1. Introduction
The Chronic Leukemia Working Committee (CKWC) met on Friday, February 21, 2019 at 12:15 p.m. The chairs, scientific director and statisticians were all presented at the meeting. Attendees were asked to have their name badges scanned at the front gate for attendance purpose and to maintain the committee membership roster.

As the scientific director of the CKWC, Dr. Wael Saber welcomed the attendees on behalf of the working committee leadership and presented Dr. Ronald Sobecks, who will present the welcome slides. Dr. Sobecks began by introducing each member of the working committee leadership. Dr. Sobecks welcomed the incoming chair, Dr. Betul Oran, from MD Anderson Cancer Center, and thanked the committee, for the opportunity to serve as a co-chair over the past 5 years. Dr. Sobecks continued the presentation explaining how to gain and maintain membership, the goals, expectations and limitations of the working committee, emphasizing the rules of authorship as well as the voting process and voting prioritization. Dr. Sobecks reiterated that each proposal was given 5 minutes for presentation and 5 minutes for discussion, and that voting scores will be used as an important aspect of deciding which proposals should be accepted. He also mentioned that a maximum of 2 proposals could be accepted.

Dr. Sobecks also emphasized that during this past year the baseline and follow-up forms for MDS and MPN disorders were divided into two sets of forms and were substantially updated for use in the future years.

2. Accrual summary
The accrual summary was referenced for review, but not formally presented. The full accrual summary was available online as part of the attachments.
3. **Presentations, Published or Submitted Papers**

The following publications or submitted papers from 2019 were referenced, as well as abstracts that have been presented at various conferences. Dr. Sobecks mentioned that it was a very productive year and emphasized the high metrics of the committee. He mentioned that CK16-02b was the most recent publication. At the time, three studies were published, one accepted to journal recently and two abstracts were presented or accepted for presentation. These include:


4. **Studies in Progress**

Due to the full agenda, studies in progress were not presented at the meeting. Dr. Sobecks mentioned that the summary of the progress of the ongoing studies was available online as part of the attachments.

a. **CK12-01** Optimal timing of allogeneic stem cell transplantation for chronic myeloid leukemia patients in the tyrosine kinase inhibitor era. (B Hu/H Lee) Submitted

b. **CK15-01** Comparison of transplant vs. non-transplant therapies for myelofibrosis. (K Ballen/RA Mesa/KL Gowin) In Press
c. **CK15-03** Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm. (V Gupta) 

*Manuscript Preparation*

d. **CK16-01** Identification of germline predisposition mutations in young myelodysplastic syndrome patients. (L Godley) 

*Data File Preparation*

e. **CK16-02b** In the era of tyrosine kinase inhibitors (TKIs), TKIs are superior to donor lymphocyte infusion for relapse of chronic myeloid leukemia post hematopoietic cell transplantation. (S Schmidt) 

*In Press*

f. **CK17-01** Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation. (T Roni/SA Giralt/J Palmer) 

*Analysis*

g. **CK17-02** Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes. (B Oran) 

*Manuscript Preparation*

h. **CK18-01** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndrome. (A Nazha) 

*Submitted*

i. **CK18-02** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. (M Mei/ R Nakamura/ R Pillai) 

*Data File Preparation*

j. **CK18-03** Impact of donor age on the outcomes of allogeneic hematopoietic stem cell transplantation for myelodysplastic syndrome (G Murthy) 

*Analysis*


*Data File Preparation*

l. **CK19-01b** Outcomes after HCT for rare chronic leukemias: Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation. (B Dholaria/B Savani/M Kharfan) 

*Protocol Development*

5. **Future/Proposed Studies**

Dr. Sobecks thanked the investigators whose proposals were submitted, but not selected for presentation, emphasizing that two other proposals were dropped due to overlaps with current studies. He also reminded the audience of the voting process.

Dr. Bart Scott then announced the presenters for the first proposal and asked the audience to stand up to the microphones and present themselves before asking the presenter about their proposed studies.

a. **PROP 1911-08** Myelodysplastic/ myeloproliferative neoplasms unclassifiable- Transplant outcomes and factors predicting survival- Retrospective analysis of chronic leukemia working party of CIBMTR. (Patnaik/Sheth/Mangaonkar)

Dr. Abhishek Mangaonkar presented the proposal. The goals of the proposal are: 1) to perform outcome analysis related on non-relapse mortality, relapse incidence, leukemia-free survival and overall survival, engraftment and GVHD; 2) to assess the relevance of IPSS/IPSS-R, CPSS and DRI scores as prognostic scores after an allogeneic HCT and compare models. We identified 281 patients with a reported diagnosis of MDS/MPN-U, above 18 years of age which received an allo-HCT from an HLA-identical sibling or unrelated donor from 97 centers between years 2012 to 2019 with a median follow-up of 24 months. Dr. Mangaonkar emphasized the importance of using CIBMTR data due to the relative rarity of this disease, which would prohibit the conduct of randomized prospective trials or large retrospective studies. Therefore, we aim to utilize the unique resources of CIBMTR to answer these important clinical questions.

The proposal was opened for comments and questions. Dr. Scott raised a concern on the misclassification at diagnosis with other syndromes. A member asked if there is molecular data available to classify these patients. Dr. Saber replied we did not have information on molecular data, but we should have path reports attached. A concern was raised on low number of patients to have a study.
on prognostic risk factors. Lastly, a member of the audience suggested to combine efforts with EBMT working party to have a larger dataset.

b. **PROP 1911-36** Clinical results of allogeneic hematopoietic stem cell transplantation for hairy cell leukemia (Chihara/Kreitman/Pavletic)

Dr. Dai Chihara presented the proposal. The goals of the proposal are: 1) to estimate the probabilities of PFS and OS, as well as the cumulative incidences of relapse, NRM, grade II-IV and III-IV acute graft-vs-host disease (aGVHD), and chronic GVHD (cGVHD) for patients with HCL undergoing allo-HCT between 1983-2018 and descriptively describe outcomes; 2) to evaluate variables that may be associated with differences in HCT outcomes as a risk factor analysis, if power allows it. Between 1983 to 2018 a total of 26 allo-HCT patients were identified in the CIBMTR database; of which 22 patients were first allo-HCT transplants and 4 received a second allo-HCT. Dr. Chihara proposed a collaborative study with the EBMT-Chronic Malignancies Working Party. The EBMT cohort consists of 23 patients. Dr. Chihara emphasized that there is an unmet need for better and curative treatments in HCL patients. Due to the rarity of allogeneic hematopoietic cell transplant for HCL, a collaboration between CIBMTR and EBMT would potentially be the most appropriate way to obtain information for these patients to provide reference and guidelines.

The proposal was opened for comments and questions. Dr. Oran commented on the study years’ timeline being too wide on this study, explaining that practices have changed over the years, and suggested a stratified analysis by incremental years. Another comment was made concerning the low number of patients and trying to contact centers for cytogenetic reports for this study would be challenging and time consuming. A concern was raised on a possible selection bias in this study due to sicker patients being selected for transplant. Lastly, Dr. Nakamura commented on the limitations on small sample and how clinicians/researchers would use the study results in their practice and transplant/non-transplant research.

c. **PROP 1911-143** Outcomes of allogeneic hematopoietic cell transplantation for Myelofibrosis based on the conditioning regime. (Murthy/ Saber)

Dr. Guru Murthy presented the proposal. The goals of the proposal is to determine the overall survival (OS), disease free survival (DFS), non-relapse mortality (NRM), engraftment, graft failure, relapse rate, incidence of acute graft versus host disease (GVHD) and chronic GVHD based on the choice of conditioning regimen used in MAC and RIC setting, for patients with MF undergoing allo-HCT. They hypothesize that the outcomes of patients with myelofibrosis (MF) who undergo allogeneic hematopoietic cell transplantation (allo-HCT) might be differ based on the choice of individual conditioning regimen used, both with myeloablative conditioning (MAC) and reduced intensity conditioning (RIC). Between years 2000 to 2018, 1161 patients allo-HCT for primary MF or post ET MF or post PV MF with MAC/RIC were identified. Dr. Murthy emphasized that the proposed study would provide information about the differences in outcomes of allo-HCT for MF based on the individual conditioning regimen utilized.

The proposal presentation was then opened for comments and questions. One comment was regarding that there had been a similar EBMT study. It was also suggested to include only more recent years of transplants. A member of the audience suggested to exclude the other regimens category or to make a stratified analysis. A comment was made that this would be a challenging study since transplant regimens are patient and center dependent. Dr. Murthy replied that we could factor in disease risk and
center effect in the multivariable analysis. Lastly, a member of the audience suggested trying to use EBMT regimen classification vs the CIBMTR standard regimen definition.

d. **PROP 1911-225 The Impact of Somatic Mutations on Allogeneic Hematopoietic Cell Transplant Outcomes in Patients with Low and Intermediate Risk Myelodysplastic Syndrome**

Dr. Shukaib Arslan presented the proposal. The goals of the proposal are: 1) to evaluate HCT outcomes in patients with “lower-risk” MDS who underwent allogeneic HCT; 2) to identify clinical risk factors for HCT outcomes; 3) characterize the mutation profile in the “lower-risk” MDS and examine potential impact of somatic mutations on HCT outcomes. They hypothesized that in patients with “lower-risk” myelodysplastic syndrome (MDS) allogeneic hematopoietic cell transplantation (HCT) is a highly effective therapy with long-term survival, and somatic mutations have prognostic relevance. Dr. Arslan emphasized that this proposed study will be the first to describe the landscape of somatic mutations in this specific patient population and will also provide a unique opportunity to re-classify the risk category (IPSS-R very low/low/intermediate) in these patients using the new criteria incorporating somatic mutations. For this purpose, they propose to assay recurrent somatic mutations using biologic samples from the NMDP repository. They plan to fund this assay using philanthropic funds dedicated for MDS research at City of Hope. A total of 621 patients with very low, low, and intermediate risk MDS with biorepository samples from 2001 through 2016 that contained bio-samples. Around 41% of the identified patients for this proposal are overlap cases from Dr. Lindsley Coleman’s study. Dr Arslan mentioned that he will collaborate with Dr. Coleman to be consistent with previous publications. The proposal presentation was opened for comments and questions. A member of the audience commented on the study not considering differences in allelic frequencies. Another comment was made on a possible selection bias in this study since patients that were transplanted may be sicker. A question was made on how many cord bloods and haploidentical transplant patients were excluded. Dr. Arslan replied that we would have to look at the data. Another member commented that Dr. Coleman’s publication did not stratify IPSS. Lastly, a question was made on the possibility of adding a non-transplant arm for comparison.

Dr. Nakamura announced the presenters for the next 3 proposals.

e. **PROP 1911-245 Outcomes of allogeneic hematopoietic stem cell transplantation for patients with B-cell prolymphocytic leukemia.**

Dr. Punita Grover presented the proposal. The goals of the proposal are: 1) to determine the outcomes of HCT for B-PLL including PFS, OS, non-relapse mortality and cumulative incidence of relapse; 2) to identify patient, disease and transplant variables associated with outcomes. They hypothesize that allogeneic HCT is associated with long term PFS and OS in patients with B-PLL. For this proposal 71 patients with B-Cell PLL from 2000-2018 were identified, 17% of these patients were from the CRF track. Dr. Grover emphasized that there is a need to determine the patient population most likely to benefit from transplant and the CIBMTR would provide the largest cohort for this purpose. The proposal presentation was opened for comments and questions. A member of the audience asked on how the PI planned to confirm real cases of the disease. Dr. Saber replied that we could provide available pathology reports for the PI to evaluate diagnosis of B-cell PLL. Another comment was made on the low numbers of patients on the CRF track which contains detailed information for studying prognostic factors. Dr. Saber replied that could make a study of prognostic factors at diagnosis and transplant that we collect on the TED track. Another member asked if any CAR-T is used for treating these patients and if CIBMTR would collect this data. Dr. Saber replied we should collect patients that received any cellular therapy.
f. PROP 1909-06/PROP1911-04 Combined proposal: Transplant outcomes for patients with large granular lymphocyte (LGL) leukemia.

Dr. Mithun Shah presented the proposal on behalf of the groups who submitted similar concepts. The goals of the proposal are: 1) to study the patient- and transplant related characteristics in LGL leukemia patients undergoing stem cell transplant and 2) analyze transplant outcomes including relapse-free (RFS), transplant-related mortality (TRM), overall survival (OS), and cumulative incidence of graft-vs-host disease (GVHD). They hypothesize that stem cell transplant is a safe and effective treatment modality for patients with T- and natural killer (NK)-cell large granular lymphocyte (LGL) leukemia. This study would include 145 LGL leukemia patients undergoing HSCT between 2000 and 2018. Dr. Shah emphasized that this would be the largest cohort of LGL leukemia patients. The largest experience currently, is from EBMT consisting of 15 heterogenous patients.

The proposal was opened for comments and questions. A member on the audience asked about the accuracy of this diagnosis that has been reported to the CIBMTR and expressed concern regarding possible misclassification of the disease. Another member suggested a collaboration with the EBMT working party to have a bigger dataset which may then allow an evaluation of prognostic factors. Another member in the audience asked if bone marrow reports are submitted to the CIBMTR. Another suggestion was made with regards to limiting to the proposal to only patients who received allogeneic transplants.


Dr. Tania Jain presented the proposal on behalf of the groups who submitted similar concepts. The goals of the proposal are: 1) to determine clinical outcomes of patients who undergo HCT using a haploidentical related donor and determine patient, donor and HCT related factors that influence these outcomes and 2) compare clinical outcomes of patients who undergo haploidentical HCT using PTCy with matched related/unrelated HCT. The hypotheses for this study are: 1) that allogeneic HCT using a haploidentical related donor and PTCy based GVHD prophylaxis in myelofibrosis results in long-term remission; and 2) outcomes with haploidentical PTCy based HCT are comparable to matched related/unrelated donor HCT. Dr. Jain emphasized the importance of using CIBMTR, which contains the largest dataset of HCT for myelofibrosis. She mentioned that haploidentical donors are a small fraction of these transplants and this is a limitation regarding how best to guide physicians of the use of such transplants for MF. For this proposal we identified 515 PTCy haploidentical HCT adult patients from years 2013 to 2018 diagnosed with primary myelofibrosis, post-polycythemia myelofibrosis, post-essential thrombocythemia myelofibrosis.

The proposal presentation was opened for comments and questions. A member on the audience asked on the possible profile change for MF patients with the introduction of Jakafi in recent years. The PI suggested we could stratify by Jakafi use if possible. Dr. Saber asked PI what is the expected difference that Dr. Jain expects. Dr. Jain replied that she expected between 10-15% differences. Dr. Saber stated that PhD Statistician had run power calculations and the study is currently underpowered for comparisons and proposed a descriptive study. Lastly, a member in the audience asked why include unrelated donors. Dr. Jain was open to eliminate this group.

2 additional proposals were submitted but not presented as listed below:

a. PROP 1911-116 Identifying the Optimal Allogeneic Transplantation Strategy for Primary and Secondary Myelofibrosis. (Patel/Prchal/Couriel) Dropped due to overlap with CK17-01 study.

b. PROP 1911-214 Retrospective Analysis of Transplant Outcomes in Patients with T-cell Prolymphocytic Leukemia (T-PLL) Treated with Allogeneic or Autologous Stem Cell Transplant (Saba/Hajja/Safah/Socola) This proposal was triaged to the Acute Leukemia WC and dropped due to overlap with CK19-01a study.
6. Study Results Presentations
Dr. Saber asked our incoming chair Dr. Betul Oran to present the results of study CK17-02 “Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes” which she presented at the 2019 ASH meeting. The goal of this study was to compare outcomes between Fludarabine/Melphalan (FM) and Fludarabine/Busulfan (FluBu) based RIC for older MDS patients (60≥) between 2007-2016. The study concluded that FM led to a lower incidence of relapse compared with FluBu, which continued to be appreciated within different MDS risk groups by CIBMTR risk score. Also, that treatment related mortality (TRM) was higher in patients with FM within the first 4 months after transplant compared to FluBu. After 5 months of transplant, TRM was comparable between the groups. Another finding was an increase in aGVHD grade II-IV, but not in aGVHD grade III-IV incidence with the use of FM compared with FluBu. Lastly, FM was associated with superior DFS and overall survival compared with FluBu due to reduced RI despite higher TRM in older MDS patients.

7. Other Business
The meeting was adjourned at 2:15 p.m.
The chairs of the working committee, scientific director and statisticians had a post-WC meeting afterwards. After the new proposals were presented, each attendee had the opportunity to vote on the proposals using the provided voting sheets. Based on the voting results, current scientific merit and impact of the studies on the field, the following study were decided to move forward as the committee’s research portfolio for the upcoming year:

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<th>Study number and title</th>
<th>Current status</th>
<th>Goal with date</th>
<th>Total hours to complete</th>
<th>Total hours to goal</th>
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<th>Hours allocated 7/1/2020-6/30/2021</th>
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<td><strong>CK12-01</strong>: Optimal timing of allogeneic stem cell transplantation for chronic myeloid leukemia patients in the tyrosine kinase inhibitor era</td>
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<td><strong>CK15-03a</strong>: Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm</td>
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<td><strong>CK16-01</strong>: Identification of germline predisposition mutations in young myelodysplastic syndrome patients</td>
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<td><strong>CK16-02b</strong>: The benefit of donor lymphocyte infusion in the tyrosine kinase inhibitors era in chronic myeloid leukemia post allogeneic hematopoietic cell transplantation</td>
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<td>CK17-01: Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation</td>
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| **Bart Scott**  
| **CK15-03** Outcome of allo-HCT for AML with history of Ph- MPN |
| **CK16-01** Identification of germline predisposition mutations in young MDS patients. |
| **CK16-02a** Contemporary role of tyrosine kinase inhibitors post allogeneic hematopoietic stem cell transplantation for advanced phase chronic myeloid leukemia. |
| **CK16-02b** Donor lymphocyte infusion vs. tyrosine kinase inhibitors in chronic myeloid leukemia post allogeneic hematopoietic cell transplantation. |
| **CK18-02** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. |
| **Ryotaro Nakamura**  
| **CK18-01** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndromes. |
| **CK17-01** Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation. |
| **CK19-01b** Outcomes after HCT for rare chronic leukemias: Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation. |
| **Betul Oran**  
| **CK20-01** Outcomes of allogeneic hematopoietic cell transplantation for Myelofibrosis based on the conditioning regime. |