CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

newsletter
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contents



# NOTICE REGARDING CIBMTR SUMMARY SLIDES

Many of you have requested downloadable versions of the annual CIBMTR Summary Slides. We are happy to inform you that effective July 2010, downloadable PowerPoint versions of the full set (formerly sets 1 and 2) of CIBMTR Summary Slides will be posted annually on our public website at www.cibmtr.org (see "Reference Center" Index).

Beginning with this edition, the Summary Slides will no longer be included in the CIBMTR Newsletter. Please let us know at contactus@cibmtr.org if you have any questions or problems accessing the data slides you need.

# PERSPECTIVES: EXTERNAL REVIEW EVALUATION

*by Stella Davies, MBBS, PhD; Chair, CIBMTR Advisory Committee*

In the time since CIBMTR hosted its external review last fall, significant progress has been made on several Review Committee recommendations. I'd like to highlight a few of these, and to thank all the people who worked so hard to make them happen.

**Recommendation: Develop strategies to bring observational studies to completion more quickly.**
**Actions taken:** Roberta King, MPH (CIBMTR-Minneapolis), and Kathy Sobocinski, MS (CIBMTR-Milwaukee), are assessing the workload of the MS statisticians. Their goal is to reduce the non-study-related tasks of this work group and engage Principal Investigators (PIs) in the process of speeding the progress of their studies.

**Recommendation: Enhance data collection and sharing with centers and cord blood banks.**
**Actions taken:** See the article on page 6 for a description of the progress we are making toward helping cord blood banks report and share data.

**Recommendation: Increase use of the Repository for immunogenetic and immunobiologic studies.**
**Actions taken:** Stephanie Lee, MD (Fred Hutchinson Cancer Research Center), and Steve Spellman, MBS (CIBMTR-Minneapolis), are working with the Immunobiology Working Committee and Histocompatibility Advisory Group. They made the following recommendations to the CIBMTR Advisory Committee at its February meeting:

- Disseminate information more widely about what is available in the Repository and develop more strategies to reach PIs with the proper expertise to do appropriate studies with these samples.
- Make sure the process for adjudication of similar studies is transparent, emphasizing and encouraging collaborative and validation studies. Emphasize inclusiveness. The first PI to submit the concept sheet on a project will continue as the collaborative study's PI.
- Make templates available describing the resource, for PIs to use in grant applications.
- Facilitate immunophenotyping/functional studies on fresh pre- and post-transplant samples for all donor/recipient pairs for which DNA and frozen cells are currently stored. Consider ways to support such studies on defined populations, in the context of prospective trials.
- Consider novel statistical approaches for data analysis.

**Recommendation: Further develop the Health Services Research Program.**
**Actions taken:** This program has been under development for the past year, and is moving forward with several projects, including a caregiver initiative and a financial impact study. Navneet Majhail, MD, and Elizabeth Murphy of the NMDP Office of Patient Advocacy are developing additional plans to move these projects forward.

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## PERSPECTIVES: EXTERNAL REVIEW EVALUATION

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**Recommendation: Develop a system for examining the overall observational research strategy, to ensure that resources are being used to address the most important issues.**
**Actions taken:** Following the 2010 BMT Tandem Meetings, CIBMTR's research priorities were established for the year. The Advisory Committee met via phone conference in May to assess these choices and provide a broad view of the observational research strategy for the organization. Several new ideas are under consideration. These discussions reiterated that CIBMTR should:

- Avoid overlap, but recognize that sometimes parallel work can accomplish results faster.
- Maximize resource use: share/collaborate.
- Use the same datasets when possible.
- Recognize there is a wide range of ideal "wants" in the scientific and medical community.
- Recognize there will always be study limitations, including cost.

**Recommendation: Develop a formal process for setting the scientific agenda of the Resource for Clinical Investigation in Blood and Marrow Transplant (RCI BMT).**
**Actions taken:** A panel convened to explore this area and made several recommendations:

- Define the criteria for RCI BMT studies more precisely.
- Establish ways to ensure that RCI BMT studies do not compete with other studies, including those of other networks.
- Establish metrics for successful completion of studies, including measures to communicate with the BMT CTN and to publicize results.
- Set up an external review in early 2011 specifically to address the RCI BMT.

So as you can see, CIBMTR is moving forward on its goals, and hopes to create even more opportunities for the scientific research community to benefit from the programs and the databases that CIBMTR makes available to them.

Best regards,
Stella Davies, MBBS, PhD

# NEW LEADERSHIP at CIBMTR

Our heartfelt thanks go to all the retiring members of the CIBMTR Advisory Committee for their hard work and dedication. The following people have been elected to take their places on the committee, with three-year terms that began March 1, 2010. As with all CIBMTR committees, member rotation is staggered so that there are always experienced members to welcome the incoming members. Please join us in greeting:

**Vice Chair North America:**
Paul Martin, MD, Fred Hutchinson Cancer Research Center, Seattle, WA
**Vice Chair Central/South America:**
Ricardo Pasquini, MD, Hospital de Clinicas, Universidade Federal do Parna, Curitaba, Brazil
**Members at Large North America:**
Koen van Besien, MD, University of Chicago Hospitals, Chicago, IL
Hillard Lazarus, MD, University Hospitals Case Medical Center, Cleveland, OH
Bart Scott, MD, Fred Hutchinson Cancer Research Center, Seattle, WA
**Members at Large Non-North America:**
Yoshiko Atsuta, MD, PhD, Nagoya University Graduate School of Medicine, Japan
Jürgen Finke, MD, Freiburg University Medical Center, Germany
Tracey O'Brien, MD, Sydney Children's Hospital, Australia

**The following members will serve CIBMTR on its Nominating Committee for 2010:**
**Chair:** David Porter, MD, Hospital of the University of Pennsylvania, Philadelphia, PA
Steven Devine, MD, Ohio State University Medical Center, Columbus, OH
*Neena Kapoor, MD, Children's Hospital of Los Angeles, CA
*Ginna Laport, MD, Stanford University, Stanford, CA
*Jeffrey Szer, MD, Royal Melbourne Hospital City Campus, Victoria, Australia
* New members

We also thank the outgoing **Working Committee Chairs,** who have led CIBMTR so diligently in meeting its research needs. Following are the newly-appointed Working Committee Chairs, who have agreed to serve five-year terms:

**Acute Leukemia:** Steven Devine, MD, Ohio State University Medical Center, Columbus, OH
**Autoimmune Diseases:** Steven Pavletic, MD, NIH-NCI Experimental Transplantation and Immunology Branch, Bethesda, MD
**Chronic Leukemia:** Matt Kalaycio, MD, Cleveland Clinic Foundation, Cleveland, OH
**Donor Health and Safety:** Michael Lankiewicz, MD, Froedtert Memorial Lutheran Hospital, Milwaukee, WI
**Graft Sources & Manipulation:** Daniel Fowler, MD, NIH-NCI Experimental Transplantation and Immunology Branch, Bethesda, MD
**Graft-vs-Host Disease:** Corey Cutler, MD, MPH, Dana-Farber Cancer Institute, Boston, MA
**Immune Deficiencies/Inborn Errors:** Harry Malech, MD, NIAID-NIH, Bethesda, MD
**Immunobiology:** Carlheinz Müller, MD, PhD, Zentrales Knochenmarkspender-Register Deutschland, Ulm, Germany
**Infection & Immune Reconstitution:** Michael Boeckh, MD, Fred Hutchinson Cancer Research Center, Seattle, WA
**Late Effects & Quality of Life:** Christine Duncan, MD, Dana-Farber Cancer Institute, Boston, MA
**Lymphoma:** David Maloney, MD, PhD, Fred Hutchinson Cancer Research Center, Seattle, WA
**Non-malignant Marrow Disorders:** Shalini Shenoy, MD, St. Louis Children's Hospital, St. Louis, MO
**Pediatric Cancer:** Carrie Kitko, MD, University of Michigan Medical Center, Ann Arbor, MI
**Regimen-Related Toxicity/Supportive Care:** Philip McCarthy, MD, Roswell Park Cancer Institute, Buffalo, NY
**Solid Tumors:** Michael Bishop, MD, NIH-NCI Experimental Transplantation and Immunology Branch, Bethesda, MD

## CIBMTR WORKING COMMITTEES

Scientific oversight for the use of CIBMTR data and statistical resources is provided by 19 Working Committees with broad, international membership. Following are two more reports in our series focusing on the work of individual Working Committees.

Each committee is responsible for designing and conducting studies relevant to their subject area, considering proposals to use CIBMTR data for pertinent studies, assessing and revising relevant sections of CIBMTR data collection forms, and planning and conducting workshops at CIBMTR meetings.

These groups set priorities for observational studies to be done using CIBMTR's large clinical databases. For more information about the Working Committees and their roles, please go to **http://www.cibmtr.org/About/WhoWeAre/Committees/Working/index.html**

## REGIMEN-RELATED TOXICITY/SUPPORTIVE CARE WORKING COMMITTEE

*by Philip McCarthy, MD, Vincent Ho, MD, Kenneth Cooke, MD, Marcelo Pasquini, MD, MS, Manza Agovi, MPH*

The scope of the Regimen-Related Toxicity/Supportive Care Working Committee (RTWC), led by Co-chairs Philip McCarthy, Vincent Ho, and Kenneth Cooke, is broader than many of CIBMTR's Working Committees, which have a disease-specific focus. This group focuses on understanding how toxicities associated with allogeneic and autologous hematopoietic cell transplantation (allo- and auto-HCT) develop. They look at how supportive care practices, patient, and transplant-related variables affect patient outcomes.

The committee wishes to thank outgoing Co-Chair Karen Ballen, (Massachusetts General Hospital), for her dedicated service to the committee. The continuing support of Scientific Director Marcelo Pasquini, and Biostatisticians Brent Logan, and Manza Agovi, (all of CIBMTR), is also much appreciated.

### Completed and nearly-completed studies

In 2009, the RTWC published an important manuscript proposing a standardized approach to defining myeloablative, reduced-intensity and non-myeloablative conditioning regimen intensities (Bacigalupo A, Ballen K, Rizzo D, Giralt S, Lazarus H, Ho V, Apperley J, Slavin S, Pasquini M, Sandmaier BM, Barrett J, Blaise D, Lowski R, Horowitz M. **Defining the intensity of conditioning regimens: working definitions.** Biol Blood Marrow Transplant 15:1628-1633, 2009). Investigators can use these definitions to compare regimen intensities and determine their effects on toxicities, GVHD, infectious complications and relapse across studies.

Also included in the wide range of recently-published studies by the RRCWC are:

- Marks DI, Ballen K, Logan BR, Wang Z, Sobocinski KA, Bacigalupo A, Burns LJ, Gupta V, Ho V, McCarthy PL, Ringden O, Schouten HC, Seftel M, Rizzo JD. **The effect of smoking on allogeneic transplant outcomes.** Biol Blood Marrow Transplant 15:1277-1287, 2009.
- Navarro WH, Agovi, M-A, Logan BR, Ballen K, Bolwell BJ, Frangoul H, Gupta V, Hahn T, No VT, Juckett MB, Lazarus HM, Litzow MR, Liesveld JL, Moreb JS, Marks DI, McCarthy PL, Pasquini MC, Rizzo JD. **Obesity does not preclude safe and effective myeloablative hematopoietic cell transplantation for acute myeloid leukemia in adults.** Biol Blood Marrow Transplantation, in press 2010.
- Schriber J, Agovi MA, Ho V, Ballen KK, Bacigalupo A, Lazarus HM, Bredeson CN, Gupta V, Maziarz RT, Hale GA, Litzow MR, Logan B, Bornhauser M, Giller RH, Isola L, Marks DI, Rizzo JD, Pasquini MC. **Second unrelated donor hematopoietic cell transplantation for primary graft failure.** Biol Blood Marrow Transplant. Feb 18, 2010 Epub ahead of print.

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## WORKING COMMITTEE: IMMUNE DEFICIENCIES/INBORN ERRORS OF METABOLISM

*By Harry Malech, MD, and Anna Hassebroek, MPH*

Immune Deficiencies and Inborn Errors of Metabolism Working Committee (IDWC) members study the impact of transplant and its outcomes in patients with rare diseases of the immune and metabolic systems. These diseases are for the most part "orphan diseases," where it is often possible to locate only a few dozen to a few hundred patients worldwide who have been transplanted for a particular disorder.

Under the leadership of Co-chairs Edwin Horwitz (Children's Hospital of Philadelphia), Paul Veys (Great Ormond Street Hospital) and Harry Malech (National Institutes of Health); statisticians Jennifer Le-Rademacher and Anna Hassebroek; and Scientific Director Mary Eapen, the committee focuses on studies that assess post-transplant outcomes for immune deficiencies and inborn errors of metabolism, collaborating with outside registries, and revising data collection forms to ensure collection of all relevant data.

The IDWC considers a wide range of issues for its studies. Immune deficiency /inborn errors of metabolism patients may be predisposed to developing secondary cancers, and transplant itself may lead to a subsequent cancer. The clinical goals of transplant for immune deficiencies/inborn errors of metabolism may ignore issues of graft-versus-tumor effects that are critical to cancer treatment-related transplants. They focus primarily on achieving adequate, stable donor engraftment within the affected cellular compartments, while minimizing development of GVHD. Many immune deficiencies/inborn errors of metabolism, such as chronic granulomatous disease and leukocyte adhesion deficiency, can be cured with low levels of donor mixed chimerism.

At the same time, many patients with an immune deficiency or inborn error of metabolism come to transplant with end organ dysfunction or infections resulting from their primary disorders. Because of these confounding issues, there is increasing interest in the use of non-myeloablative or sub-ablative conditioning, alternate donors such as unrelated cord blood, and immune-conditioning and GVHD prevention regimens that maximize the development of donor graft tolerance.

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## REGIMEN-RELATED TOXICITY/SUPPORTIVE CARE WORKING COMMITTEE

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- Uberti JP, Agovi M, Tarima S, Haagenson M, Gandham S, Anasetti C, Baker KS, Bolwell BJ, Bornhauser M, Chan KW, Copelan E, Davies SM, Finke J, Hale GA, Kollman C, McCarthy PL, Ratanatharathorn V, Ringdén O, Weisdorf DJ, Rizzo JD. **Comparative analysis of busulfan and cyclophosphamide versus cyclophosphamide and total body irradiation in full intensity unrelated marrow donor transplantation for acute myelogenous leukemia, chronic myelogenous leukemia and myelodysplasia.** Bone Marrow Transplant, in press, 2010.


A study presented at the 2009 American Society of Hematology (ASH) meeting showed that obese children with severe aplastic anemia undergoing allo-HCT experience higher treatment-related mortality and shorter overall survival *(Barker et al)*. This is an important observation; otherwise excellent outcomes after transplants for severe aplastic anemia were diminished in obese pediatric patients.

Another study presented at ASH demonstrates a decrease in transplant-related mortality (TRM) over the past two decades, and improvements in overall survival among patients with AML in remission undergoing related and unrelated myeloablative allo-HCT *(Horan et al)*. This reaffirms that advancements in supportive care have rendered full-intensity allo-HCT safer for patients.

### Biologic markers for transplant-related toxicity

The RTWC conducts studies using CIBMTR data and sample repositories, that correlate biomarkers with post-transplant outcomes. A study examining TGF-beta-1 promoter and signal peptide polymorphisms as risk factors for renal dysfunction in HCT patients treated with cyclosporine A *(Shah et al)* did not show an association between the study gene polymorphisms and post-transplant renal dysfunction. However, polymorphisms associated with higher levels of TGF-beta-1 that were presumed to be linked to cyclosporine A-related kidney injury were present in a minority of patients.
The lack of association observed in this study may be related to small sample size.

*Hahn et al* obtained NHLBI funding for a genome-wide association study of genetic polymorphisms and HCT-related mortality in donor/recipient pairs in unrelated donor allo-HCT. Its purpose is to understand how genetics contribute to TRM after unrelated donor allo-HCT. It will be conducted with the Immunobiology Working Committee. A study proposed by *Artz et al* will link pre-transplant C-reactive protein to transplant outcomes in unrelated donors. Using the unrelated donor sample repository with donor-recipient pairs broadens the scope of these studies.

### Assessing organ failure after transplantation

One RTWC protocol will examine the incidence of long-term severe renal toxicity requiring hemodialysis following allo-HCT, and the associated outcomes of end stage renal disease in comparison to allo-HCT patients not on dialysis. This study will be done by matching and merging CIBMTR data with data from the U.S. Renal Data System.

Regimen-related toxicity in the liver is commonly seen after transplant. Although hepatic veno-occlusive disease may be less prevalent with less intensive conditioning and busulfan pharmacokinetics, drugs such as gemtuzumab ozogamicin and rapamycin are associated with significant liver toxicity. A study by *Smiley et al* is looking at the use of these agents and liver toxicities.

Predictors of post-transplant lung toxicity are not well defined. Associations with certain haplotypes (HLA A1B3DR3) and lung toxicity have been reported, and will be further tested in a study with a larger sample size proposed by *Liu et al.*

### Prediction and treatment of toxicities

Predicting post-transplant complications from data available prior to transplant is a main objective of the RTWC. This will help physicians choose the appropriate transplant modality to minimize or avoid complications. *Sorror et al* demonstrated that particular comorbidities are associated with poor outcomes. CIBMTR is currently collecting data on these comorbidities with the Pre-Transplant Essential Data (Pre-TED) form to assess how they affect outcomes in a large independent cohort.

It is believed that massive splenomegaly delays engraftment after HCT. Through the RTWC, *Akpek et al* are assessing the effect of splenomegaly, splenectomy and splenic irradiation on engraftment and TRM, compared to a group of patients with splenomegaly transplanted without these interventions.

Primary graft failure after myeloablative HCT is a devastating complication. It results in poor long-term survival despite second allo-HCT. The RTWC solicited proposals from committee members to study prognostic factors for primary graft failure. Three proposals were combined into a study to assess pre- and post-transplant factors that may predict primary graft failure after myeloablative marrow or peripheral blood HCT *(Olsson et al).*

The *Bunin et al* study is looking at the effects of obesity on transplant outcomes in children with malignant disease. The RTWC is also examining outcomes of second allo-HCT in patients with relapsed hematologic malignancies after initial allo-HCT *(Akpek et al).*

### Conditioning regimens and impact on toxicities

Reduced-intensity conditioning decreases upfront toxicity, but may increase the risk of relapse. Since reduced-intensity conditioning transplants rely primarily on the graft-versus-tumor effect, disease risk categorization previously established for ablative HCT may not be applicable for these transplants. Investigators from Seattle recently proposed a new disease risk scoring system for patients undergoing non-myeloablative HCT. The RTWC accepted a proposal to validate this scoring system using CIBMTR data *(Baron et al)*. Another study will examine conditioning regimen intensity and outcomes after haploidentical donor allo-HCT (*Ciurea et al)* in collaboration with investigators from Johns Hopkins, and will include patients treated with reduced-intensity conditioning and post-transplant cyclophosphamide.

### Future endeavors

As supportive care evolves and complications of HCT are better defined, refinements have been made to CIBMTR's data collection forms to capture elements to facilitate future studies. Input is encouraged from the CIBMTR community for improvements in data collection. Not all changes can be made immediately, due to FormsNet and SCTOD technical priorities; however prioritizing forms changes is an important RTWC function to enhance our ability to improve patient outcomes.

**IMMUNE DEFICIENCIES/INBORN ERRORS OF METABOLISM**

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**The IDWC has several studies published and/or in progress that address the topics outlined above:**

- **ID98-05:** HCT for infantile osteopetrosis *(P Orchard, A Fasth).*
- **ID99-02:** The role of HCT in Langerhans cell histiocytosis *(RM Egeler, A Filipovich).*
- **ID00-01:** Describe secondary cancers after transplant for primary immune deficiency *(N Kamani)*
- **ID02-02:** Collaboration with EBMT to describe patients with leukocyte adhesion deficiency (Qasim W, Cavazzana-Calvo M, Davies EG, Davis J, Duval M, Eames G, Farinha N, Filopovich A, Fischer A, Friedrich W, Gennery A, Heilmann C, Landais P, Horwitz M, Porta F, Sedlacek P, Seger R, Slatter M, Teague L, Eapen M, Veys P. **Allogeneic hematopoietic stem-cell transplantation for leukocyte adhesion deficiency.** Pediatrics. Mar; 123(3):836-840, 2009.)
- **ID06-03:** Collaboration with EBMT and Eurocord to assess survival and toxicity after HCT in Hurler Syndrome patients *(JJ Boelens, V Rocha).*
- **ID09-01:** Long-term survival and late deaths after HCT for primary immune deficiencies and inborn errors of metabolism *(M Eapen).*

**In addition, two new proposals were accepted for study at the 2010 BMT Tandem meetings:**

- **ID10-01:** Follow-up of patients with pre-symptomatic meta-chromatic leukodystrophy *(P Shaw, J Kurtzberg).*
- **ID10-02:** HCT for DNA repair disorders *(A Gennery).*

The CIBMTR databases provide the transplant community with an opportunity to study immune deficiencies and inborn errors of metabolism in larger numbers than are available from single institutions. The IDWC encourages those interested to take advantage of this opportunity and welcomes new members and proposal ideas.

## 2010 BMT TANDEM MEETINGS: BIGGER AND BETTER THAN EVER...

*by D'Etta Waldoch, CMP*

Highly Successful **2010 BMT Tandem Meetings** took place February 24-28 in Orlando, Florida. Scientific Program Chairs were Jeffrey Szer, MD, representing CIBMTR, and Joseph Antin, MD, for ASBMT.

A record-breaking 2,570 attendees from 45 countries gathered at the Rosen Shingle Creek Convention Center to listen to and present the latest developments in HCT. The 2010 agenda included five plenary sessions, 13 concurrent sessions, 108 oral abstracts, two poster sessions and seven corporate-supported symposia.

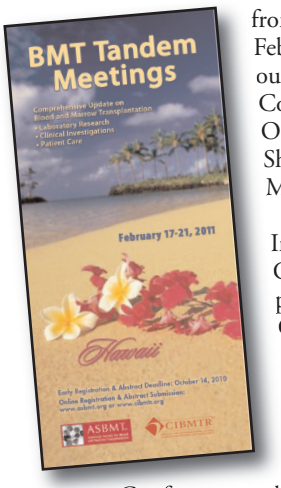
A new feature this year was the presence of more than 275 Advanced Practice Professionals, who met for two days during the Tandem Meetings. Because of the high level of interest in these meetings, an additional day is planned for 2011.

Much to her surprise, CIBMTR Chief Scientific Director Mary M. Horowitz was recognized for her 25 years of service to the meetings during the CIBMTR General Assembly on Wednesday. Dr. Ricardo Pasquini, Chief Medical Director for Hospital de Clinicas in Curitiba, Brazil, became the first recipient of the CIBMTR Distinguished Service Award. Rounding out this jam-packed evening was a presentation by Professor Alois Gratwohl, Medical Director of Kantonsspital Basel, Switzerland, of this year's Mortimer M. Bortin Lecture entitled, "The Evolution of Hematopoietic Stem Cell Transplantation: A Darwinian View."

Meeting organizers were pleased to receive 498 abstracts from investigators in 35 countries. Accepted abstracts are indexed and accessible online at **www.cibmtr.org**, as well as published in the February 2010 issue of *Biology of Blood and Marrow Transplantation* (vol. 16, no. 2, supplement 2). Audio recordings, slides and agenda from the meetings are also available on the CIBMTR website.

Conference evaluations and transcripts for continuing medical education or allied health professional contact hours were again available online. Additional questions about CME transcripts may be directed to **info@condorregistration.com.**

## ...AND LOOKING FORWARD TO HAWAII IN 2011!




The BMT Tandem Meetings will change U.S. coastlines from east to west for 2011. The meetings are scheduled for February 17 to 21 (that's Thursday to Monday, rather than our typical Wednesday to Sunday) at the Hawaii Convention Center in Honolulu, on the beautiful island of Oahu, Hawaii. The Scientific Program Chairs are Thomas Shea, MD, representing CIBMTR, and Elizabeth Shpall, MD, for ASBMT.

In addition to five intensive days of scientific, clinical and CIBMTR/ASBMT business meetings, the related peripheral meetings will include: the BMT CTN Steering Committee, BMT CTN Coordinator and Investigator Sessions, FACT Training Workshops, Clinical Research Professionals Data Management Conference, BMT Center Administrative Directors Conference, BMT Pharmacists Conference, Advanced Practice Professionals Conference, Transplant Nurses Conference, and BMT Center Medical Directors Conference. Sessions related to pediatric cancer will be held on Friday, February 18.

Detailed information about the 2011 BMT Tandem Meetings are updated on the CIBMTR (www.cibmtr.org) and ASBMT (www.asbmt.org) websites as it becomes available. Online conference registration, hotel reservations and the abstract submission program ***(abstract deadline is October 14, 2010)*** will be posted in summer. For general information, please e-mail D'Etta Waldoch, CMP, at the conference office at bmttandem@cs.com.

### 2011 Meeting Topics:

Acute GVHD
Acute Leukemia (MDS)
Acute Lymphoblastic Leukemia
Bioethical Issues in HCT Research
CLL and Lymphoma
Conditioning Regimens
Gene Modified T Cells
Genomics
GVL
Haploidentical vs. Cord Blood Debate
Infection
Induced Pluripotent Stem Cells
Innate Immunity
Myeloma Debate
Minimal Residual Disease
Novel Strategies in Cord Blood
T Regulatory Cells
ISCT, NMDP and WBMT Sessions

Ricardo Pasquini, MD, Chief Medical Director for Hospital de Clinicas, Universidade Federal do Parana, Curitiba, Brazil, was presented with CIBMTR's first ever Distinguished Service Award for his dedication to promoting hematopoietic stem cell transplantation research in developing countries. He is shown here after receiving the award at the 2010 BMT Tandem Meetings, flanked by his son Marcelo Pasquini, MD, MS, and Mary Horowitz, MD, MS, both of CIBMTR-Milwaukee.

## STEM CELL THERAPEUTIC OUTCOMES DATABASE (SCTOD)

*by J. Douglas Rizzo, MD, MS, Jenni Bloomquist and Carol Doleysh, BS, CPA*

The C.W. Bill Young Cell Transplantation Program and SCTOD are very interested in the increasing use of umbilical cord blood as hematopoietic cell source. We put extensive efforts into ensuring the completeness and quality of cord blood data. Our recent initiatives can be grouped into those focused on the input stage at the transplant centers, and those focused on the end users – cord blood banks (CBBs) and others using the data for research.

### Input: Transplant Centers

To assist centers in submitting high quality, timely data to CIBMTR, we developed training materials and hosted training sessions about Infusion Form completion (Form 2006), emphasizing cord blood product data. An Instruction Manual for this form was released this year and is available at www.CIBMTR.org, and a cord blood data Webinar is also being posted to the CIBMTR website. Although they focus on cord blood, these Infusion Form instructions can benefit any CIBMTR data professional.

CIBMTR and transplant center staff members have worked diligently to resolve discrepant data for cord blood HCT, including reconciliation of recipient, product and bank identifiers.

For their accreditation and internal quality control programs, CBBs need product thaw and recipient engraftment data close to the event dates. To help them, we now ask transplant centers to submit cord blood Baseline (2000) and Infusion (2006) forms by 21 days post transplant, and 100-Day Reports (2100) by 120 days post transplant, rather than at the routine deadlines for these forms.

Stem cell thaw and processing reports are often difficult to interpret. We are collecting these reports from centers for all cord blood transplants to help us better assess what additional training may be needed for submitting these complex data. Our staff is trained by CBB staff on how to read and interpret stem cell thaw and processing records. This helps them answer questions for transplant center staff with questions on how to report these data. Some transplant centers have allowed cell processing laboratory staff to enter the infusion form data directly into FormsNet™2.

### End Users: Cord Blood Banks

CIBMTR data is used to provide regular Recipient Outcomes Reports to CBBs for the units they provide. These data are used for internal quality control programs, accreditation applications, and for supporting their licensure. Bank licensure is critical to the ready availability of cord blood units for transplantation. With help from the Cord Blood Data Working Group, CIBMTR continues to improve these reports.

The Cord Blood Data Working Group has established processes at CBBs to help ensure their reports are as complete and up-to-date as possible. For example, some CBBs give us a list of units they have shipped for transplant, which allows us to proactively ensure that all the units are registered in FormsNet and attributed to the correct CBB.

Some CBBs have started collecting the CIBMTR Recipient CRID number from centers when it is available before transplant. This makes it easier for us to review these cases once we receive shipment lists.

The Cord Blood Data Working Group has worked with us to establish validation parameters for cord blood data, including numerical ranges for values such as cell counts, and other validations for thaw data and expected manipulations. CIBMTR staff can now query cord blood data against these validations and work with transplant centers to resolve discrepancies.

## BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK (BMT CTN)

*by Sarah Mull, Program Coordinator*

Already, 2010 has proven itself a productive year for the BMT CTN. Highlights include:

- As of April 30th, more than 3,000 patients have been enrolled on 19 different trials (since November 2003, when the Network's first clinical trial opened to accrual), that address important issues in HCT.
- BMT CTN 0603 (Phase II trial, haplo-identical transplant in adults) successfully closed to accrual May 17, well ahead of projections.
- On March 31, BMT CTN 0604 (Phase II trial of double cord blood transplant in adults) successfully closed to accrual, also well ahead of projections. This study just opened in December 2008.

**New studies:**

- BMT CTN 0802 (Phase III trial of acute GVHD treatment) opened to accrual in February and BMT CTN 0801 (chronic GVHD treatment) opened in April.
- The highly anticipated BMT CTN 0702 (multiple myeloma) opened to accrual in May 2010. Three additional protocols are anticipated to open this year.
- Another successful BMT CTN Coordinators' meeting was held in February during the BMT Tandem Meetings. More than 120 data coordinators attended the $1^1/_2$ day sessions.
- The 2010 BMT CTN Progress Report is now available at www.bmtctn.net or by contacting the CIBMTR.
- As reported to the Network during the February Steering Committee meeting, it is the intention of NCI and NHLBI to issue a Request for Applications in summer 2010 for renewal of the BMT CTN.

## RESOURCE FOR CLINICAL INVESTIGATIONS IN BLOOD AND MARROW TRANSPLANT (RCI BMT)

*by Willis Navarro, MD, and Rebecca Drexler*

The RCI BMT was developed to conduct smaller clinical trials than the BMT CTN. It features:

- Statistical, medical, and logistical clinical trials expertise;
- Data management services for multi-center phase I/II trials including electronic data capture;
- Use of CIBMTR's large observational database to help plan trials and identify transplant centers that will optimize accrual;
- Long-term follow-up beyond primary study endpoints; and
- Collaboration with investigators to seek and secure necessary funding and support for trial completion.

RCI BMT currently has three protocols open and accruing patients:

- **05-DCB:** Double cord blood HCT after myeloablative conditioning for acute myelogenous leukemia, acute lymphocytic leukemia and myelodysplastic syndrome. This trial is funded by a grant from the U.S. Office of Naval Research.
- **07-REV:** Evaluating the safety and tolerability of lenalidomide after allogeneic HCT for myeloma. This study is funded by the Celgene Corporation.
- **06-DON or RDSafe:** A multi-institutional prospective study of hematopoietic stem cell donor safety, and quality of life in related donors. This study will provide a comprehensive analysis of the related donor experience, and is funded by an R01 grant from NCI.

RCI BMT has three protocols under development:

- **09-PLEX:** A prospective trial of safety and efficacy of plerixafor for mobilizing and transplantation of sibling donors in patients with hematological malignancies. This study is funded by the Genzyme Corporation.
- **09-MRD:** A prospective trial to examine the utility of two minimal residual disease assays to predict outcomes in pediatric acute myelogenous leukemia.
- **09-SQOL:** A study to assess the feasibility of collecting quality of life data for the SCTOD.

RCI BMT has several other ongoing projects, including a financial impact study for patients undergoing HCT, sample acquisition for a study of KIR mismatch, a long-term safety study for unrelated donors examining the incidence of malignancies and autoimmunity, and a collaboration with the Pediatric Blood and Marrow Consortium for infrastructure development for pediatric transplant clinical trials. Work has also begun on a sample management module for the **09-MRD** protocol, supported by funding from the St. Baldrick's Foundation.

## CLINICAL RESEARCH PROFESSIONALS AND DATA MANAGERS HAVE THEIR CHANCES TO SHINE!

*by Diane Knutson, Manager of Clinical Research*

A large crowd of eager learners registered for the CIBMTR Fall Clinical Research Professionals/Data Management (CRP/DM) Conference in November 2009, in conjunction with the NMDP Council Meeting. The first day included an in-depth look at successful completion of the CIBMTR Infusion Form (2006) by M. Jo Lauppe (M.D. Anderson Cancer Center, Houston, TX) and Jenni Bloomquist (CIBMTR). Other highlights included a FormsNet™2 lab conducted by CIBMTR Clinical Research Coordinators (CRCs), and the Mentors Reception, which celebrated CIBMTR's 5th anniversary with a trivia contest.

The next day included a popular panel facilitated by Amy Prentice (CIBMTR), which shared GVHD data collection advice from Cindy Delbrook (National Cancer Institute), Roby Nicklow, RN (University of Minnesota, Minneapolis, MN), and Erin Richardson (Cancer Care Manitoba, Canada). For those looking to streamline their center's data collection efforts, Marita Whede, RN, BSN, and Sharon Von Harz, RN, MSN (both of Barnes-Jewish Hospital, St. Louis, MO), shared the "Lean Process" that their center conducted with amazing results. Navneet Majhail, MD, MS (CIBMTR, University of Minnesota) clarified the details of Report Form Data from a Health Policy perspective.

A few months later, the 2010 CRP/DM Conference at the BMT Tandem Meetings was divided into tracks for beginners, conducted by CIBMTR CRCs, and for experienced Data Managers. The track for experienced managers included a lesson on molecular genetics by Phillip Rowlings, MD, MS (Calvary Mater Newcastle Hospital, Newcastle, Australia), pulmonary toxicity by Vincent Ho, MD (Dana-Farber Cancer Institute, Boston, MA), and chronic GVHD by Stephanie Lee, MD, MPH (Fred Hutchinson Cancer Research Center, Seattle, WA).

An adult vs. pediatrics track included an explanation of multiple myeloma by Parameswaran Hari, MD (CIBMTR, Medical College of Wisconsin), and pediatric non-malignant diseases with pinch-hitting speaker Christine Duncan, MD (Dana-Farber Cancer Institute, Boston, MA).

Many of the CRP/DM sessions from the BMT Tandem Meetings are audio recorded and available for review at: http://www.cibmtr.org/Meetings/Materials/CRPDMC/index.html. We encourage CRP/DMs to consider submitting an abstract for the BMT Tandem Meetings scheduled for February 17-21, 2011, in beautiful Honolulu, Hawaii. The abstract due date is October 14, 2010.

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