November 2014 Newsletter

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Perspectives

By Paul Maris, MD

My wife and I joke that the second most gratifying sentence for me to hear is “You were right.” The CIBMTR has received 146 new research proposals for review during the 2015 BMT Tandem Meetings. The Working Committees will evaluate these proposals based on their scientific merit, feasibility, and the CIBMTR’s ability to complete the study in a timely fashion. Let me explain how “You were right” relates to these proposals.

During a laboratory meeting early in my fellowship training, a senior audience member challenged one of my ideas. I replied, “Well, it’s just a hypothesis.” The audience member was rightly outraged, because I had unwittingly trampled on the most sacred intellectual core of science. On another occasion several years later, I sought help from a faculty member after a grant application had received a poor review. After some discussion, he asked a simple question: “What is your hypothesis?” I was quite taken aback because I had not previously viewed the project from that perspective. With some quick thinking, I managed to articulate a reasonable hypothesis based on my preliminary data. He then asked, “Why don’t
you test your hypothesis?” The resubmitted application received a favorable review because I had framed each aim around a test of this hypothesis.

Working Committees have been encouraged to emphasize impact and feasibility as the primary considerations when proposed studies are evaluated. High impact studies have the potential to change clinical practices, improve clinical outcomes, or enhance biological understanding in a way that would enable the development of better treatment strategies. High impact studies fill important gaps in knowledge about HCT, for example, by providing preliminary data for a clinical trial or information to support insurance coverage. Studies are most feasible when the necessary data and the scientific and statistical expertise are already available within the CIBMTR.

The hypothesis is a frequently underemphasized element in study proposals and Working Committee evaluations. During the 2014 BMT Tandem Meetings, Working Committees reviewed 88 proposed new studies. The minutes of these discussions used the word “hypothesis,” “hypotheses,” “hypothesize,” or “hypothesized” only 12 times.

Retrospective observational studies using the CIBMTR Research Database can come across as descriptive “data mining.” To paraphrase Lewis Carroll, if you don’t know where you are going, any road will get you there. Without question, these studies often yield very interesting and informative results that can have significant impact, but in essence, the reports are saying, “Look what we found!”

In Section III of the Study Proposal Outline, investigators are asked to state the hypothesis of the study, which is described as the “scientific assumption that is the basis of the study.” The hypothesis involves a specific prediction to be tested, or as Lewis Carroll might have put it, “When we take this path, we will meet the Red Queen.”

Instead of combing through the mine in hopes of finding something valuable so that we could say, “Look what we found;” we should say, “When we look here with this method, we will find the diamond.” Finding the diamond then becomes more a matter of predictive insight and skill and less a matter of luck. For me, at least, showing how I was right is much more gratifying than showing how I was lucky.

Graft Sources and Manipulation Working Committee

The Graft Sources and Manipulation Working Committee (GSWC) addresses scientific questions related to the comparative effectiveness of the three most commonly used graft types, quality, and manipulation. It is one of the most active and prolific committees of the CIBMTR. This committee has collaborated with other registries, national and international, and the resulting publications have led to practice changes with respect to graft choices when considering HLA-matched sibling and unrelated donor transplantations for leukemia, the use of T cell depletion in reduced intensity transplants, selection of cord units, and the use of cord blood as a stem cell source for patients with hematological malignancies. Our primary collaborators are Eurocord and the Acute Leukemia Working Party of the EBMT.

The committee is chaired by Daniel Fowler, MD (NIH-NCI Experimental Transplantation and Immunology Branch); Miguel-Angel Perales, MD (Memorial Sloan Kettering Cancer Center); and Vanderson Rocha, MD (Churchill Hospital). The chairs are assisted by Scientific Director, Mary Eapen, MD, MS, and statisticians Junfang Chen, MS, MA, and Mei-Jie Zhang, PhD, as well as Stephen Spellman, MBS, Director for Immunobiology Research.

Committee membership is comprised of investigators of diverse backgrounds and experience in clinical transplantation and cell processing and manipulation, providing the opportunity for synergy in scientific interactions, stem cell technology development, and new ideas. The committee has a significant publication track record with 17 publications in the past 5 years, and several of the publications in high impact journals were conducted jointly with Eurocord and EBMT. A full list of the GSWC’s studies, including recent publications in available on the CIBMTR website.

The committee was one of three committees that were recognized as outstanding by the CIBMTR Advisory Committee after the 2013-2014 review of the CIBMTR’s Scientific Working Committees. “These committees were identified because of their strong promotion of studies that will have a notable impact on the field, willingness to forgo studies that will not have a significant impact on the field, and focus on the effective use of CIBMTR resources. In addition, these committees have cultivated external collaborations and are notably well-organized and highly productive.”

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The committee has several on-going projects that address current issues related to donor and/or graft selection for allogeneic transplantation. The success of the committee is dependent on scientific interactions, new ideas, and active participation of junior and senior investigators. Please contact one of the Chairs or the Scientific Director to learn more about the committee or to discuss ideas and new projects.

**Late Effects and Quality of Life Working Committee**

The Late Effects and Quality of Life Working Committee (LEWC) conducts clinical research on late effects following HCT. The committee takes advantage of the large clinical database of the CIBMTR to study these effects, many of which are relatively rare in individual centers.

The LEWC is headed by three co-chairs who are internationally recognized experts in the field. The current co-chairs are: Christine Duncan, MD (Dana Farber Cancer Institute); Bipin Savani, MD (Vanderbilt University Medical Center); and Mary Flowers, MD (Fred Hutchinson Cancer Center). The chairs are assisted by the Scientific Director, Bronwen E Shaw, MD, PhD, who has very recently succeeded Navneet S. Majhail, MD, MS. Additionally, the chairs are assisted by statisticians Ruta Brazauskas, PhD, and Heather Millard, MPH.

The committee meets annually in person at the BMT Tandem Meetings, and the co-chairs (with CIBMTR support staff) meet monthly by teleconference to ensure the timely completion of projects as well as to reassess priority areas and promote and develop the scientific agenda.

Previously, the committee identified target areas of post-transplant late-effects that deserve specific attention, including fertility and liver toxicity. These interests have led to several publications in these topics, which help to inform those working in the field of incidence and risk factors and also to recommend practice.

With this in mind, in 2013 the LEWC sent a survey to the international membership to identify key areas where recent or comprehensive clinical guidelines were lacking. Almost 100 members responded, and based on the priorities identified, the first topic area (second malignancy screening) has already been addressed by an active working group, with a manuscript soon to be published. A second topic will be launched soon.

Another area of intense interest to the committee is quality of life and patient-reported outcomes following transplant. Efforts are actively underway in the committee to harmonize and generalize the collection and analysis of such data. A full list of the LEWC's studies, including recent publications, is provided on the [CIBMTR website](http://www.cibmtr.org).

**2015 BMT Tandem Meetings Return to San Diego**

**By D'ette Waicloch, CMP**

The BMT Tandem Meetings - the combined annual meetings of the CIBMTR and ASBMT - are North America's largest international gathering of blood and marrow transplant clinicians and investigators, laboratory technicians, advanced practice professionals, transplant nurses, pharmacists, administrators, and clinical research associates since 1999.

Leading experts will convene at the Manchester Grand Hyatt San Diego February 11-15 to present the latest developments in blood and marrow transplantation during the BMT Tandem Meetings. Scientific Program Chairs for the 2015 meetings are Paul Veys, MD, for the CIBMTR and Krishna Komanduri, MD, for ASBMT.

Keep an eye on [www.cibmtr.org](http://www.cibmtr.org) or [www.asbmt.org](http://www.asbmt.org) to create your own personal meeting agenda. The online registration and housing deadline is January 9, 2015. After registering, take advantage of special conference guest room rates at the Manchester Grand Hyatt and neighboring hotels. Remember to reserve your ticket to the Saturday evening Tandem Reception aboard the USS Midway to end a memorable week with colleagues and good friends!

Questions regarding support opportunities at the 2015 BMT Tandem Meetings may be directed to Sherry Fisher at [sfisher@mcs.edu](mailto:sfisher@mcs.edu).

For general information, please email the conference office at [bmttandem@cs.com](mailto:bmttandem@cs.com).

We look forward to seeing you in San Diego!
Blood and Marrow Transplant Clinical Trials Network

By Amy Fodey, MA

The BTCTN, with its 20 core and approximately 100 affiliate centers, has enrolled over 7,000 patients since 2003. The CIBMTR shares administration of the BTCTN Data and Coordinating Center with NMDP and The Emmes Corporation. Together, these three organizations support all BTCTN activities.

The BTCTN Steering Committee is currently under the leadership of Chair Fred Appelbaum (Fred Hutchinson Cancer Research Center), Steve Devine (Ohio State University Medical University) continues to serve as Vice Chair, and Gina Laport (Stanford University) is serving as Immediate Past Chair.

2014 State of the Science Symposium: Learn More

The BTCTN hosted a two-day State of the Science Symposium (SOSS) during the 2014 BTCTN Tandem Meetings. The Symposium had two purposes: 1) review recent scientific advances in the field of stem cell transplantation and 2) identify the most compelling opportunities for clinical research appropriate for the BTCTN in the next several years.

A report from the SOSS will be presented at the ASH Annual Meeting in San Francisco. See the article below for details and registration!

In addition, a summary of the SOSS proceedings and decisions has been published in the BMJ:


Clinical Trials: Open Enrollment

The BTCTN encourages widespread transplant community participation in clinical trials. If your center is interested in participating, please visit the BTCTN website at http://www.bmtctn.net.

There are eight trials open, one released to sites, and three in development. The following BTCTN trials are open or will soon be opened for enrollment:

- **BMT CTN 0903** - Phase II study for allogeneic transplantation for hematologic malignancy in HIV+ patients
- **BMT CTN 1101** - Phase II study comparing HLA-haploidentical related donor bone marrow vs. double umbilical cord blood (haplo vs. double cord) with RIC for patients with hematologic malignancy
- **BMT CTN 1102** - Biologic assignment trial comparing RIC HCT to hypomethylating therapy or best supportive care in patients aged 50-75 with intermediate-2 and high-risk myelodysplastic syndrome
- **BMT CTN 1202** - Prospective cohort of biologic samples for the evaluation of biomarkers predicting risk of complications and mortality following allogeneic HCT
- **BMT CTN 1203 PROGRESS I** - Randomized Phase II study of novel approaches for GVHD prophylaxis compared to CIBMTR controls
- **BMT CTN 1204** - RIC for children and adults with hematopoietic syndromes or selected primary immune deficiencies
- **BMT CTN 1205** - Easy-to-read Informed consent for HCT clinical trials
- **BMT CTN 1301 PROGRESS II** - Randomized, Phase III trial of calcineurin inhibitor-free interventions for prevention of graft-versus-host disease
- **BMT CTN 1304 / DFCI 11-010** - Phase III study comparing conventional dose treatment using a combination of lenalidomide, bortezomib, and dexamethasone (RVD) to high-dose treatment with peripheral stem cell transplant in the Initial management of myeloma in patients up to 65 years (Note: this study is managed by Dana Farber Cancer Institute, but BTCTN has endorsed the study and is providing accrual credit to BTCTN centers)

Recent Presentations
Leveraging Resources to Design, Conduct, and Analyze Hematopoietic Stem Cell Transplant Clinical Trials: The Ongoing Collaboration between the Center for International Blood and Marrow Transplant Research and the Blood and Marrow Transplant Clinical Trials Network.

Interscience Conference on Antimicrobial Agents and Chemotherapy, September 2014

BMT CTN D01: William Hope

Relationship between Voriconazole Concentrations and the Probability of Breakthrough Fungal Infections.

Recent Publications

There are 47 BMT CTN published articles, including 14 primary analyses. The following manuscripts were recently accepted / published. (Manuscripts reporting primary results are bolded.)


Social Media Accounts Launched!

To get up-to-date information about BMT CTN studies, meetings, and news:

- Like us on Facebook: www.facebook.com/bmtctn
- Follow us on Twitter: @BMTCTN

Registration Open for Symposium: Report from BMT CTN SS14

The NMDP/Be The Match® recently opened registration for A Report from the Blood and Marrow Transplant Clinical Trials Network State of the Science Symposium 2014 preceding the 2014 ASH Annual Meeting. Earlier this year, the BMT CTN selected the highest priority projects for the next 7 years after bringing together 12 committees in HCT to address critical issues and present proposals for the future.

This CME symposium will allow attendees to quickly learn about the prioritized clinical trials in areas including: AML/MDS, non-Hodgkin lymphoma, myeloma, post-transplant care, and eight other research priorities. During an interactive panel discussion, attendees will talk with clinical trial leaders about strategies for conducting successful clinical trials in the current healthcare era.
The symposium will be held on Friday, December 5, 2014, from 7:00 to 11:00 a.m. in the Moscone Center, in San Francisco, CA. Pre-registration is encouraged. Registration and additional information, including a program description and other event details, are available on the Be The Match website. Encourage your colleagues in transplant and those who refer for transplant to attend, too.

Recent Accomplishments of the RCI BMT
By Rebecca Drexler

The RCI BMT is a CIBMTR program that offers infrastructure and support for a wide array of clinical studies, including multi-center trials, surveys, and quality of life assessments. Since the recent departure of Dr. Willis Navarro, Dr. Dennis Confer, CIBMTR Associate Scientific Director, has assumed oversight of the program with the assistance of the Senior Manager, Rebecca Drexler, and her team. Together with guidance from the senior leadership of the CIBMTR, the RCI BMT continues to develop new projects and support ongoing studies and projects.

Highlights of Recent Accomplishments
We closed the adult accrual to RDSafe, our multi-institutional study of HCT donor safety and quality of life. In May 2013. Pediatric accrual closed in July of this year. A total of 1,507 adults and 300 pediatric donors were accrued. An abstract has been accepted for the 2014 ASH meetings reporting on the adult population. Two abstracts have also been submitted to the 2015 Tandem meetings: 1) comparison of early toxicities of related vs. unrelated donors and 2) comparison of quality of life of older adult related donors vs. younger ones.

The RCI BMT has been involved in a collaboration with the Pediatric Blood and Marrow Transplant Consortium (PBMTC) since 2009, which continues to be active and productive.

- The initial study, 09-MRD, to investigate the role of minimal residual disease (MRD) testing before and after HCT for pediatric AML, continues to enroll patients with H9 enrolled of the targeted 150 or 99% of goal.
- In September 2013, the second PBMTCT trial was opened, 11-TREO, a multi-center study evaluating a fixed regimen of treosulfan, fludarabine, and low dose total body irradiation in children with AML or MDS undergoing allogeneic HCT. Accrual for this study was quicker than expected and completed with our total of 40 on May 2, 2014.
- The third project, 12-MOXE, a phase II, open-label, non-randomized, prospective study to evaluate the activity, safety, and feasibility of administration of moxetumomab pasudotox in the pre-allogeneic HCT setting to patients with B-lineage ALL who have pre-transplant MRD is currently awaiting a response from the FDA to proceed with site preparations.
- The fourth project, 13-TLEC study, will prospectively collect comprehensive information about HCT late effects with particular emphasis on renal, cardio-metabolic, and skeletal toxicities. In addition, it will establish a biologic sample repository from this large cohort of survivors of childhood HCT. This study is in the process of site preparation and activation. Accrual is expected to begin early this winter.

The RCI BMT continues to support a number of other studies and projects including collaboration with the Health Services Research Program to develop a randomized study supported by a federal PCORI (Patient-Centered Outcomes Research Institute) grant. The study will compare an individualized survivorship care plan template with usual care. Site preparation and activation is in process with accrual expected to begin early this winter.

Health Services Research Program’s Many Projects
By Navneet Majhail, MD, MS, and Ellen Denzer, MS

The holidays are a time for rejoicing and things usually slow down (at least on the transplant inpatient units). However, the CIBMTR Health Services Research (HSR) Program, which is conducted in partnership with Be The Match Patient and Health Professional Services, continues to remain busy with several ongoing projects.

The big kahuna project within the program is the PCORI funded project, “Individualized Care Plans for Hematopoietic Cell Transplant Survivors”. We were really proud to receive this grant and have dedicated most of our mojo and sweat into making sure we successfully get this project off the ground. The study has two parts. The first phase, which has already been completed, involved focus groups of
three populations to understand what / how / when they wanted a treatment
summary and survivor care plan:

- Patients and their caregivers
- Transplant center doctors, mid-level providers, nurse coordinators, and
  social workers
- Primary care and hematology-oncology doctors and mid-level providers.

Our HSR team then tirelessly toiled through approximately 80 interview transcripts
to identify common themes. (They had the help of qualitative analysis software).
Using this information, we came up with a template that provides a personalized
survivor care plan based on published long-term follow-up guidelines plus
individual patient data submitted by centers to the CIBMTR.

We are currently on act two of this study, and we are getting ready to roll out a
randomized trial to one- to two-year survivors, where half will get the individualized
care plan and the other half won’t. We will then see whether there is any impact on
their understanding of survivorship care and healthcare behaviors. Thanks to
the courage, dedication and devotion of our RCI BMT team, we will be starting this
500 patient study at approximately 20 centers soon. Hats off to the protocol team,
especially our patient representatives, who keep reminding us of what is really
important to our patients and caregivers. We have also learned through this
process that compared to actually doing the study, getting the grant is usually
the easier part of the project (although it never feels that way when the grant is being
written / submitted).

The HSR Program is also participating in the BMT CTN 1206 (Easy To Read
Informed Consent – ETRIC) study. This trial has a sub-study that involves semi-
structured interviews of transplant center principal investigators, coordinators, and
IRB administrators to understand what it will take for centers to implement a better
consent form. Two of our team members, Ellen Denzen and Heather Moore, went
around to 10 BMT CTN centers and interviewed approximately 80 people. After
their first set of interviews, they learned that having candies at hand goes a long
way in soothing and bringing out the best in people. Our team really appreciated
the willingness of these centers to participate and the help they received locally to
set up the interviews. We are currently transcribing and analyzing the interview
transcripts. Although this involved a lot of hard work and coordination, Ellen and
Heather were able to rake in some frequent flier miles.

We continued our quest for additional projects and worked with NMDP’s Payor
Policy and Medical Marketing departments to successfully obtain the National
Comprehensive Cancer Network’s Independent Grant for Learning and Change in
order to identify practice gaps and improve care of patients with rare cancers. The
project, titled “Payer-partnered approach to community based referral for HCT,” will
conduct a market survey of referring hematologists-oncologists to understand their
perceptions, knowledge, and referral practices for transplantation and will partner
with a payer to investigate educational interventions for physicians who refer
patients to transplant centers. We are currently developing a protocol for this
project.

The NMDP’s System Capacity Initiative continues in full force, and the HSR
Program supports several of its activities. A survey of transplant provider burnout
and wellbeing is under development (finally, something about our quality of life),
and a survey of patient housing and caregiver needs is nearing completion. Last
but not least, we are data geeks and can spend endless hours talking about claims
data. We continue to try our best to figure out if ICD9 codes can be used to learn
something about quality and costs of transplantation.

As always, we are ever eager to work with collaborators. If you have ideas, please
do not hesitate to contact Ellen (edenzen@nmdp.org) – and yes, you will get
special consideration if you share our excitement about ICD9 codes.

**CPI Program for Autologous Transplants**

*By Janet Brunner, PA-C, and Marie Matlack*

On September 30, the CIBMTR announced that, over the next year, we will be
phasing in a CPI program for autologous transplants. This program will include
autologous transplants that occurred on or after December 3, 2007. Reporting for
autologous transplants that occurred prior to December 3, 2007, will still be
ongoing but will not be included in this new CPI program. The first phase was
launched in early October when CRCs sent transplant centers in the US a CPI
forms due report listing the autologous forms due at their center.

Below is the comprehensive implementation plan:

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January 2015 reporting period: Monitor only
Monitor autologous forms submission with the earliest completion date of December 3, 2007, through August 31, 2014.

May 2015 reporting period: Partial Implementation at 75%
To meet CPI “good standing” criteria, 75% of the autologous forms with the earliest completion date of December 3, 2007, through December 31, 2014, must be submitted and completed.

September 2015 reporting period: Fully Implemented at 90%
To meet CPI “good standing” criteria, 90% of the autologous forms with the earliest completion date of December 3, 2007, through April 30, 2015, must be submitted and completed.

If any center has concerns about being able to achieve the CPI “good standing” criteria by September 2015, they should contact their CRC to work with them to develop an individual plan tailored to meet the specific needs of their center.

Three New Study Summaries Posted for Patients
By Jessica Gillis-Smith, MPH
The CIBMTR Consumer Advocacy Committee was created in 2005 as a subcommittee of the Advisory Committee to communicate CIBMTR research results and data to the non-medical community and to provide patient and donor perspectives during the development of the CIBMTR research agenda. Many members have personal experience as a donor, recipient, or family member. One of the main initiatives of this committee is to assist in translating published research articles into lay summaries.

Committee members determine which research articles are most applicable to patients and family members, and the lay summary is created collaboratively with the CIBMTR’s Medical Writer, the first author of the research article, Consumer Advocacy Committee members, and members of the NMDP Patient Services Writing Team. In the past few months, three new summaries have been added to the CIBMTR Patient Resources webpage:

- **Very Few Donors have Severe Side Effects from Donation: Blood Stem Cell Donors have Fewer than Bone Marrow Donors (PDF)**
- **Alo Transplant Helps Some Older Patients with AML (PDF)**
- **Alo Transplant Helps Some Children with Neuroblastoma (PDF)**

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CIBMTR Advisory Committee
The Advisory Committee, made up of members from across the globe, maintains careful oversight of the CIBMTR research agenda. The **2014 committee members are listed on the CIBMTR website**, and we sincerely thank all of our committee members for their time and efforts.

Our Supporters
The CIBMTR is supported by Public Health Service Grant / Cooperative Agreement U24-CA76518 from the NCI, NHLBI, and NIAID; a Grant / Cooperative Agreement 5U10HL69294 from NHLBI and NCI; a contract HHSF250201200016C with HRSA / DHHS; two Grants N00014-13-0039 and N00014-14-0028 from the Office of Naval Research; and grants from our corporate and private contributors, which are listed on the CIBMTR website.

Abbreviations
Need an acronym defined? **Review our list of common abbreviations.**
CIBMTR® (Center for International Blood and Marrow Transplant Research®) is a research collaboration between the National Marrow Donor Program®/Be The Match® and the Medical College of Wisconsin.