meeting was adjourned at 4:35 pm.

**Working Committee Overview Plan for 2013-2014**

R02-09 Evaluation of donor leukocyte infusions to treat relapsed hematologic malignancies after related and unrelated donor myeloablative allogeneic hematopoietic stem cell transplantation. The study will be combined with a similar proposal and transferred to cellular therapy working committee. Previously collected supplemental data collection will be used to enhance the study.

LK04-01 Comparison of autologous and allogeneic hematopoietic stem cell transplantation for patients with acute promyelocytic leukemia (APL) in second complete remission. The analysis is completed and manuscript is under preparation. We plan to submit the paper by June 2013.

LK07-03c: Reduced intensity or non-ablative hematopoietic cell transplantation in older patients with Non-Hodgkin Lymphoma: encouraging survival for patients ≥55 years. The revised manuscript is nearly completed. We plan to submit the paper by June 2013.

LK09-02: Impact of monosomal karyotype in the outcome of hematopoietic cell transplantation for Acute Myeloid Leukemia and Myelodysplasia. Protocol will be finalized in April 2013 and since the data file preparation is almost complete already, we plan to finish analysis by June 2013. Submission is anticipated by June 2014.

LK10-02: Effect of pre-transplant consolidation chemotherapy on outcomes of RIC Allogeneic transplant for adults with AML in CR1. Draft manuscript has been circulated with feedback received. Additional modest analysis is needed from PhD statistician and we plan to submit paper before June 2013.

LK10-03: The outcome of adults with Philadelphia positive acute lymphoblastic leukemia comparing reduced intensity conditioning and myeloablative conditioning allogeneic stem cell transplantation. The draft manuscript is complete and has been circulated within the Writing Committee in March. Submission of paper is expected by June 2013.

LK11-01: Impact of extramedullary disease on the outcome of allogeneic HCT in AML. Data file preparation ongoing and will be ready for analysis by June 2013. Submission of paper is expected by June 2014.
h. **LK12-01**: Chemotherapy versus Allogeneic Hematopoietic Cell Transplantation in Philadelphia negative chromosome negative adult ALL. Protocol revision is underway and plan to move to data file preparation by June 2013. We plan to finish analysis and complete the manuscript by June 2014.

i. **LK12-02**: FLT3/ITD mutation in acute myeloid leukemia remains a poor prognostic factor compared to conventional cytogenetics with increased risk of relapse and decreased overall survival after allogeneic stem cell transplantation in first complete remission. Protocol revision is underway and will be moved to data file preparation by June 2013. We plan to finish analysis and complete the manuscript by June 2014.

j. **LK13-01** (PROP 1112-38): Evaluating outcomes of reduced intensity conditioning allogeneic SCT in older adult lymphoblastic leukemia patients reported to the CIBMTR and EBMT. We anticipate developing the study protocol after July 2013 and prepare data file to be ready for analysis by June 2014.

k. **LK13-02** (PROP 1112-35): Prognostic significance of cytogenetic abnormalities in patients with Philadelphia-negative acute lymphoblastic leukemia undergoing allogeneic hematopoietic stem cell transplantation in complete remission. We anticipate developing the study protocol after July 2013 and prepare data file for detailed review by the PI and to be ready for analysis by June 2014.

l. **LK13-03** (PROP 0712-04): Allogeneic transplantation for Acute Biphenotypic Leukemia: Disease characteristics, complications and outcomes. We anticipate developing the study protocol after July 2013. All cases will have a pathology report reviewed by PI. We plan to finish data file preparation and review of cases by June 2014.

### Oversight Assignments for Working Committee Leadership (February 2013)

**Daniel Weisdorf**

- **LK07-03c**: Reduced intensity or non-ablative hematopoietic cell transplantation in older patients with Non-Hodgkin Lymphoma: encouraging survival for patients ≥55 years
- **LK12-01**: Chemotherapy versus Allogeneic Hematopoietic Cell Transplantation in Philadelphia negative chromosome negative adult ALL
- **LK13-02**: Prognostic significance of cytogenetic abnormalities in patients with Philadelphia-negative acute lymphoblastic leukemia undergoing allogeneic hematopoietic stem cell transplantation in complete remission

**Marcos de Lima**

- **LK09-02**: Impact of monosomal karyotype in the outcome of hematopoietic cell transplantation for Acute Myeloid Leukemia and Myelodysplasia
- **LK11-01**: Impact of extramedullary disease on the outcome of allogeneic HCT in AML
- **LK13-01**: Evaluating outcomes of reduced intensity conditioning allogeneic SCT in older adult lymphoblastic leukemia patients reported to the CIBMTR and EBMT
Steven Devine

LK04-01: Comparison of autologous and allogeneic hematopoietic stem cell transplantation for patients with acute promyelocytic leukemia (APL) in second complete remission

LK10-02: Effect of pre-transplant consolidation chemotherapy on outcomes of RIC Allogeneic transplant for adults with AML in CR1

LK10-03: The outcome of adults with Philadelphia positive acute lymphoblastic leukemia comparing reduced intensity conditioning and myeloablative conditioning allogeneic stem cell transplantation

Donald Bunjes

LK12-02: FLT3/ITD mutation in acute myeloid leukemia remains a poor prognostic factor compared to conventional cytogenetics with increased risk of relapse and decreased overall survival after allogeneic stem cell transplantation in first complete remission

LK13-03: Allogeneic transplantation for Acute Biphenotypic Leukemia: Disease characteristics, complications and outcomes