November 2018 Newsletter

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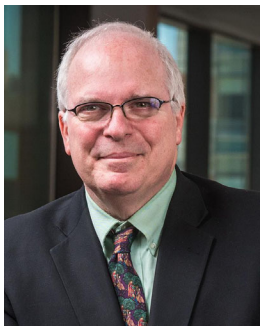
Perspectives

By Robert Soiffer, MD



A Prospective Randomized Double-Blind Trial of ... vs. ..., That's the Holy Grail, what we clinical investigators are always itching for. In the past 16 years, the BMT CTN has performed a number of relatively large prospective randomized trials covering many areas. Most, unfortunately have been negative studies. Voriconazole prophylaxis did not improve fungal free survival after allo-transplant. Mobilized peripheral blood stem cell transplant did not improve relapse, transplant-related mortality, or survival compared to bone marrow from matched unrelated donors. Sirolimus prophylaxis did not improve GVHD free survival compared to methotrexate. Double umbilical cord blood transplantation was not superior to single cord transplant in pediatric patients. Radiolabeled CD20 antibody did not reduce relapse rates when added to BEAM conditioning. Mycophenolate mofetil did not improve GVHD response and survival in patients with newly diagnosed GVHD. Tandem autologous / allogeneic transplantation was not superior to tandem auto-transplant (biologic assignment). Reduced intensity transplantation was not superior (and clearly inferior in some subsets) in patients aged 18-65 transplanted for AML / MDS. Now we are not batting .000. We did demonstrate that lenolidomide maintenance after auto-transplant for myeloma leads to superior progression free and overall survival. There are currently three trials which have completed accrual (sirolimus vs. prednisone for low risk acute GVHD, haplo vs. cord for RIC transplant, and CD34

selection vs. PTCy vs. tac / mtx as GVHD prophylaxis) that is hoped to be read out in 2019. One trial testing gilteritinib as maintenance after transplant for FLT3-ITD+ AML is currently accruing. Also, a randomized Phase II trial, post-transplant cyclophosphamide was superior to CIBMTR concurrent controls in terms of chronic GVHD free relapse free survival and will now be the subject of a prospective randomized trial.

So what have we learned and what can we do? My predecessor as Chair of the CIBMTR Advisory Committee, Paul J. Martin, MD, Fred Hutchinson, has taught us over and over again not to believe everything we see, even it is with our own eyes. He has pointed out that the road to perdition is paved with "promising" Phase II trials that often do not pan out when subjected to the scrutiny of a randomized controlled trial. Why is that?

1. It might be that the patients studied in an initial single arm trial are highly selected and not representative of the broader population participating in a multicenter randomized trial.
2. The initial interpretation of successful outcomes in the single arm trial may be overstated.
3. The randomized trial may be underpowered to demonstrate a significant difference between arms because we underestimate the performance of the control therapy.
4. For practical purposes, we overestimate benefits in trial design because we simply do not have enough patients available to answer the question properly and therefore unwittingly doom the trial to failure. Maybe if some controls were included in the initial Phase II trials rather than having relied on historical comparisons, we would have had a more accurate sense of the potential success of some of our large Phase III undertakings.

However, we should not hang our heads about negative results from so many of these trials. In fact, we should not even use the word "negative". In many of these studies, we have demonstrated that our transplant community should not necessarily be so eager to adopt the new kid on the block, just because the cool kids have done so. For instance, it is critically important to know that mycophenolate mofetil does not improve outcomes of patients with GVHD or that peripheral blood use in matched unrelated ablative transplants does not improve survival and leads to worse chronic GVHD, etc. Without these trials we would be doing our current and future patients a grave disservice.

It is surely tempting to proceed with single arm trials, particularly with new agents. The FDA has traditionally required randomized trial for registration but recently approved a spate of therapies including IDH1 and IDH2 inhibitors for patients with AML carrying those mutations, CD19 CAR T cells for patients for lymphoma and ALL, and even ibrutinib for steroid refractory chronic GVHD all based on modestly sized single arm Phase II experiences. However, when contrasting available therapies, I confess I still am addicted to the Phase III prospective randomized trial, but we need to be aware of the limitations of the single arm data on which these trials are based. The CTN and CIBMTR are working hard to develop novel trial designs with sophisticated statistical modeling to help answer critical questions in our field whether through single arm or randomized studies. But they can only succeed with the participation and dedication of all our constituent institutions accruing to trials rapidly in the service of our present and future patients.

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2019 | TCT Transplantation and Cellular Therapy Meetings of ASBMT and CIBMTR

By Tia Houseman

The TCT | Transplantation & Cellular Therapy Meetings of ASBMT and CIBMTR (formerly known as BMT Tandem Meetings) is the combined annual meetings of the CIBMTR and ASBMT. This has been 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.

Scientific Program Co-Chairs for the 2019 Meeting, Jane Apperley, MD, (CIBMTR), and Gay Crooks, MD, (ASBMT), along with the scientific organizing committee and session chairs have put together an amazing program. Over the course of five

days, leading experts in the field of transplantation and cellular therapy from around the world will present the latest developments during plenary, concurrent, oral abstract, and poster sessions.

Registration and Housing

Registration and additional details can be found on the 2019 TCT Meetings webpage. The last day for general registration rate is Tuesday, January 22. Once you have registered, take advantage of special conference guest room rates offered at several hotels in the TCT Meetings housing block. All hotels in the housing block are located within 0.6 miles of the TCT Meeting venues.

TCT Meetings Reception on Saturday, February 23

Reminder to reserve your ticket to the Saturday, February 23, evening TCT Reception at the Hilton Americas-Houston to end a memorable week with colleagues and friends!

Networking Opportunities

several networking opportunities are offered during the TCT Meetings including poster sessions, networking reception, TCT Meetings Reception, and more.

Support Opportunities and Additional Information

Questions regarding support opportunities for this year's TCT Meeting, may be directed to the TCT Meetings Conference Office.

We look forward to seeing you at the Hilton Americas-Houston and George R. Brown Convention Center (GRB) in Houston, Texas, February 20-24, 2019.

Join the Conversation: #TCTM19

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Plasma Cell Disorders and Adult Solid Tumors Working Committee

Committee Leadership

Co-Chairs

Tomer M. Mark, MD, University of Colorado Hospital

Shaji Kumar, MD, Mayo Clinic Rochester

Nina Shah, MD, University of California San Francisco Medical Center

Scientific Director	Assistant Scientific Director	Statistical Director	Statistician

[Parameswaran Hari, MD, MS](), CIBMTR Milwaukee

[Anita D'Souza, MD](), CIBMTR Milwaukee

[Raphael Fraser, PhD](), CIBMTR Milwaukee

[Omar Dávila-Alvelo, MPH, MS](), CIBMTR Milwaukee

Multiple myeloma is the most common indication for HCT in the US. The Plasma Cell Disorders and Adult Solid Tumors Working Committee works with investigators from around the world to define the optimal utilization of transplantation for not only multiple myeloma but also other plasma cell disorders, such as light chain amyloidosis, Waldenstrom macroglobulinemia, and plasma cell leukemia. Since 2014, adult solid tumors are also included within our focus.

We have six ongoing projects, including cell transplantation for primary plasma cell leukemia, impact of bortezomib in light chain amyloidosis, racial discrepancy in clinical outcomes of multiple myeloma with cytogenetic abnormalities, age discrepancy in clinical outcomes of multiple myeloma patients, deriving a prognostic score for multiple myeloma patients undergoing HCT, and others. Noteworthy accomplishments from this committee in the last year include seven peer-reviewed publications between 2017 and 2018, two presentations at the American Society of Hematology Annual Meeting, one presentation at Genitourinary Cancers Symposium of the American Society of Clinical Oncology, and one presentation at the European Society for Blood and Marrow Transplantation Annual Meeting.

This past year we received 18 proposals, 10 of which were presented at the 2018 BMT Tandem Meetings; 3 were accepted as studies. The Plasma Cell Disorders and Adult Solid Tumors Working Committee is always seeking interesting and novel ideas for study as well as encouraging involvement of junior investigators and those wanting to break into the field of BMT and outcomes research. We believe early involvement encourages long-term participation of young investigators in committee activities.

Our committee provides a platform for consolidating ideas from oncologists across the country regarding the role of transplant in the management of multiple myeloma, light chain amyloidosis, Waldenstrom's macroglobulinemia, and germ cell tumors. The CIBMTR houses the largest set of data related to transplantation outcomes for these disorders. By serving as a partner for researchers, we leverage the power of big data to undertake projects and answer questions that would be impossible for a single institution to accomplish. This is particularly relevant for the rare plasma cell disorders for which no institution would have adequate numbers to answer any critical questions related to treatment. As a byproduct of the collaborative process, stronger connections and commitment to the overall mission of the CIBMTR are achieved, and a positive feedback loop results. The vision of the committee is to keep the positive feedback loop alive and have it lead to greater national and international integration of transplant-related research that will accelerate discovery of cures for patients afflicted by these diseases.

The success of the Committee depends on new ideas and testable hypotheses as well as participation by individuals with different perspectives and scientific backgrounds. The Plasma Cell Disorders and Adult Solid Tumors Working Committee encourages all investigators with an interest in our disease focus to propose a study. Information on how to propose a study can be found on the CIBMTR How to Propose a Study webpage.

To learn more or to discuss your research ideas and proposals, contact one of the members of the Working Committee leadership team.

We encourage our 345 current Working Committee members to actively participate. We look forward to seeing everyone at the upcoming February 2019 TCT Meetings in Houston, Texas.

View planned, in-progress, and completed studies and publications on the Plasma Cell Disorders and Adult Solid Tumors webpage.

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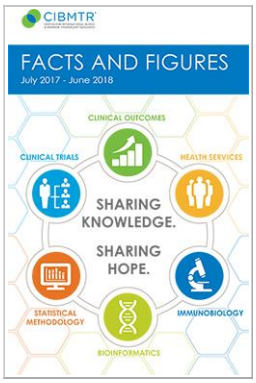
CIBMTR 2018 Facts and Figures



The CIBMTR fiscal year 2018 Facts and Figures document is now available to view on the CIBMTR Administrative and Progress Reports webpage.

This document provides an annual summary of the CIBMTR's accomplishments in each research program, key publications, and high priority initiatives.

Email contactus@cibmtr.org if you would like a printed copy or copies mailed to you.

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CIBMTR Trivia

The CIBMTR's Research Database has information on more than _____ transplant patients.

A. 415,000
B. 435,000
C. 465,000
D. 495,000

Enter your answer online. If you answer correctly, you will be entered into a drawing to win a CIBMTR prize.

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RCI BMT Monitoring Program

By Erin Leckrone

The RCI BMT monitors clinical studies to ensure integrity of data and to verify fulfillment of investigator obligations. The RCI BMT utilizes a risk-based approach to identify, evaluate, and mitigate risks that could impact the quality or safety of a study and to ensure resources target those institutions at highest risk for study and safety compliance. For this process, monitors who understand the cellular therapy product being investigated and are trained in good clinical practice (GCP) either travel to participating hospitals to verify accuracy of data or review data remotely.

The standard monitoring program includes the following visits and associated tasks, which may be conducted onsite or remotely:

- Initiation Visits: Onsite or WebEx training to ensure site staff (PI and data coordinator at minimum) understand the required elements of the study.
- Interim Visits: Review of subject consenting process, data entered into study database against medical records, compliance to protocol, adverse events, and regulatory documents.
- Close-Out Visit: Final review of data and study documents.

Each clinical study receives a customized monitoring plan based upon study phase and type, subject population, enrollment goal, number of participating centers, and desired amount of data review. During the course of study enrollment and follow-up, RCI BMT team members review key indicators of study compliance and safety status to make data-driven decision regarding which centers should receive next visits or enhanced monitoring. Trigger indicators include the following:

- Safety events
- Protocol deviations
- Informed consent form non-compliance
- Status of data entry (late or on-time)
- Status of IRB approval
- Unresolved required corrective actions
- Change in study personnel by site

To learn about current RCI BMT activities, contact Erin Leckrone or Steven Devine, MD.

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Data Management Conference Held in Rio de Janeiro, Brazil

The third meeting of Data Managers in Bone Marrow Transplantation was held in August 2018 prior to the the Brazilian Society of Bone Marrow Transplantation (SBTMO) Conference. A core group of Brazilian data managers (Anderson Simione, Cinthya Correa da Silva, and Heliz Regina Alves das Neves) along with Marcelo Pasquini, MD, MS, Senior Scientific Director, CIBMTR, were instrumental in planning and facilitating this meeting. This year, several CIBMTR Scientific Directors including Bronwen Shaw, MD, PhD, and Wael Saber, MD, MS, presented topics important for data collection:

- AML including a case study
- Multiple myeloma including a case study
- Myelodysplastic syndrome (MDS) / myelofibrosis including a case study
- HLA and donor classification
- Data quality

Following the Data Managers meeting, Janet Brunner-Grady, PA-C, CIBMTR Data Operations Program Manager, facilitated a session for data managers to get assistance with difficult forms questions or concerns they have with data collection at their center.

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Senior Manager of Clinical Data Management

Opportunity to join the CIBMTR leadership team in Minneapolis, Minnesota, as Senior Manager of Clinical Data Management. This position directly impacts data integrity to support research.

Seeking qualified individual to provide overall leadership and management of a team within Data Operations. This position will handle the collection, validation / acceptance testing, and standardization of clinical data sourced from a global network that is used to conduct research. This role will also oversee ensuring data integrity to optimize data value for research.

Qualified candidates may apply on the NMDP/Be The Match website.

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Three New Patient-Level Summaries of CIBMTR Research

Three new patient-level summaries of CIBMTR research publications recently were posted on the Study Summaries for Patients webpage:

- New consent form helps people talk about treatment options
  - Easy-to-read consent form leads to better discussions between people and their doctors.
- Two-part transplant helps people with Hodgkin lymphoma
  - Splitting an autologous transplant into two doses of cells with more medicines may help people live longer than giving one transplant, a review of two studies showed.
- Transplant prep for follicular lymphoma has less risk
  - FCR combo before transplant may lower risk of chronic GVHD.

Summaries are created through a collaborative process involving CIBMTR Consumer Advocacy Committee members, CIBMTR Medical Writers and Communications Consultant; NMDP/Be The Match Patient Education Specialists, and CIBMTR Scientific Directors. Developing these summaries is one of the main initiatives of the Consumer Advocacy Committee.

The 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.

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CIBMTR on Facebook and Twitter

Like us on Facebook and follow us on Twitter to stay up-to-date with important news and events. We promote our publications, share important content from other organizations, and advertise our key meetings and events. Join us today!

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Our Supporters

The CIBMTR is supported primarily by Public Health Service Grant/Cooperative Agreement 5U24CA076518 from the National Cancer Institute (NCI), the National Heart, Lung and Blood Institute (NHLBI) and the National Institute of Allergy and Infectious Diseases (NIAID); a Grant/Cooperative Agreement 1U24HL138660 from NHLBI and NCI; a contract HHSH250201700006C with Health Resources and Services Administration (HRSA/DHHS); Grants N00014-17-1-2388, N00014-17-1-2850 and N00014-18-1-2045 from the Office of Naval Research HHSH250201700006C; and grants from our corporate and private contributors.

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Abbreviations

Need an acronym defined? Review our list of common abbreviations.

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Last Updated: 9/22/2021 11:10 AM

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