CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

newsletter
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contents

CIBMTR WORKING COMMITTEES IN THE SPOTLIGHT

The 19 Working Committees of the CIBMTR provide scientific oversight for the use of CIBMTR data and statistical resources. The major responsibilities of Working Committees are to:

- Review and rank study proposals that use CIBMTR data relevant to the committee's subject area, and assist leadership in the proposal approval process;
- Design and conduct studies relevant to their subject area involving CIBMTR data, statistical resources, networks, and/or centers;
- Periodically assess and revise relevant sections of CIBMTR data collection forms;
- Plan and conduct workshops at CIBMTR meetings.

The observational studies conducted under Working Committees are a core activity of CIBMTR. For a full listing of the 19 Working Committees and their leadership, visit the CIBMTR website.

The work of each of the Working Committees is highlighted in our newsletters. In this newsletter, we focus on the Acute Leukemia Working Committee and the Health Policy and Psychosocial Issues Working Committee.

ACUTE LEUKEMIA WORKING COMMITTEE

Acute leukemia remains the most common indication for allogeneic stem cell transplantation. The last few years have seen rapid advances in the identification of cytogenetic and molecular prognostic markers with a potential impact on the outcome of stem cell transplantation. The major changes in the practice of allogeneic stem cell transplantation have been the expanding use of alternative donors and reduced-intensity conditioning regimens. Therefore, the activities

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HEALTH POLICY AND PSYCHOSOCIAL ISSUES WORKING COMMITTEE

The Health Policy and Psychosocial Issues Working Committee (HPWC), one of the younger CIBMTR committees, made its debut at the 2005 BMT Tandem Meetings. The HPWC comprises an enthusiastic group of investigators who use CIBMTR data to address issues related to disparities in HCT access and outcomes, practice variation and quality of care, structure- and process-based predictors of patient outcomes, resource utilization and

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ABBREVIATIONS USED IN THIS NEWSLETTER:

ALWC	Acute Leukemia Working Committee
ALL	acute lymphoblastic leukemia
AML	acute myeloid (myelogenous) leukemia
ASBMT	American Society for Blood and Marrow Transplantation
ASH	American Society of Hematology
BMT	blood and marrow transplantation
BMT CTN	Blood and Marrow Transplant Clinical Trials Network
CARs	chimeric antigen receptors
CED	coverage with evidence development
CIBMTR	Center for International Blood and Marrow Transplant Research
CLL	chronic lymphocytic leukemia
CMS	Center for Medicare and Medicaid Services
CMV	cytomegalovirus
EBV	Epstein-Barr virus
ETRIC	easy-to-read informed consent
GVHD	graft-versus-host disease
HCT	hematopoietic (stem) cell transplant
HLA	human leukocyte antigen
HPWC	Health Policy and Psychosocial Issues Working CommitteeTransplantation
HRSA	Health Resources and Services Administration
HSR	Health Services Research
MAvRIC	myeloablative vs. reduced-intensity conditioning regimens
MDS	myelodysplastic syndrome
NCI	National Cancer Institute
NHLBI	National Heart, Lung, and Blood Institute
NIAID	National Institute for Allergy and Infectious Disease
NMDP	National Marrow Donor Program
Ph+ALL	Philadelphia chromosome positive acute lymphoblastic leukemia
RCI BMT	Resources for Clinical Investigation in Blood and Marrow Transplantation
SCTOD	Stem Cell Therapeutic Outcomes Database
SEER	Surveillance, Epidemiology, and End Results
STaMINA	Stem Cell Transplantation for Multiple Myeloma Incorporating Novel Agents
TNF	tumor necrosis factor

ACUTE LEUKEMIA WORKING COMMITTEE

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of the Acute Leukemia Working Committee (ALWC) have focused on three areas:

1. Evaluating the impact of cytogenetic and molecular markers on the outcome of allogeneic stem cell transplantation;
2. Assessing the influence of reduced-intensity conditioning regimens and the use of alternatives on the results of transplantation;
3. Utilizing the large database of the CIBMTR to study outcomes of allogeneic stem cell transplantations in rare subtypes of acute leukemia.

The ALWC is led by three co-chairs: Donald Bunjes, MD, University Hospital Ulm, Germany; Steven Devine, MD, Ohio State Medical Center – James Cancer Center; and Marcos de Lima, MD, Case Western Reserve University – University Hospitals Case Medical Center. The Scientific Director is Daniel Wiesdorf, MD, University of Minnesota, and the CIBMTR statisticians are Mei-Jie Zhang, PhD, and Hailin Wang, MPH.

Continuing to improve the quality and efficiency of the ALWC, the Committee is guided by the principles established by the CIBMTR Advisory Committee:

1. Publish peer-reviewed publications of high scientific impact;
2. Complete work products within a reasonable time period;
3. Ensure inclusiveness and fairness within the study process.

The ALWC's recent academic activity includes two presentations at the 2013 BMT Tandem Meetings and three manuscripts published during the past year. The ALWC has also submitted four manuscripts, which are currently under review.

Eleven proposals were submitted to the ALWC for the 2013 BMT Tandem Meetings, and eight were presented and discussed by the committee. These numbers reflect the high level of interest of the BMT community in the data trove maintained by the CIBMTR and provided by the participating centers and investigators.

Accrual summary of acute leukemia cases in the CIBMTR database, 1995-2012

Type of Transplant	Number of Cases Providing Transplant Essential Data (TED) – Level Data	Number of Cases Providing Comprehensive Report Forms (CRF) – Level Data
AML Allogeneic	22,776	19,854
ALL Allogeneic	12,710	10,827
AML Autologous	4,582	1,304
ALL Autologous	730	218

The ALWC leadership stated, "The success of the ALWC is a reflection not only on the vibrant team of CIBMTR statisticians and data managers, but ultimately it also reflects the commitment of the transplant groups in the US and abroad who provide outcomes research, trustworthy data collection, and attention to detail. We can only expect more high quality research in the future, and we welcome proposals from our colleagues interested in AML or ALL!"

HEALTH POLICY AND PSYCHOSOCIAL ISSUES WORKING COMMITTEE

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economic aspects of HCT, and psychosocial aspects of HCT. Steven Joffe, MD, MPH, (Dana Farber Cancer Institute) and Theresa Hahn, PhD, (Roswell Park Cancer Institute) are the Committee's current co-chairs.

As Rabindranath Tagore once said, "Age considers, youth ventures." This observation holds true for the HPWC – although still in its adolescence, the committee has conducted a number of high-impact research projects. The committee leadership is also dedicated to promoting young investigators and encourages fellows and junior faculty to propose and lead research projects.

HPWC studies have led to 15 publications, with an additional two under review. Published and ongoing studies can be reviewed on the CIBMTR website.

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HEALTH POLICY AND PSYCHOSOCIAL ISSUES WORKING COMMITTEE

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Completed studies include:

- **HS05-01 – Race and socioeconomic status and outcomes of unrelated donor HCT:** This study showed inferior survival and higher treatment-related mortality after unrelated donor HCT among African-Americans and among patients with low socio-economic status. (Baker KS et al. Biology of Blood and Marrow Transplantation. 2009 Dec 01;15(12): 1543-1554.)

- **HS06-02 – Race and outcomes of cord blood transplantation:** This study showed that African-Americans have inferior survival compared to Whites after single umbilical cord blood transplantation but that survivals are similar when well-matched cords and those with adequate cell doses are used. (Ballen KK et al. Biology of Blood and Marrow Transplantation. 2012 Jun 01;18(6):903-912.)

- **HS06-03 – Survival trends among adolescents and young adults with AML:** This study demonstrated that improvements in survival among adolescents and young adults who received allogeneic HCTs for AML have not lagged behind those of children and older adults. (Majhail NS et al. Biology of Blood and Marrow Transplantation. 2012 Jun 01;18(6):861-873.)

- **HS06-06 – Access to HCT:** Using data from CIBMTR and the SEER Cancer Registry, this study found that, as compared with White patients, African-Americans have a lower likelihood of receiving autologous and allogeneic HCT for leukemia, lymphoma, and multiple myeloma. (Joshua TV et al. Cancer. 2010 Jul 15;116(14):3469-3476.)

- **HS07-01 – Trends in allogeneic HCT utilization and outcomes over time:** Using CIBMTR data to describe trends in utilization of allogeneic HCT from 1994-2005, this study showed that survival has significantly improved over time. (Hahn T et al. Journal of Clinical Oncology. In press.)

- **HS07-02 – Financial impact of allogeneic HCT:** This pilot study showed that it is feasible to capture patient and caregiver out-of-pocket costs over the first three months after transplantation. (Pederson K et al. Bone Marrow Transplantation. In press.)

The HPWC's portfolio consists of 11 active studies. Examples of ongoing research include:

- **HS08-03 – Prevalence of HCT survivors in the US:** This analysis used CIBMTR data to estimate the prevalence of autologous and allogeneic HCT survivors in the US and to make projections regarding the anticipated number of survivors by 2030. (PI: Navneet Majhail, MD, MS; manuscript under review.)

- **HS11-02 – Comparison of hospital length of stay among alternative graft sources:** This study will investigate resource utilization through the first 100 days post-transplant among recipients of umbilical cord blood and unrelated donor HCT. (PI: Karen Ballen, MD; protocol under development.)

- **HS12-03 – Survival trends for unrelated donor HCT by race:** Trends in survival after unrelated donor HCT over time will be compared between Whites and African-Americans. (PI: Ellen Denzen, MS; protocol under development.)

- **HS13-01 – Association of depression with HCT outcomes:** This study will investigate the association of pre-transplant depression with HCT outcomes. (PI: Areej El-Jawahri, MD; protocol under development.)

In addition to pursuing studies such as those outlined above, the HPWC collaborates with the Health Services Research Program, a joint effort of the CIBMTR and Be The Match Patient Services Department. The Health Services Research Program conducts investigator-initiated studies requiring expertise and resources beyond those needed for typical CIBMTR committee studies (e.g., research using other databases, qualitative research, or additional external funding). The capture of socioeconomic data has substantially improved since 2007 with the introduction of electronic data submission to CIBMTR using FormsNet. Variables that are crucial to health services and health policy research, such as recipient income, education, occupation, and zip code of residence, are much more complete than they were in the past. Because of this, studies investigating the association of these factors with various aspects of transplantation have become increasingly feasible and central to the HPWC's portfolio.

Another rich resource for health policy research is the Center-Specific Outcomes Analysis dataset. As required by the Stem Cell Therapeutic Outcomes Database contract, the CIBMTR conducts an annual analysis of allogeneic HCT outcomes by transplant center. Important questions related to center practices, outcomes and trends can be addressed using this dataset.

The HPWC is an invaluable resource for studying health policy and psychosocial issues related to HCT. Leadership welcomes inquiries about potential studies from both new and established investigators. Committee contacts are its Scientific Director (Navneet Majhail, MD, MS, nmajhail@nmdp.org) and Statisticians (Ruta Brazauskas, PhD, ruta@mcw.edu, and Zhiwei (Jerry) Wang, MS, zwang@mcw.edu).

Perspectives: OLDER AND BETTER!!

by Thomas Shea, MD

Chair, CIBMTR Advisory Committee; Professor, Department of Medicine - Division of Hematology and Oncology, & Director, Bone Marrow and Stem Cell Transplantation Programs, University of North Carolina

In recent years, the age of patients eligible for allogeneic transplant has increased significantly as a result of improved supportive care and the successful increase in use of reduced intensity and non-ablative conditioning regimens.[1] Accompanying this trend has been data suggesting comparable outcomes for matched unrelated and matched related donors with some reports indicating improved outcomes with the use of younger as opposed to older unrelated donors when comparable matches are available.[2,3,4] It is not surprising that the effect of donor age was not appreciated until the use of unrelated donors became more widespread, as siblings tend to be close to one another in chronological age; whereas, the unrelated donor pool covers a much larger age range. The increase in older patients has, however, often raised the question of whether such patients would differentially benefit from an older sibling donor or a younger, comparably matched, unrelated donor.

This dilemma was addressed in a recent publication by Alousi et al. from the CIBMTR that reported on the use of 8/8 matched sibling donors over age 50 as compared to comparably matched unrelated donors under age 50 for allograft recipients with lymphoma or leukemia.[5] The study was limited to patients over 50 and donors under age 67. Researchers found that use of siblings was associated with improved non-relapse mortality, overall survival, and lower relapse for patients with performance status of 90 or above as well as comparable outcomes for patients with lower performance status. Thus, in contrast to the apparent benefit of using younger unrelated donors when a matched sibling was not available, the Alousi trial confirmed an advantage for using sibling donors up to age 67 as opposed to an unrelated donor of any age for patients over the age of 50.

While this paper did not control for the co-morbid illnesses that make older individuals less than ideal stem cell donors, it nevertheless emphasizes the importance and value of working up older siblings who may have some medical limitations but should not otherwise be disqualified as donors. The lesson here is that while younger unrelated donors are likely better candidates than older unrelated ones, we should not discount or disqualify older matched siblings without good reason, as they are likely to be the best donor of all.

References

1. Pasquini MC, Wang Z. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR Summary Slides, 2011. http://www.cibmtr.org.
2. Kollman C, Howe CW, Anasetti C, et al. Donor characteristics as risk factors in recipients after transplantation of bone marrow from unrelated donors: the effect of donor age. Blood. 2001; 98(7):2043-2051.
3. Gupta V, Tallman MS, He W, et al. Comparable survival after HLA-well-matched unrelated or matched sibling donor transplantation for acute myeloid leukemia in first remission with unfavorable cytogenetics at diagnosis. Blood. 2010;116(11):1839-1848.
4. Lee SJ, Klein J, Haagenson M, et al. High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation. Blood. 2007;110:4576-4583.
5. Alousi AM, Le-Rademacher J, Saliba RM, et al. Who is the better donor for older hematopoietic transplant recipients: an older-aged sibling or a young, matched unrelated volunteer? Blood. 2013;121(13):2567-2573.

FormsNet[SM]3 Launched!

by Marie Matlack and Janet Brunner, PA-C

Release of the FormsNet3 recipient module on Dec. 4, 2012, marked the completion of the first phase of a multi-year project to upgrade FormsNet, CIBMTR's electronic data capture system. Development of the recipient module was a collaborative effort of the CIBMTR Donor and Recipient Clinical Research Coordinators, Clinical Trials, Audit, Data Entry and Imaging, and CIBMTR Information Technology teams. The successful release was the end result of nearly two years of work documenting requirements for new functionality (including requests from network transplant center users) as well as analyzing, designing, developing and testing the system. Jeanne Burkart, Liz Johnson, and Kristy Nutter were the subject matter experts, representing users of the application, and they worked closely with CIBMTR Information Technology staff throughout the project.

FormsNet3 builds upon the capabilities in FormsNet2 and provides features and functions that users requested, e.g., easier site navigation and auto population. Some of the new functionality in FormsNet3 includes:

- Improved user experience and increased efficiency;
- Better data capturing,
  - Auto populating the current key fields and author information,
  - Enabling and disabling, showing only questions that require data;
- Improved validation, leading to higher quality of data collected.

All in all, the release of FormsNet3 was deemed a success with few defects noted in the first month of use. To date, there have been four high priority defects (or 'bugs' as some refer to them) identified and resolved. One example was the post-release fix to improve the time it took to load a form. The Clinical Research Coordinators and Subject Matter Experts have been triaging FormsNet3 related concerns.

The next module to be upgraded to FormsNet3 is the Donor module. This module is in the Analysis and Design Phase, and a timeline is being developed for its release. Clinical Trials will be the last module to be upgraded.

The next project for the Recipient Module is Forms Revisions, which will incorporate the revision of 26 forms in the first phase and 12 forms in the second phase. Form revisions have been designed to utilize the enhanced features of FormsNet3. For example, if a recipient is participating in a BMT CTN clinical trial and that option is selected on the Pre-TED (form 2400), a drop down box will appear listing all the current BMT CTN studies, allowing the specific study to be selected. The forms are being defined by the recipient data management team. The CIBMTR Information Technology project for implementing phase 1 forms has begun, and the release is planned for fall of 2013. Once initial revisions have been completed, plans include revising all Recipient forms on a three year cycle.

BMT TANDEM MEETINGS

by D'Etta Waldoch

The 2013 BMT Tandem Meetings held in Salt Lake City are thrilled to report a record-breaking attendance of more than 2,800 attendees! That's about 300 people more than the previous record. What was it that contributed to the overall popularity this year? Was it the venue, the skiing or the science?

The 2013 annual meeting is over, and the evaluations are in. We're betting you're not surprised that for every three persons asked, there were three different opinions regarding a ski vs. sun venue for the BMT Tandem Meetings. Was it the skiing that contributed to this year's high attendance? We can tell you that every year we have more than one person asking to go back Keystone, even though our last "ski" meeting was held there in 2007. Alas, we have long outgrown the hallowed hills west of Denver.

At the same time, there were also many comments in favor of returning to the warmer climates of San Diego, Orlando, and Honolulu. Yes, some like it hot, and some like it cold. Some feel the Salt Palace was too big and long for the intimacy of a smaller meeting, and some think it was just right and can't wait to return! While we would be delighted to please 100% of the people 100% of the time and control the weather, perhaps it really is the educational value of the conference that keeps our attendance figures climbing. Consider a sampling of comments from this year's evaluations:

…This is probably the best ASBMT-CIBMTR meeting ever. Congratulations to Cath Bollard and Vanderson Rocha. Feeling of collegiality was felt throughout the meeting… Plenary sessions on CARs and cellular immunotherapy (anti-EBV, anti-CMV…) were truly outstanding.

…Attending this conference has inspired me to keep abreast of current issues relating to BMT, which will help to provide better patient care.

…Change in my practice will be incremental. I have been coming to these meetings for 15 years and have been implementing bits and pieces of knowledge. By doing so, our survival has increased 2% annually.

…The conference allows the opportunities to hear of new clinical trials, publications, and the latest in data management procedures. These updates are brought back to the research team and implemented as appropriate.

…This session was extremely helpful at pointing out the varying practice decisions of the community at large, and the rationale for many of the different decisions. It was one of the most effective sessions at the conference.

…The fact that the meeting is not that big, as compared to ASH, allows more interaction with speakers and other attendees, which is always invaluable.

So there you have it. As one of the exhibitors was overheard commenting, perhaps we should just forget about wondering why more and more people show up each year – it is simply a really good meeting!

The 2014 BMT Tandem Meetings, which are already taking shape under the watchful eye of an Organizing Committee that addresses the educational objectives of both the CIBMTR and ASBMT, will be held February 26 - March 2 at the Gaylord Texan hotel and convention center in Grapevine, Texas, a few short minutes from the Dallas airport. Industry-supported satellite sessions and product theaters will broaden the spectrum of state-of-the-art offerings. In addition to an outstanding scientific program, the 2014 Meetings will again offer peripheral sessions for BMT pharmacists, BMT center administrators, coordinators, investigators, medical directors, clinical research professionals/data managers, transplant nurses, and advanced practitioners.

Keep an eye on the CIBMTR website or the ASBMT website as the program starts to take shape this spring. Email broadcasts will give you the green light to register and make housing reservations this summer. We're hoping for another record-breaker next year!

BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK

by Amy Foley

The Blood and Marrow Transplant Clinical Trials Network (BMT CTN), with its 20 core and approximately 100 affiliate centers, has enrolled over 5,300 patients since 2003. CIBMTR shares administration of the BMT CTN Data and Coordinating Center with NMDP and The EMMES Corporation. These three organizations together support all BMT CTN activities.

The BMT CTN Steering Committee is currently under the leadership of Chair Ginna Laport (Stanford University), Chair-Elect Fred Appelbaum (Fred Hutchinson Cancer Research Center), and Vice Chair Steve Devine (Ohio State University Medical University).

Clinical Trials: Open Enrollment

The BMT CTN encourages widespread transplant community participation in clinical trials. If your center is interested in participating, please visit the BMT CTN website.

There are nine trials open, one released to sites, and five in development. The following BMT CTN trials are open or will soon be opened for enrollment:

- BMT CTN 0301—Phase I/II allogeneic marrow transplantation from unrelated donors for patients with **aplastic anemia**
- BMT CTN 0601—Phase II unrelated donor HCT for patients with **sickle cell** using reduced-intensity conditioning
- BMT CTN 0702—Phase III single autologous transplant with or without consolidation versus tandem autologous transplant with lenalidomide maintenance; also known as stem cell transplantation for **multiple myeloma** incorporating novel agents (STaMINA)
- BMT CTN 0801—Phase II/Phase III trial comparing sirolimus plus prednisone vs. sirolimus/calcineurin inhibitor plus prednisone for **chronic GHVD treatment**
- BMT CTN 0803/0903 – Phase II studies for allogeneic transplantation for hematologic malignancy in **HIV+ patients**
- BMT CTN 0804/CALGB 100701 – Phase II study comparing reduced-intensity allogeneic HCT in **high-risk CLL** patients
- BMT CTN 0805/SWOG 0805 – Phase II trial of chemotherapy plus dasatinib regimen for newly-diagnosed Ph+ALL patients
- BMT CTN 0901 – Phase III study comparing **myeloablative vs. reduced-intensity conditioning regimens** (MAvRIC) in multiple sclerosis or AML
- BMT CTN 1101 – Phase III study comparing HLA-haploidentical related donor bone marrow vs. double umbilical cord blood (**haplo vs. double cord**) with reduced-intensity conditioning for patients with hematologic malignancy (released to sites)
- BMT CTN 1202 - Prospective cohort of biologic samples for the evaluation of **biomarkers** predicting risk of complications and mortality following allogeneic HCT

Presentations

Tandem 2013:

Three BMT CTN oral abstracts were presented at this year's Tandem meeting:

- **BMT CTN 0403: Greg Yanik** - Randomized, double blind, placebo-controlled trial of a TNF inhibitor (etanercept) for the treatment of idiopathic pneumonia syndrome (IPS) after allogeneic stem cell transplant (SCT). A Blood and Marrow Transplant Clinical Trials Network (BMT CTN) study.
- **BMT CTN 0501: Joanne Kurtzberg** - Superior survival after single unit umbilical cord blood transplantation (UCBT) in children with hematological malignancies treated on Blood and Marrow Transplant Clinical Trials Network (BMT CTN) 0501 relative to the Cord Blood Transplantation (COBLT) Trial.
- **BMT CTN 0802: Javier Bolaños-Meade** - A multi-center, randomized, double blind, Phase III clinical trial comparing steroids/placebo vs. steroids/mycophenolate mofetil as initial therapy for acute graft-versus-host disease. Blood and Marrow Transplant Clinical Trials Network Study 0802.

Publications

There are 29 BMT CTN published articles, including nine primary analyses. The following manuscripts were accepted/published since the last CIBMTR newsletter:

- Pasquini M, Devine S, Mendizabal A, Baden L, Wingard J, Lazarus H, Appelbaum F, Keever-Taylor C, Horowitz M, Carter S, O'Reilly R, Soiffer R. **Comparative outcomes of donor graft CD34+ selection and immune suppressive therapy as graft-vs-host disease prophylaxis for patients with acute myeloid leukemia in complete remission undergoing HLA-matched sibling allogeneic hematopoietic cell transplantation.** Journal of Clinical Oncology. 2012 Sep 10; 30(26):3194-3201. Epub 2012 Aug 6.
- Mauskopf J, Chirila C, Graham J, Gersten I, Mullins D, Maziarz R, Baden L, Bolanos-Meade J, Brown J, Walsh T, Horowitz M, Kurtzberg J, Marr K and Wingard J. **Cost-effectiveness analysis of voriconazole compared with fluconazole for prevention of invasive fungal infection in patients receiving allogeneic hematopoietic cell transplants.** American Journal of Health-System Pharmacy. [In Press]

RESOURCE FOR CLINICAL INVESTIGATION IN BLOOD AND MARROW TRANSPLANT

by Becky Drexler

The Resource for Clinical Investigation in Blood and Marrow Transplant (RCI BMT) conducts prospective research within the CIBMTR, providing researchers in the field of HCT with infrastructure and expertise in HCT clinical trial conduct and analysis. The goal is to generate data allowing novel and innovative ideas to move into the larger Phase II or Phase III setting through such groups as the National Institutes of Health BMT CTN or the national cooperative groups.

The RCI BMT continues to develop new projects and support ongoing studies and projects.

The RCI BMT submitted two abstracts for the 2013 BMT Tandem Meetings, and both were accepted for oral presentations. The first was titled **Phase I/II multicenter clinical trial of lenalidomide maintenance after allogeneic hematopoietic cell transplant (alloHCT) in patients with high risk (HR) multiple myeloma (MM)** and was presented by Dr. Pam Becker. The second was presented by Dr. Juliet Barker and was titled **Results of a prospective multi-center myeloablative double-unit cord blood transplantation trial in adult patients with acute leukemia and myelodysplasia.**

Our collaboration with the Pediatric Blood and Marrow Transplant Consortium continues to be productive. In addition to the actively enrolling 09-MRD trial, we expect to open the second trial, 11-TREO, by spring of 2013. 09-MRD is a multi-center study to determine the role of treating minimal residual disease before and after HCT for pediatric acute myeloid leukemia with accrual at 47% of goal. 11-TREO is a multi-center study evaluating a fixed regimen of treosulfan, fludarabine, and low dose total body irradiation in children with AML or MDS undergoing HCT from allogeneic donors. During the past several months, we have been working on a new project, 12-MOXE, with the Pediatric Blood and Marrow Transplant Consortium. Protocol development activities have been initiated as we finalize funding options.

The 09-PLEX study, a Phase II study evaluating the safety and efficacy of intravenous Plerixafor for the mobilization and transplantation of HLA-matched sibling donor hematopoietic stem cells in recipients with hematological malignancies, opened to accrual on May 14, 2013. The remaining sites are actively pursuing their required internal approvals.

RCI BMT has a number of other projects, new and ongoing, along with a number of inquiries for potential studies in the coming year that keep the team engaged and productive.

HEALTH SERVICES RESEARCH PROGRAM

Jaime Preussler, MS; Ellen Denzen, MS; Tammy Payton; Heather Moore, MPH, CHES; and Navneet Majhail, MD, MS

The CIBMTR, in collaboration with the NMDP's Patient Services department, established the Health Services Research (HSR) program in 2009 to complement activities of the Health Policy and Psychosocial Issues Working Committee. The HSR program focuses on several areas of health services research related to HCT, such as access and health care disparities, quality of care, and economic aspects of transplantation.

HSR Program Studies

Examples of ongoing HSR program studies include:

- **Transplant provider and center factors and outcomes of allogeneic hematopoietic cell transplantation.** HCT center and provider characteristics ("center effects") can impact the organization and delivery of care, and they can potentially impact overall patient outcomes. We conducted a national survey of U.S. transplant centers to obtain information about transplant center personnel, infrastructure, and models of care delivery. The response rate to our survey was 79%, and this study is in the analysis phase.

- **Variation in Medicaid coverage for hematopoietic cell transplantation.** In this policy analysis, we obtained information on 2012 HCT coverage benefits from state Medicaid websites and offices as well as NMDP network transplant centers. States

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were graded on coverage for: (1) transplant procedure and disease indications; (2) donor search; (3) medications; (4) clinical trials; and (5) patient food, lodging, and transportation. No state met the recommended minimum coverage benefit criteria in all five categories, and there was substantial variation in coverage by state. A poster on this study was presented at the 2013 BMT Tandem Meetings, and a manuscript is under review.

- **Identifying HCT housing and caregiver challenges and potential interventions.** Housing and caregiver issues were identified among barriers to successful HCT by the NMDP's System Capacity Initiative. This study will use focus groups and a survey of transplant center providers (social workers, coordinators) to identify barriers and potential interventions to address patient housing and caregiver needs. The focus group phase has been completed, and the survey is under development.

- **Easy-to-read informed consent (ETRIC) for hematopoietic cell transplantation clinical trials.** Given their complexity, the consent process for HCT clinical trials can be a challenge for patients. Through a competitive grant award from the National Heart, Lung, and Blood Institute as a supplement to the BMT CTN funding, this study will: (1) conduct a randomized study of ETRIC vs. standard consent form to evaluate whether the former enhances patient comprehension and satisfaction and decreases anxiety related to the consent process for BMT CTN 0901 and 1101 trials, and (2) identify barriers and facilitators to the implementation of ETRIC at transplant centers through semi-structured interviews of site investigators and Institutional Review Board personnel.

HSR Program Publications

Representative recent publications from the HSR program include:

- Preussler JM, Denzen EM, Majhail NS. **Costs and cost-effectiveness of hematopoietic cell transplantation**. Biology of Blood and Marrow Transplantation. 2012 Nov 01;18(11): 1620-1628. Epub 2012 Apr 3.

- Majhail NS, Mau LW, Denzen EM, Arneson TJ. **Costs of autologous and allogeneic hematopoietic cell transplantation in the United States: a study using a large national private claims database.** Bone Marrow Transplantation. 2013 Feb 01;48(2):294-300.

- Denzen EM, NS Majhail, Ferguson SS, Anasetti C, Bracey A, Burns L, Champlin R, Chell J, Leather H, Lill M, Maziarz RT, Medoff E, Neumann J, Schmit-Pokorny K, Snyder EL, Wiggins L, Yolin Raley DS, Murphy EA. **Hematopoietic cell transplantation in 2020: summary of year II recommendations of the National Marrow Donor Program's System Capacity Initiative.** Biology of Blood and Marrow Transplantation. 2013 Jan 01;19(1):4-11.

- Moore HK, Burton Santibañez ME, Denzen EM, Carr DW, Murphy EA. **Barriers to accessing healthcare for hematopoietic cell transplant recipients living in rural areas: perspectives from healthcare providers.** Clinical Journal of Oncology Nursing. [In Press]

- Majhail NS, Rizzo JD, Hahn T, Lee SJ, McCarthy PL, Ammi M, Denzen E, Drexler R, Flesch S, James H, Omondi N, Pedersen TL, Murphy E, Pederson K. **Pilot study of patient and caregiver out-of-pocket costs of allogeneic hematopoietic cell transplantation.** Bone Marrow Transplantation. [In Press]

The HSR program continues to evolve as a resource for conducting health services research studies in HCT. It also looks forward to broader participation of the transplant community and health services researchers. For more information about the program or to discuss potential opportunities for collaboration, please review the CIBMTR website or contact Navneet Majhail, MD, MS, at nmajhail@nmdp.org.

STEM CELL THERAPEUTIC OUTCOMES DATABASE

by J Douglas Rizzo, MD, MS and Carol Doleysh, BS, CPA

The Stem Cell Therapeutic Outcomes Database (SCTOD) is part of the US Health Resources and Services Administration (HRSA)-funded C. W. Bill Young Cell Transplantation Program, which collects data on all allogeneic hematopoietic cell transplants performed in the United States as well as data on transplants performed elsewhere using cellular products that originated in the US. Several activities of the SCTOD, including the contract renewal, center-specific outcomes analysis forum, and the Center for Medicare and Medicaid Services (CMS) MDS project, are highlighted below.

HRSA Renews SCTOD Contract

The CIBMTR successfully competed for, and was awarded, renewal of the SCTOD contract with HRSA. This contract was first awarded to CIBMTR in 2006. The outcomes registry of the CIBMTR currently contains information for more than 350,000 transplant recipients as well as critical data to continually evaluate the operations of the national transplant program.

"CIBMTR is privileged to continue to operate the Outcomes Database on behalf of the C.W. Bill Young Cell Transplantation Program," said J. Douglas Rizzo, MD, MS, Professor of Medicine at the Medical College of Wisconsin, Associate Scientific Director at CIBMTR, and Principal Investigator of the SCTOD. "CIBMTR delivers value by using the Outcomes Database to provide clinicians, scientists, patients, and policymakers the information they need to make the best possible clinical decisions. It is a beneficial platform to expand important research to advance the field, plan clinical trials, facilitate quality improvement, and perform studies on behalf of policymakers. The major goal of the program is to make blood and marrow transplants available to all who need them and to increase their safety and effectiveness."

In addition, HRSA recently awarded other C.W. Bill Young Cell Transplantation Program contracts to the NMDP, in order to continue the Program's work through the Office of Patient Advocacy/Single Point of Access for transplant patients, the Bone Marrow Coordinating Center, and the Cord Blood Coordinating Center.

Center-Specific Outcomes Analysis Forum

Outcomes reporting in allogeneic HCT is necessary to provide information requested by patients, insurers, and government agencies and to comply with current laws. In order to maintain a transparent process to generate fair, scientifically valid center-specific survival reports for related and unrelated HCT performed in the United States, CIBMTR hosts a Center-Specific Outcomes Analysis Forum every other year. The purpose of this meeting is to review the methods, processes and results for the center-specific survival report, which includes related and unrelated HCT, and to consider revisions to the methods and processes.

Review of the data elements collected by CIBMTR to support the risk-adjustment performed in the center-specific survival analysis is another important topic. Forum participants include patient advocates, representatives of HCT centers, experts in center outcomes reporting not involved in HCT, members of the ASBMT Quality Outcomes Committee, statisticians, government project officers, and representatives of the CIBMTR and NMDP. A few specific recommendations from the 2012 Forum include: continued collection of the HCT comorbidity index, collection of pre-HCT cytogenetics and other risk factors for acute leukemia and MDS, and revisions to the website hosting the publicly available center-specific survival data. A summary of the meeting, and the recommendations from the 2012 Forum as well as those held in previous years, are posted on the CIBMTR website.

The 2012 center-specific survival report, which includes first allogeneic HCTs performed between 2008 and 2010, was recently distributed to transplant center medical directors. A description of the methodology used in generating this report can be found on the CIBMTR website. These data were used to refresh the Transplant Center Directory located at bethematch.org/access.

MDS

This study is an example of how CIBMTR infrastructure can be used to quickly address both scientific and health policy needs regarding hematopoietic cell transplantation in the United States. MDS is primarily a disease of the elderly. Before 2010, Medicare had not established a National Coverage Determination for this disease. Therefore, many of these patients in the US did not have access to HCT because of lack of reimbursement for the procedure by Medicare.

A CMS decision of August 2010 stated that transplant procedures could be covered if patients were enrolled in a trial designed to provide CMS with further evidence regarding the efficacy of the procedure (coverage with evidence development, CED). Detailed requirements for trials that would satisfy CMS's needs for data were described in the Decision Memo. Using the data collection platform for required reporting of allogeneic HCT in the US specified in the SCTOD, the CIBMTR worked closely with CMS to develop a study to assess the outcomes in Medicare beneficiaries. The study plan was approved by CMS under CED in December 2010; patients began to be enrolled immediately after approval. The primary objective of this study is to compare the 100-day survival of patients age 65 and older (including Medicare beneficiaries) who receive allogeneic HCT for treatment of MDS with that of patients age 55-64. To date, more than 90 US centers have activated this study, and more than 420 patients 65 or older have enrolled. This study ensures that virtually all CMS beneficiaries with MDS have access to HCT. Between 2010 and 2012, the number of patients aged 65 or older registered with the CIBMTR who received a first allogeneic transplant at a US center for MDS has more the doubled. More details regarding the study and participation information can be found on the CIBMTR website.

Public Website

The HRSA Blood Cell Transplant website recently received a new look; it was updated to be more consistent with other HRSA webpages. The site features basic transplant, cord blood and donor information, a description of the C. W. Bill Young Cell Transplantation Program and its contractors, and a search feature for patient survival and center volumes data. Check it out at bloodcell.transplant.hrsa.gov. Feedback or suggestions can be provided using the Contact HRSA link.

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2013 CIBMTR Advisory Committee Members

Please address correspondence to:

CIBMTR Milwaukee Campus
Medical College of Wisconsin
Jessica Gillis-Smith, MPH, Editor

9200 W. Wisconsin Ave., Ste. C5500
Milwaukee, WI 53226 USA

Telephone: (414) 805-0700
Fax: (414) 805-0714

Website: www.cibmtr.org
Email: contactus@CIBMTR.org

MEDICAL COLLEGE OF WISCONSIN

CIBMTR Minneapolis Campus
National Marrow Donor Program

3001 Broadway St., Ste 110
Minneapolis, MN 55413-1753 USA

Telephone: (612) 884-8600
Fax: (612) 884-8661

Website: www.cibmtr.org
Email: contactus@CIBMTR.org

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