CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

newsletter

VOLUME 15 ISSUE 1 AUGUST 2009

contents

This issue of the CIBMTR newsletter is made possible through an unrestricted educational grant from

Otsuka
Otsuka America Pharmaceutical, Inc.

Making CIBMTR Even Better: External Reviews

by Roberta King, MPH, Vice President-CIBMTR Minneapolis

To ensure that the CIBMTR continues to optimally serve the hematopoietic cell transplantation community, this year we are conducting a review of our processes and a review of our scientific agenda.

The process review was held in June, led by a consultant with expertise in this type of analysis. Three primary processes within the CIBMTR were analyzed: forms revision, data management and conducting observational studies. Staff examined the steps in each of these processes and then made recommendations for improving each process for both efficiency and quality. Twenty-one recommendations were adopted for immediate implementation.

For the scientific agenda review, we have invited experts from a variety of perspectives to review CIBMTR scientific activities, and to participate in a one-day forum with CIBMTR staff and scientific leadership in September. The resulting recommendations will be presented to the CIBMTR Advisory Committee in November and used to establish the scientific agenda for the next five years. ■

CIBMTR Working Committees

Scientific oversight for the use of CIBMTR data and statistical resources is done by 19 CIBMTR Working Committees with diverse membership from the transplant community. Following is another installment 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 hardworking groups set priorities for observational studies to be done using CIBMTR's large clinical database. For more information about the Working Committees and their roles, please go to http://www.cibmtr.org/COMMITTEES/Working_Committees/index.html.

Plasma Cell Disorders Working Committee

by Smriti Shrestha, MS, MA; Parameswaran Hari, MD, MS; Angela Dispenzieri, MD; Gustavo Milone, MD; and Sagar Lonial, MD

The Plasma Cell Disorders Working Committee (PCDWC) focuses on research into the use of HCT for multiple myeloma (MM) and other plasma cell disorders. The committee was formed several years ago under the name "Multiple Myeloma Working Committee." In the past few years, it has been among the most productive committees in generating research proposals to address a wide range of issues in the field.

PCDWC research focuses on defining the optimal role of transplantation for MM patients. Recent studies have examined prognostic factors (the International Staging System, role of response), subgroups of patients with myeloma (non-secretory myeloma, IgD and IgM myeloma, the elderly,

>> Continued on Page 4

Non-Malignant Marrow Disorders Working Committee

by Jeanette Carreras, MPH; Mark Walters, MD; Mouhab Ayas, MD; Joachim Deeg, MD; and Mary Eapen, MD, MS

Stem cell, bone marrow and cord blood transplantation have emerged as major therapeutic options for a number of non-malignant disorders, including aplastic anemia, congenital disorders of hematopoiesis, autoimmune cytopenias and others. The Non-Malignant Marrow Disorders Working Committee (NMMDWC) focuses on cellular therapy for these types of diseases.

The committee was one of the first established within IBMTR, and has been among its most prolific in addressing a wide range of issues in HCT for patients with non-malignant hematopoietic disorders. It sets priorities for Non-Malignant Marrow Disorders observational studies using the large clinical database of the CIBMTR.

>> Continued on Page 5

Stem Cell Therapeutic Outcomes Database (SCTOD)

by Carol Doleysh, BS, CPA

It has been almost three years since the U.S. Health Resources and Services Administration (HRSA) awarded the SCTOD contract to CIBMTR for the C.W. Bill Young Cell Transplantation Program. Since that time, a main focus has been developing our electronic data collection system, FormsNet™ 2.0, to help transplant centers meet their new reporting requirements. Recent activity has centered on enhancing FormsNet™ 2.0 and testing the AGNIS (A Growable Network Information System) messaging system. Following are some highlights of our progress.

FormsNet™ 2.0

All U.S. centers have been activated in FormsNet™ 2.0 and the number of forms submitted through this system continues to increase. As of June 2009, 277 centers were using FormsNet™ to enter at least some of their data, and more than 200,000 forms had been processed. Enhancements to FormsNet™ 2.0 are ongoing. Forms Due reports were released in January 2009. These reports help centers manage their workload and ensure that forms are completed and submitted on time. Forms revisions needed for AGNIS were included in the February 2009 FormsNet™ release. Comprehensive Report Form (cRF) changes are scheduled for release in August 2009.

AGNIS

Work continues on the AGNIS system to enhance electronic data exchanges between transplant center databases and CIBMTR databases. Data elements are being "curated" with the NCI's cancer data standards repository (caDSR) so that all data will comply with a national data standard. Data elements found on more than one form are being identified so they can be curated identically. The first release of AGNIS and several curated forms took place in March. Transplant centers that have prepared their systems for AGNIS can now submit Transplant Essential Data (TED) through AGNIS to the CIBMTR. For more information about the specifics of this release, refer to the AGNIS Release Notes at www.cibmtr.org.

Centers interested in learning more about electronic messaging via AGNIS are encouraged to refer to www.AGNIS.net, or contact the AGNIS team at agnis@nmdp.org.

Cord Blood Reports

Substantial progress was made recently in cord blood transplant reporting. CIBMTR is working with transplant centers, National Cord Blood Inventory banks, and the Cord Blood Coordinating Center via the newly-formed Cord Blood (CB) Data Working Group. This group is identifying and addressing issues specific to cord blood banks, especially barriers to data collection. CIBMTR has been working with centers and banks to provide complete outcome reports for the banks. This is essential for their quality assurance, accreditation, and FDA compliance activities.

The first meeting of the CB Data Working Group in December focused on ideas for linking transplant center data with cord blood unit data from the banks and determining the most useful format for reports. These meetings helped identify both issues and solutions, which are now being implemented. The CIBMTR Recipient ID (CRID) is a critical component for banks and centers, to be certain their units are properly tracked in CIBMTR systems. Centers can expect that cord blood banks shipping units directly to them will request a recipient CRID prior to shipment to facilitate tracking outcomes.

Center Outcomes Data

A forum in September 2008 generated recommendations for the most equitable and understandable ways to perform transplant center-specific outcomes analysis – another SCTOD contract requirement. Center directors received a report in December that was discussed at the Medical Directors' conference at Tandem. Discussions included the following issues:

- ***When will data be analyzed?***
  The 2009 report will include only unrelated donor transplant information, as in the past. Related donors will be included on the 2010 report, once data for transplants performed in 2008 under SCTOD and one year of follow-up data are collected.
- ***What outcomes will be measured?***
  The primary outcome is one-year survival. In the future, 100-day mortality will also be reported.
- ***Will outcomes be risk adjusted?***
  Factors including patient volumes, clinical trial participation, co-morbidities, economic status, and others found to affect outcomes will be built into the statistical model.
- ***Will pediatric and small centers be handled differently than adult centers?***
  Forum participants agreed that the same methods should be used for all centers. Larger confidence intervals around the one-year survival estimates will offer protection from over-interpretation of any individual year's results to smaller centers.
- ***How will center outcomes be made available to centers and the public?***
  Center outcomes will be posted to the web-site http://bloodcell.transplant.hrsa.gov. Prior to posting, transplant centers will have the opportunity to review, correct, and provide commentary on their center's report.
- ***What should a center do if its outcomes are outside the norms?***
  Steps may include reviewing data submitted to CIBMTR for accuracy, reviewing their center's treatment patterns over the time period, or looking for differences, trends, changes, or new practices compared to the center's own past practices or national norms.
- ***Are steps being taken to prevent unintended consequences?***
  The purpose of outcomes reporting is quality improvement. CIBMTR is carefully considering how to analyze and present the reports and how to give centers the tools they need to improve quality. A biennial review process will start in 2010. CIBMTR will incorporate the feedback it receives, as appropriate, in our reports to HRSA.

Website Redesign

CIBMTR is in the process of redesigning its website, www.cibmtr.org, to improve navigation and add new content. The first phase is targeted for fall 2009. The revisions will include additional access to information about the C.W. Bill Young Cell Transplantation Program and SCTOD.

Advisory Council

The Advisory Council on Blood Stem Cell Transplantation (ACBSCT) of the U.S. Department of Health and Human Services is responsible for supervising the C.W. Bill Young Cell Transplantation Program. Three open public meetings were held in 2008, and one so far in 2009. Discussion topics included:

- Definition of a high quality cord blood unit,
- Adult donor recruitment,
- Confidentiality policies for cord blood donors, and
- Public funding for required data collection.

Other information about SCTOD issues can be found on the HRSA website, http://bloodcell.transplant.hrsa.gov. ■

BMT Tandem Meetings Convene In Florida

by D'Etta Waldoch Benson, CMP

The combined annual meetings of the CIBMTR and the American Society for Blood and Marrow Transplantation (ASBMT) have been North America's largest international gathering of blood and marrow transplant clinicians and investigators, laboratory technicians, transplant nurses, pharmacists and clinical research associates since 1995.

2009 BMT Tandem Meetings Wrap-Up

The 2009 BMT Tandem Meetings were held February

Perspectives

Happy Anniversary CIBMTR!

by Stella Davies, MBBS, PhD

Chair, CIBMTR Advisory Committee,
Cincinnati Children's Hospital, Cincinnati, OH, USA

While a gift of wood may be traditional when a marriage reaches a five-year anniversary, a gift of blood, sweat and tears might be more appropriate to celebrate the fifth anniversary of the CIBMTR in July 2009. It's hard to believe we have reached this milestone already! Many people have given a lot to make this happen.

Perhaps the wedding song five years ago was, "We've only just begun." The affiliation that created the CIBMTR brought together the strengths of two great organizations (IBMTR and NMDP) with extensive experience in HCT-related research. It would take an entire newsletter to describe everything that has been done by CIBMTR in the last five years, but I'd like to note a few significant highlights here.

A major transformation took place in September 2006, when CIBMTR received a contract from HRSA to administer the ***Stem Cell Therapeutic Outcomes Database*** **(SCTOD)**. The NMDP was awarded contracts to operate three other components of the C.W. Bill Young Cell Transplantation Program. The Program's goal is to increase the access to, safety of, and effectiveness of HCT.

Mostly as a result of the SCTOD, many information technology advances have taken place, the biggest being ***FormsNet™ 2.0***, which was launched in December 2007. This was CIBMTR's first comprehensive electronic data collection system. FormsNet™ gives transplant centers many new, desired capabilities, such as on-line validation of data, immediate randomization of recipients to either the TED or cRF track, and the ability to print a PDF from electronically submitted data.

The first release of ***AGNIS (A Growable Network Information System)*** took place in March 2009. AGNIS allows transplant centers to electronically message data between their databases and the CIBMTR database. Currently, only TED data can be sent via AGNIS by those centers that are beta test sites for AGNIS. Eventually, any center will be able to transmit TED and cRF data through AGNIS. That day will be a huge leap forward from the "old days" when transplant centers filled out paper forms and sent them through the mail to CIBMTR for manual entry.

When the CIBMTR affiliation was established, the number of scientific ***Working Committees*** expanded from 12 to 17. In the past year, two more Working Committees were established: International Studies and Cellular Therapy. More than 200 active studies are in progress every year, and the number of proposals for new ones increases annually. Because CIBMTR has more than doubled its number of statisticians, it is now able to approve record numbers of proposals to move forward.

A milestone was reached in October 2008, when **CIBMTR total publications passed 400 articles**. The number of staff members has also increased during the five years of CIBMTR's existence, to about 65 at each campus.

CIBMTR continues to work together with NMDP and The EMMES Corporation to manage the BMT CTN Data and Coordinating Center, a process that began even before the affiliation. You can read about some of its accomplishments on page six. You can also read about the achievements of the RCI BMT, a new CIBMTR resource for small clinical trials that increases our knowledge about HCT, on page six.

In collaboration with the NMDP Office of Patient Advocacy, CIBMTR is working to increase understanding and conduct research in health policy and services issues as they relate to HCT. This new emphasis on ***Health Services Research*** will address topics that affect health and well-being during the HCT process, including cost-effectiveness and financing, patient and population health status and quality of life, outcomes of health care interventions, practice patterns and many more.

CIBMTR also participated in the evolution of the ***Worldwide Network for Blood and Marrow Transplantation*** **(WBMT)** as one of its founding member societies, along with the European Group for Blood and Marrow Transplantation, NMDP, the World Marrow Donor Association and the Asian-Pacific Blood and Marrow Transplantation Group. WBMT was recently invited by the World Health Organization to partner as a non-governmental organization to provide a single voice for HCT globally.

Perhaps the most important achievement of all since CIBMTR was created, however, has been the **spirit of unprecedented collaboration and cooperation** that has arisen between the individuals, the organizations, and the Network personnel engaged in a common mission: conducting HCT research leading to better outcomes for patients. This is a noteworthy feat, and everyone involved should be proud of what has been accomplished in a few short years.

These and many other initiatives have resulted in accomplishments well beyond what was envisioned at the time of the affiliation. Happy fifth anniversary, congratulations, and thank you to everyone who helped make it happen! ■

11-15 in Tampa, Florida. There were 2,457 attendees, with registrants from 45 countries – a new record. Investigators representing 29 countries submitted 470 abstracts. The abstracts are indexed and available online at www.cibmtr.org. They were also published in the February 2009 issue of *Biology of Blood and Marrow Transplantation* (vol. 15, no. 2, Supplement).

Audio CDs, synchronized audio/visual CDs and MP3 downloads of the 2009 sessions, including peripheral conferences of transplant nurses, clinical research professionals, center administrators and BMT pharmacists, are available for purchase online.

Looking Ahead To 2010

A short hop across Florida will take the BMT Tandem Meetings to Orlando, February 24-28, 2010, at the Rosen Shingle Creek Convention Center. Scientific Program Chairs are Drs. Jeffrey Szer for CIBMTR and Joseph Antin for ASBMT.

In addition to a full scientific program, peripheral meetings will include: the BMT CTN Steering Committee, Coordinator and Investigator Sessions, FACT Training Workshops, Clinical Research Professionals Data Management Conference, BMT Center Administrative Directors Conference, BMT Pharmacists Conference, Transplant Nurses Conference, BMT Center Medical Directors Conference, and (new this year!) a Mid-level Practitioner (NP, PA) Conference and an ISCT meeting. Sessions targeted to pediatric cancer will take place February 25.

Up-to-date information about the 2010 meetings can be found on the CIBMTR (www.cibmtr.org) and ASBMT (www.asbmt.org) websites. Online registration, hotel reservation and abstract submission is now live.

For general information about Tandem, please e-mail D'Etta Waldoch Benson, CMP, at the conference office at bmttandem@cs.com. Support opportunity questions may be directed to Sherry Fisher at slfisher@mcw.edu. ■

Plasma Cell Disorders Working Committee
Continued from Page 1

and the obese), and defining the role of allogeneic transplant and the graft versus myeloma effect. Another focus has been on the recent controversy over the timing and incremental benefit of autotransplant for myeloma. The curative intent of transplant approaches such as allogeneic transplant and donor lymphocyte therapy are also of great interest.

The CIBMTR Statistical Center and the PCDWC would like to acknowledge the leadership and scientific contributions of David H. Vesole, MD, PhD, and Donna E. Reece, MD, who served as committee co-chairs for more than a decade. The committee is now chaired by Angela Dispenzieri, MD (Mayo Clinic Transplant Center, Rochester, MN); Gustavo Milone, MD (Angelica Ocampo-Fundaleu, Argentina) and Sagar Lonial, MD (Winship Cancer Institute, Atlanta, GA), and assisted by Scientific Director Parameswaran Hari, MD, MS, and statisticians Smriti Shrestha, MS, MA, and Mei-Jie Zhang, PhD, of the Medical College of Wisconsin.

The most widely used guideline for assigning disease response for MM was developed more than 10 years ago by this committee, in collaboration with the European Group for Blood and Marrow Transplantation. It is internationally known as the Blade Criteria and may be found at:

- Blade J, Samson D, Reece D, Apperley J, Bjorkstrand B, Gahrton G, Gertz M, Giralt S, Jagannath S, Vesole D. Criteria for evaluating disease response and progression in patients with multiple myeloma treated by high-dose therapy and haematopoietic stem cell transplantation. *Br J Haematol.* 1998: 102;1115-1123.

The productivity of the PCDWC is shown by the following manuscripts, which are either published or in press:

- Reece DE, Bredeson C, Pérez WS, Jagannath S, Zhang MJ, Ballen KK, Elfenbein GJ, Freytes CO, Gale RP, Gertz MA, Gibson J, Giralt SA, Keating A, Kyle RA, Maharaj D, Marcellus D, McCarthy PL, Milone GA, Nimer SD, Pavlovsky S, To LB, Weisdorf DJ, Wiernik PH, Wingard JR, Vesole DH. Autologous stem cell transplantation in multiple myeloma patients <60 versus ≥60 years of age. *Bone Marrow Transplant.* 2003: 32;1135-1143. **(MM98-01).**
- Vesole DH, Pérez WS, Akasheh M, Boudreau C, Reece DE, Bredeson CN, Bashey A, Brunvand MW, Dispenzieri A, Freytes CO, Gale RP, Gibson J, Giralt SA, Holland HK, Kyle RA, Lazarus HM, McCarthy PL, Milone GA, Schiller G, Siegel D, Wiernik PH. High-dose therapy and autologous hematopoietic stem cell transplantation for patients with primary systemic amyloidosis: A Center for International Blood and Marrow Transplant Research study. *Mayo Clinic Proc.* 2006: 81;880-888. **(MM00-01).**
- Anagnostopoulos A, Hari PN, Pérez WS, Ballen K, Bashey A, Bredeson CN, Freytes CO, Gale RP, Gertz MA, Gibson J, Goldschmidt H, Lazarus HM, McCarthy PL, Reece DE, Vesole DH, Giralt SA. Autologous or allogeneic stem cell transplantation in patients with Waldenstrom's macroglobulinemia. *Biol Blood Marrow Transplant.* 2006: 12;845-854. **(MM01-01).**
- Bashey A, Pérez WS, Zhang MJ, Anderson KC, Ballen K, Berenson JR, To LB, Fonseca R, Freytes CO, Gale RP, Gibson J, Giralt SA, Kyle RA, Lazarus HM, Maharaj D, McCarthy PL, Milone GA, Nimer S, Pavlovsky S, Reece DE, Schiller G, Vesole DH, Hari P. Comparison of twin and autologous transplants for multiple myeloma. *Biol Blood Marrow Transplant.* 2008: 14;1118-1124. **(MM00-02).**
- Kumar S, Pérez WS, Zhang M-J, Ballen K, Bashey A, To LB, Bredeson CN, Cairo MS, Elfenbein GJ, Freytes CO, Gale RP, Gibson J, Kyle RA, Lacy MQ, Lazarus HM, McCarthy PL, Milone GA, Moreb JA, Pavlovsky S, Reece DE, Vesole DH, Wiernik PH, Hari P. Comparable outcomes in non-secretory and secretory multiple myeloma after autologous stem cell transplantation. *Biol Blood Marrow Transplant.* 2008: 14;1134-1140. **(MM02-02).**
- Hari P, Zhang M-J, Roy V, Pérez WS, Bashey A, To LB, Elfenbein G, Freytes CO, Gale RP, Gibson J, Kyle RA, Lazarus HM, McCarthy PL, Milone GA, Pavlovsky S, Reece DE, Schiller G, Vela-Ojeda J, Weisdorf D, Vesole D. Is the International Staging System superior to the Durie Salmon staging system? A comparison in multiple myeloma patients undergoing autologous transplant. *Leukemia.* E-pub Mar. 26, 2009. **(MM04-01).**

Four abstracts from the committee were presented at the ASH meeting in 2008. The committee is proud to report it has 12 ongoing projects, listed below.

- Comparison of second autologous transplant versus related or unrelated non-myeloablative allogeneic HCT in patients with multiple myeloma who relapse after autologous transplantation. (PIs Cesar Freytes and David Vesole, **MM02-01/D01-117**).
- The graft-versus-myeloma effect in patients receiving non-myeloablative conditioning. (PI Olle Ringdén, **MM02-03/MM03-01**).
- Clinical outcome of patients with IgD and IgM multiple myeloma undergoing autologous hematopoietic stem cell transplants: A CIBMTR retrospective study. (PIs Donna E. Reece and David H. Vesole, **MM05-01**).
- Effect of obesity on outcome in patients with multiple myeloma undergoing autologous stem cell transplantation. (PIs Dan Vogl and Edward Stadtmauer, **MM05-02**).
- Outcomes among African-Americans versus whites after autologous hematopoietic cell transplantation for multiple myeloma. (PIs Paulette Mehta and Parameswaran Hari, **MM06-03/HS06-01**).
- Comparison of outcomes of patients undergoing autologous transplantation after achieving less than a partial response to initial chemotherapy compared with those receiving additional salvage chemotherapy prior to undergoing autologous transplantation. (PIs Ravi Vij, Shaji Kumar and Donna E. Reece, **MM06-04**).
- Time trends in allogeneic HCT for myeloma. (PI Shaji Kumar, **MM08-01**).
- HLA specificities and predisposition to the development of multiple myeloma. (PI Meral Beksac, **MM08-02**).
- Effect of renal failure after autologous HCT for myeloma. (PI Baldeep Wirk, **MM08-03**).
- Plasma cell leukemia: outcomes with autologous or allogeneic transplant. (PIs Anuj Mahindra, Jorge Vela, Matt E. Kalaycio and David H. Vesole, **MM09-01**).
- Outcome of salvage second auto transplant in relapse multiple myeloma. (PIs Ayman Saad, Laura Michaelis and David H. Vesole, **MM09-02**).
- DLI for relapse/persistent MM post allo HCT. (PI Baldeep Wirk, **MM09-04**).

We encourage all members of the HCT community to actively participate in our committee. The next PCDWC meeting will be held in February 2010 at the BMT Tandem meetings. ■

Non-Malignant Marrow Disorders Working Committee Continued from Page 1

This committee has contributed significantly to scientific research, submitting many abstracts to ASH. Since it began, the NMMDWC has reported on its activities in 12 published/submitted papers, with three more in preparation. Its major strengths include outstanding leadership and a dynamic membership roster of investigators who actively participate on the writing committees to provide critical insight and feedback on all studies.

At the 2009 BMT Tandem meetings, outgoing NMMDWC Co-Chair Ricardo Pasquini, MD, was recognized for his significant contributions to the committee over the past decade. We look forward to his continued participation as a committee member and investigator. The remaining co-chairs, Mark Walters, MD, and Mouhab Ayas, MD, are delighted to welcome Joachim Deeg, MD, as a new co-chair. The co-chairs are responsible for promoting and developing the scientific agenda, establishing priorities based on input from the Working Committee members, and ensuring the progress of the research studies and publications. They are assisted by CIBMTR Scientific Director, Mary Eapen, MD, MS, and statisticians Jeanette Carreras, MPH, Jennifer Le Rademacher, PhD, and Mei-Jie Zhang, PhD.

The committee encourages all members of the transplant community to actively participate in committee activities by submitting new proposals or participating in the design and conduct of studies. Encouraging the participation of new investigators is a major goal of the CIBMTR. The next NMMDWC meeting will be held in February 2010 at Tandem.

In addition to the following studies published by the NMMDWC, several other studies are in process, with data collection and analysis ongoing.

- Pasquini R, Carreras, J, Pasquini MC, Camitta BM, Fasth AL, Hale GA, Harris RE, Marsh JC, Robinson AJ, Zhang M-J, Eapen M, Wagner JE. HLA-matched sibling hematopoietic stem cell transplantation for Fanconi anemia: comparison of irradiation and non-irradiation containing conditioning regimens. *Biol Blood Marrow Transplant.* 2008. 14;1141-1147. **(AA00-03).**
- Perez-Albuerne ED, Eapen M, Klein JP, Gross TG, Lipton JM, Baker KS, Woolfrey AE, Kamani NR. Outcome of unrelated donor stem cell transplantation for children with severe aplastic anemia. *Br J Haematol.* 2008:141;216-223. **(D00-03).**
- Wagner JE, Eapen M, MacMillan ML, Harris RE, Pasquini R, Boulad F, Zhang MJ, Auerbach AD. Unrelated donor bone marrow transplantation for the treatment of Fanconi anemia. *Blood.* 2007: 109;2256-2262. **(D01-04).**
- Panepinto JA, Walters MC, Carreras J, Marsh J, Bredeson CN, Gale RP, Hale GA. Horan J, Hows JM, Klein JP, Pasquini R, Roberts I, Sullivan K, Eapen M, Ferster A. Matched-related donor transplantation for sickle cell disease: report from the Center for International Blood and Transplant Research. *Br J Haematol.* 2007: 137;479-485. **(AA01-01).**
- Schrezenmeier H, Passweg JR, Marsh JC, Bacigalupo A, Bredeson CN, Bullorsky E, Camitta BM, Champlin RE, Gale RP, Fuhrer M, Klein JP, Locasciulli A, Oneto R, Schattenberg AV, Socie G, Eapen M. Worse outcome and more chronic GVHD with peripheral blood progenitor cells than bone marrow in HLA-matched sibling donor transplants for young patients with severe acquired aplastic anemia. *Blood.* 2007: 110;1397-1400. **(AA00-01).**
- Champlin RE, Pérez WS, Passweg JR, Klein JP, Camitta BM, Gluckman E, Bredeson CN, Eapen M, Horowitz MM. Bone marrow transplantation for severe aplastic anemia: a randomized controlled study of conditioning regimens. *Blood.* 2007: 109;4582-4585. **(AA98-03).**
- Passweg JR, Pérez WS, Eapen M, Camitta CM, Gluckman E, Hinterberger W, Hows JM, Marsh JC, Pasquini R, Schrezenmeier H, Socié G, Zhang M-J, Bredeson CN. Bone marrow transplants from mismatched related and unrelated donors for severe aplastic anemia. *Bone Marrow Transplant.* 2006: 37;641-649. **(AA98-02).**
- Roy V, Pérez WS, Eapen M, Marsh JC, Pasquini M, Pasquini R, Mustafa MM, Bredeson CN. Bone marrow transplantation for diamond-blackfan anemia. *Biol Blood Marrow Transplant.* 2005: 11;600-608. **(AA00-02).**
- Burt RK, Rowlings PA, Traynor A. Hematopoietic stem cell transplantation for severe autoimmune disease: know thyself. In: *Hematopoietic Stem Cell Therapy.* 2000: (Ball ED, Lister J, Law P, eds.), Churchill Livingstone, Philadelphia, PA, pp. 203-215. **(AA98-04).**
- Saso R, Marsh J, Cevreska L, Szer J, Gale RP, Rowlings PA, Passweg JR, Nugent ML, Luzzato L, Horowitz MM, Gordon-Smith EC. Bone marrow transplants for paroxysmal nocturnal hemoglobinuria. *Br J Haematol.* 1999: 104;392-396. **(AA98-05).**
- Hows J, Stone JV, Camitta B. Alternative donor bone marrow transplantation for severe acquired aplastic anemia. In: *Aplastic Anemia–Pathophysiology and Treatment.* 1999: (Schrezenmeier J, Bacigalupo A, eds.), Cambridge University Press, Cambridge, United Kingdom, pp. 258-274. **(AA98-01).**
- Horan JT, Carreras J, Tarima S, Camitta BM, Gale RP, Hale GA, Hinterberger W, Marsh J, Passweg JR, Walters MC, Eapen M. Risk factors affecting outcome of second HLA-matched sibling donor transplantations for graft failure in severe acquired aplastic anemia. *Biol Blood Marrow Transplant.* 2009: 15;626-631. **(AA03-01).** ■

Welcome Aboard!

The following individuals were elected to serve CIBMTR on its Advisory Committee, with terms that began March 1, 2009. New members are:

Chair-Elect:

Thomas Shea, University of North Carolina-Chapel Hill

Vice-Chair Europe:

Jane Apperley, Imperial College, UK

Vice-Chair Asia/Africa/Australia:

Mammen Chandy, Christian Medical College and Hospital, Tamil Nadu, South India

At Large North America Advisory Committee Members:

- Brenda Sandmaier, Fred Hutchinson Cancer Research Center, Seattle
- Marcos de Lima, MD Anderson Medical Center, Houston
- Robert Soiffer, Dana-Farber Cancer Institute, Boston

At Large Non-North America Advisory Committee Members:

- Jonas Mattsson, Karolinska Institute at Huddinge Hospital, Huddinge, Sweden
- Peter Dreger, University of Heidelberg, Germany
- Judith Marsh, St. George's Hospital, UK

On behalf of the entire transplant community, we thank our outgoing Advisory Committee members, who have given us all countless hours of dedicated service:

- Sergio Giralt (past-Chair)
- Eliane Gluckman
- Jeffrey Szer
- Jeff Lipton
- Nancy Bunin
- Steve Mackinnon
- Katarina LeBlanc

We also thank Donna Wall (Chair) and Jose Borbolla Escoboza, who served on the Nominating Committee for these elections.

New 2009 Nominating Committee Members:

- Steven Devine, Ohio State University, Columbus
- David Porter, University of Pennsylvania, Philadelphia

The BMT CTN At Work

by Sarah Mull, Program Coordinator

The Blood and Marrow Transplant Clinical Trials Network (BMT CTN) was established in October 2001 to conduct large, multi-institutional clinical trials addressing important issues in HCT. Sixteen Core Clinical Centers and more than 90 Affiliate Centers nationwide are working collaboratively to improve outcomes for transplant patients. Since opening its first protocol in November 2003, more than 2,800 patients have been enrolled on 18 clinical trials.

There are currently 11 protocols actively accruing patients. Seven more are under development and six trials have successfully completed accrual. Six new concepts were approved during the past year by the BMT CTN Steering Committee for protocol team formation. The Network is eager to activate these trials in the near future. They include:

- A phase II/III randomized, multicenter trial comparing sirolimus plus prednisone, sirolimus/photopheresis plus prednisone, and sirolimus/calcineurin inhibitor plus prednisone for the treatment of chronic graft versus host disease **(BMT CTN 0801)**.
- Initial systemic treatment of acute GVHD: a phase III randomized trial evaluating mycophenolate mofetil plus corticosteroids versus corticosteroids and placebo **(BMT CTN 0802)**.
- High dose chemotherapy with autologous stem cell rescue for aggressive B cell lymphoma and Hodgkin Lymphoma in HIV-infected patients **(BMT CTN 0803)**.
- Phase II study of reduced-intensity allogeneic stem cell transplant for high risk chronic lymphocytic leukemia **(BMT CTN 0804/CALGB 100701)**.
- A multi-center phase III study comparing myeloablative to nonmyeloablative transplantation in patients with myelodysplastic syndrome or acute myelogenous leukemia **(BMT CTN 0901)**.
- A phase III randomized, multicenter trial testing whether exercise and/or stress management improves functional status and symptoms of autologous and allogeneic recipients **(BMT CTN 0902)**.

Study Results

Four abstracts were presented in 2008 (three at ASH and one at ASCO). It is important to the BMT CTN and transplant community that findings are published as quickly as possible. We are proud to report that our first manuscript with outcome data from a Network study **(BMT CTN 0302)** was published this summer in *Blood*:

- Alousi A, Weisdorf D, Logan B, Bolanos-Meade J, Goldstein S, Ho V, Hayes-Lattin B, Wingard J, Horowitz M, Levine, J. Etanercept, mycophenolate, denileukin or pentostatin plus corticosteroids for acute graft vs. host disease: a randomized phase II trial from the BMT CTN. *Blood. 2009:* 114;511-517.

Although most BMT CTN trials are still in progress, several have already yielded findings that have impacted clinical practice and research. These early publications include:

- Wingard JR. Design issues in a prospective randomized double-blinded trial of prophylaxis with fluconazole versus voriconazole after allogeneic hematopoietic cell transplantation. *Clin Infect Dis.* 2004: 39;Suppl 4:S 176-180.
- Ho V, Cutler C, Carter S, Martin P, Adams R, Horowitz M, Ferrara J, Soiffer R, Giralt S. Thrombotic microangiopathy (TMA) after hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant.* 2005: 11;571-575.
- Logan BR. Optimal two-stage randomized phase II clinical trials. *Clin Trials.* 2005: 2;5-12.
- Weisdorf D, Carter S, Confer D, Ferrara J, Horowitz M. Blood and Marrow Transplant Clinical Trials Network (BMT CTN): addressing unanswered questions. *Biol Blood Marrow Transplant.* 2007: 13;257-262.
- Ferrara JL, Anasetti C, Stadtmauer E, Antin J, Wingard J, Lee S. Levine J, Schultz K, Appelbaum F, Negrin R, Giralt S, Bredeson C, Heslop H, Horowitz M. Blood and Marrow Transplant Clinical Trials Network State of the Science Symposium 2007. *Biol Blood Marrow Transplant.* 2007: 13;1268-1285.
- Cutler C, Stevenson K, Kim HT, Richardson P, Ho VT, Linden E, Revta C, Ebert R, Warren D, Choi S, Koreth J, Armand P, Alyea E, Carter S, Horowitz M, Antin JH, Soiffer R. Sirolimus is associated with veno-occlusive disease of the liver after myeloablative allogeneic stem cell transplantation. *Blood.* 2008: 112(12);4425-4431.
- Logan B, Leifer E, Bredeson C, Horowitz M, Ewell M, Carter S, Geller N. Use of biological assignment in hematopoietic stem cell transplantation clinical trials. *Clin Trials.* 2008: 5(6);607-16.

Future Network Activity Update

The BMT CTN continues to be actively involved in securing approval from NCI and NHLBI for renewal in 2011. For more information about the BMT CTN or any of its activities, please visit our public Website at www.bmtctn.net. ■

Resource For Clinical Investigations In Blood And Marrow Transplantation (RCI BMT)

by Marcie Tomblyn, MD, MS, Willis Navarro, MD, and Rebecca Drexler

It has been just over four years since the RCI BMT held its first Clinical Trials Advisory Committee (CTAC) meeting. As with everything in the CIBMTR, we continue to grow exponentially. The past several months have seen exciting activities taking place.

Two trials are actively accruing patients: Double cord blood HCT after myeloablative conditioning for hematologic malignancies **(05-DCB)**, and Evaluating the safety and tolerability of lenalidomide after allogeneic HCT **(07-REV)**. A third trial, Related donor safety and quality of life **(RDSafe or 06-DON)**, will open later this year. Interest in our trials activity continues to increase, with more transplant centers asking to participate. More importantly, RCI BMT received three proposals for discussion at the CTAC meeting at Tandem: Two were from investigators new to RCI BMT.

In another exciting development, we are now collaborating with the Pediatric Blood and Marrow Transplant Consortium (PBMTC). This partnership will facilitate early phase pediatric transplant trials for both malignant and non-malignant conditions. The initial partnership activities are funded, in part, by an infrastructure grant awarded to the PBMTC from St. Baldrick's Foundation.

This summer we began a project to further develop the FormsNet™ platform to include functions for clinical trials management. This is a large task, but it will provide RCI BMT with its own electronic data capture and management system. The first trial to utilize this functionality will be the RDSafe **(06-DON)** trial. Additional functionality and infrastructure projects are in the planning stages.

In July, Dr. Marcie Tomblyn stepped down as Scientific Director of the RCI BMT because of her move from the University of Minnesota to Moffitt Cancer Center in Florida. During her years as Scientific Director, she was central to the development of this program and we thank her for all her efforts. Dr. Tomblyn transferred the program direction to Dr. Willis Navarro, a Medical Director at the National Marrow Donor Program. Dr. Navarro is looking forward to taking on this role and being part of the continued evolution of this important program. ■

CIBMTR Summary Slides

by Marcello Pasquini, MD, MS, and Zhiwei Wang, MS

The Summary Slides are an annual report on data submitted to the CIBMTR. Part I focuses on trends in the use of hematopoietic cell transplantation (HCT) according to donor type, graft sources, patient age and transplant regimes. Early outcomes such as mortality rates at day 100 post HCT and causes of death are also included in this series. Graphs with total transplant numbers (slides 7 & 8) are estimates based on data reported to the CIBMTR adjusted according to transplant type. These adjustment factors are derived from comparisons with other national and international databases.

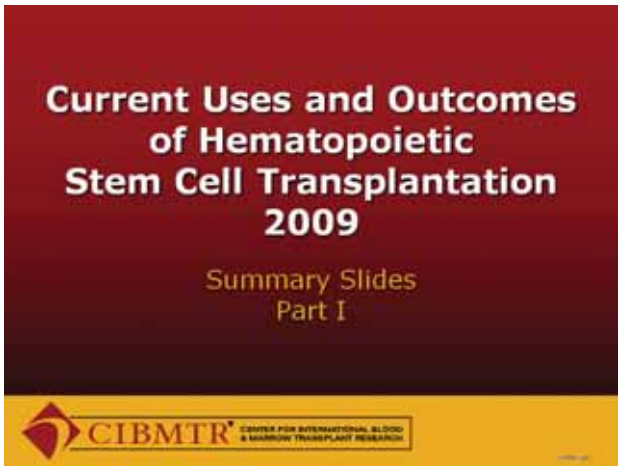
Acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), and chronic myelogenous leukemia (CML) are classified as early (first complete remission [CR1] or first chronic phase [CP1]), intermediate (second or subsequent CR or CP or accelerated phase [AP]), and advanced (primary induction failure, active disease, or blastic phase) disease. Myelodysplastic syndrome (MDS) is divided into early (refractory anemia [RA] or refractory anemia with ringed sideroblasts [RARS]), and advanced (refractory anemia with excess of blasts [RAEB] or chronic myelomonocytic leukemia [CMML]) disease. Lymphoma is classified according to sensitivity to prior chemotherapy (chemosensitive or chemoresistant).

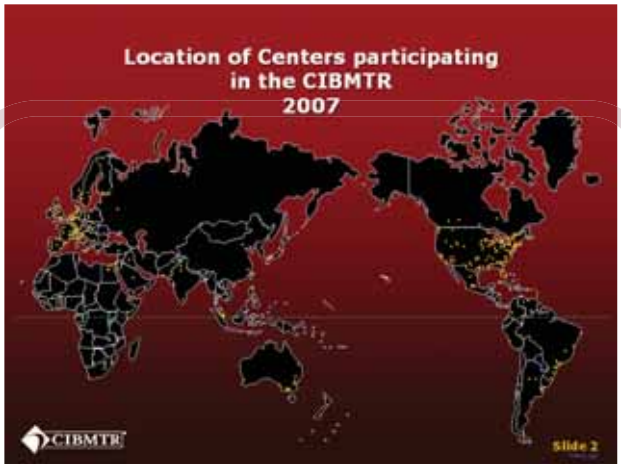
The classification of conditioning regimen intensities is based upon the agents, doses and schedules used. Several classifications are available, and for this report we used a composite classification. Cases defined as using reduced-intensity conditioning by the transplant center were classified as such. Cases without such information and with available data on chemotherapy agents, radiation and doses were classified according to the CIBMTR operational definition of conditioning regimen intensity:

Myeloablative conditioning regimen: regimens with total body irradiation doses of ≥500 cGY, single fractionated doses of ≥800 cGY, busulfan doses of >9mg/kg, or melphalan doses of >150 mg/m2 given as single agents or in combination with other drugs.

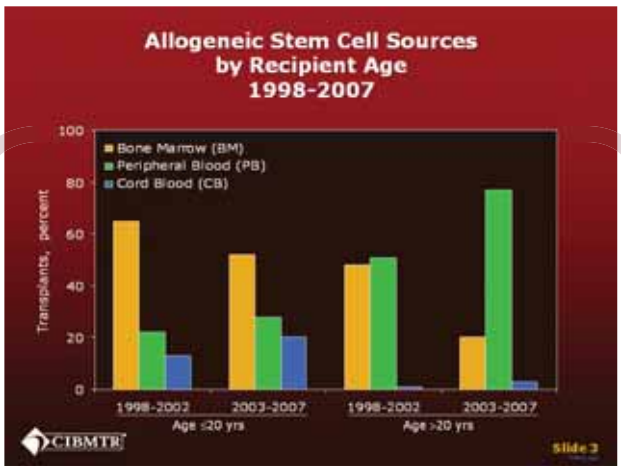
Reduced-intensity conditioning regimen: regimens with lower doses of total body irradiation, fractionated radiation therapy, busulfan, and melphalan than those used to define a myeloablative conditioning regimen (above).

This article may be cited as follows: Pasquini MC, Wang Z. Current use and outcome of hematopoietic stem cell transplantation: Part I CIBMTR summary slides, 2009. CIBMTR Newsletter [serial online], 2009; (15)1:7-11. It may be found online at: http://www.cibmtr.org/PUBLICATIONS/Newsletter/index.html.

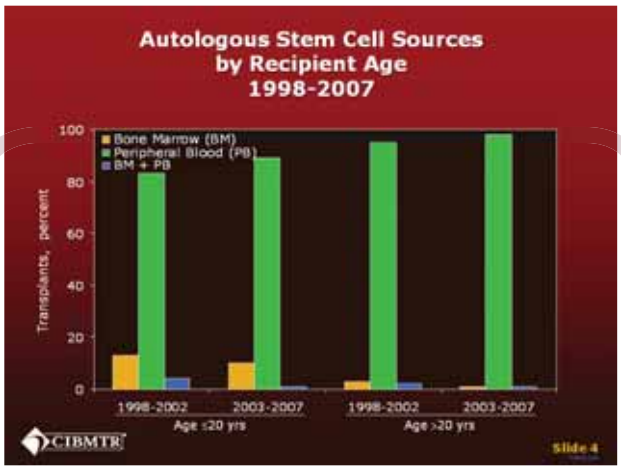




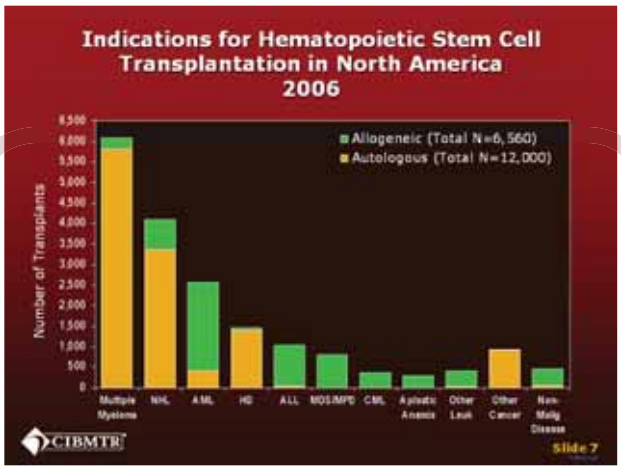
Slide 2: The CIBMTR database includes data reported by more than 500 centers in 54 countries worldwide.



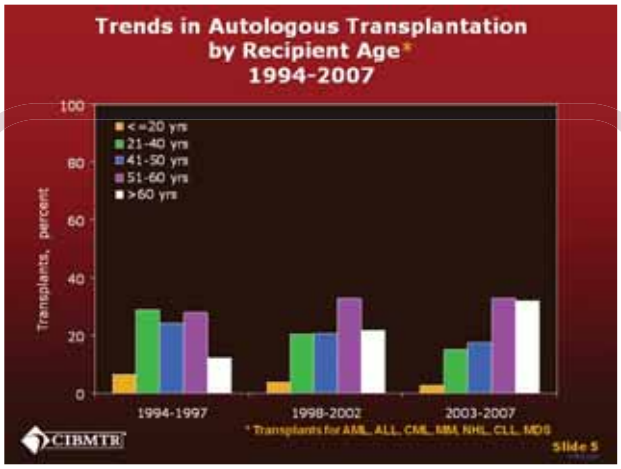
Slide 3: Bone marrow is the primary graft source for transplantation in children, though the use of peripheral blood and umbilical cord blood grafts is increasing. During the period 2003 to 2007, peripheral blood grafts accounted for 28%, and cord blood accounted for 20% of allotransplants in patients younger than 20 years of age. Among adults older than 20 years, peripheral blood is the most common source of allogeneic grafts.

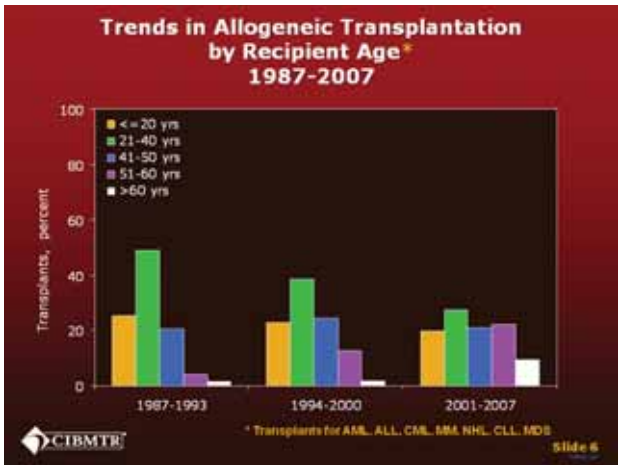


Slide 4: Mobilized peripheral blood progenitor cells are currently the main graft source for autologous HCT, accounting for greater than 90% of transplants in children. The practice of combining bone marrow with peripheral blood stem cells in patients unable to mobilize optimal cell doses has decreased in both adults and children (1%). Better mobilization regimens and patient selection may account for this trend.

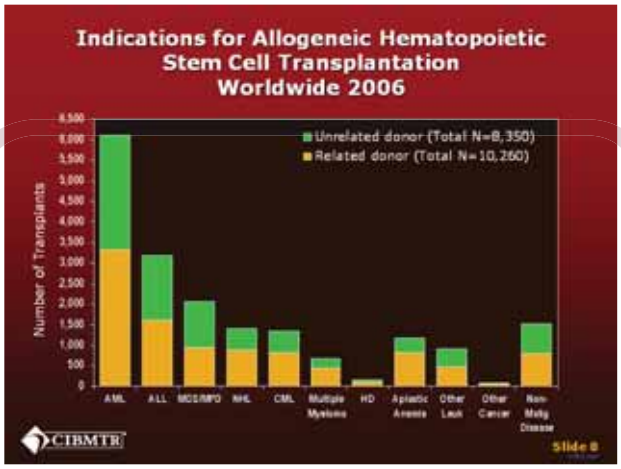


Slide 7: The most common indications for HCT in North America in 2006 were multiple myeloma and lymphoma, accounting for 63% of all HCTs. Multiple myeloma was the most common indication for autotransplantation and acute myeloid leukemia was the most common indication for allogeneic transplantation.

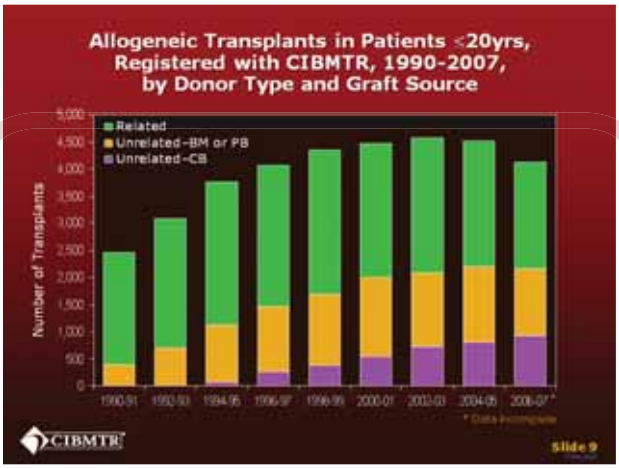


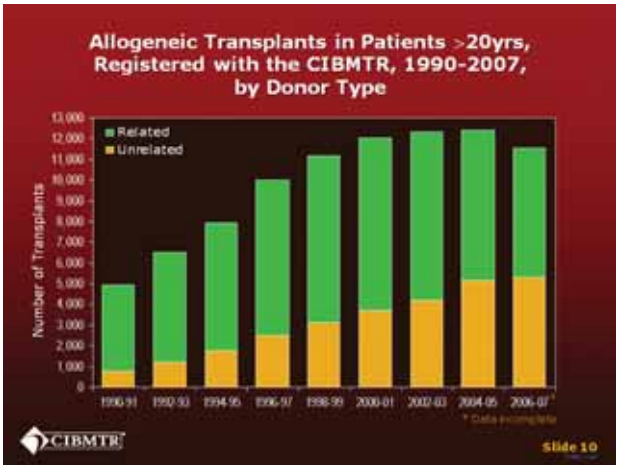


Slides 5 & 6: The numbers of autologous and allogeneic HCTs for treatment of the most common malignant disease indications in patients older than 60 continue to increase. Thirty-two percent of autograft recipients and 10% of allograft recipients in 2003-2007 were older than 60 years of age. The majority of autograft recipients (65%) are older than 50 years in this later period.

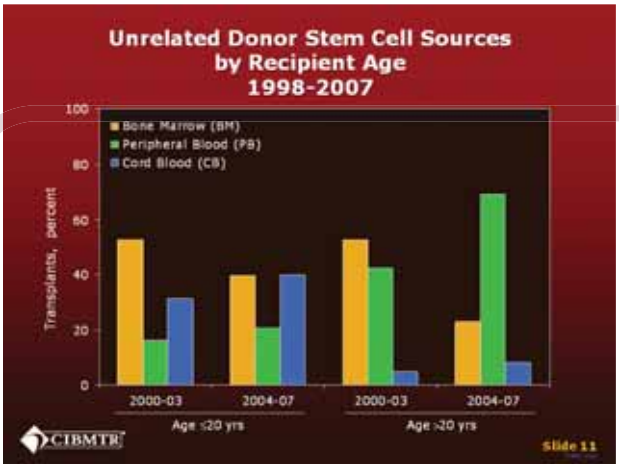


Slide 8: Approximately 45% of all allotransplants performed worldwide are from unrelated donors. Use of alternative donors depends on the disease indication, recipient's age, and lack of a related donor. Patients with acute leukemias and myelodysplasias most commonly receive unrelated allografts. The proportion of unrelated transplants performed in acute leukemias and myelodysplasia are 47% and 55% respectively.

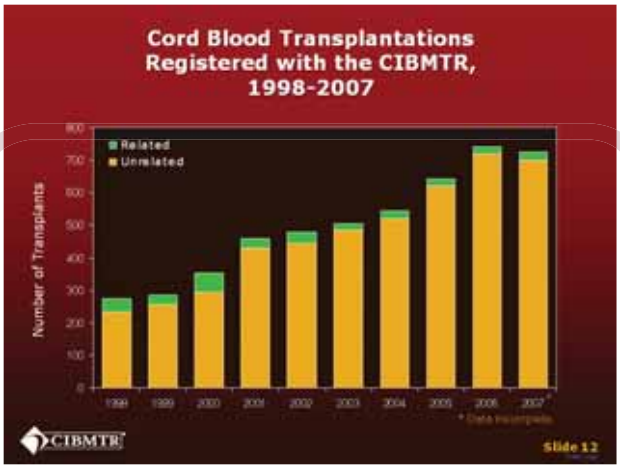




Slides 9 & 10: The proportion of transplants from unrelated donors is steadily increasing for both children and adults. For patients younger than 20, the proportion of unrelated transplants is 53%, with 23% utilizing cord blood as the graft source in 2006-2007. The same general trend is observed in patients older than 20 as well, with 46% of patients receiving unrelated donor transplants. Studies demonstrating similar outcomes between unrelated and related donor transplants, the increased availability of unrelated donors, and the increase in use of cord blood for the pediatric population are all responsible for this increase.

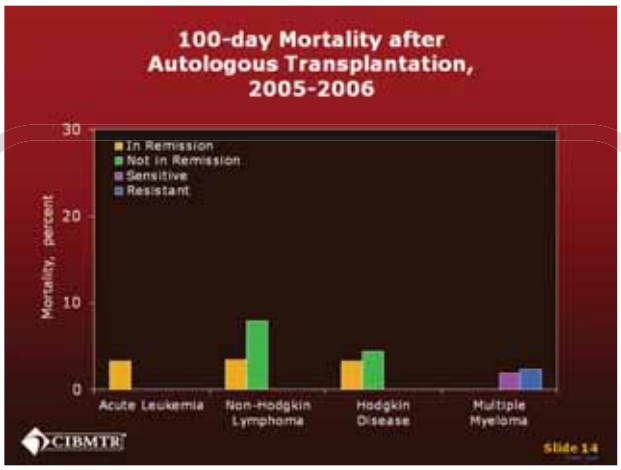


Slide 11: Graft selection for unrelated donor transplantation has shifted from bone marrow to other sources of hematopoietic cells. Among patients younger than 20 years, marrow was used for 40% of unrelated donor transplants in 2004-2007, compared to 53% in 2000-2003. Among patients older than 20 years, marrow accounted for 23% of unrelated donor transplants in 2004-2007, compared to 53% in 2000-2003. The use of cord blood, however, has increased only modestly in patients older than 20 years, reaching just 7%. Limited numbers of cells in single cord blood units is the main barrier for widespread use of this graft source in adults. Similar to related donor allogeneic transplantation, peripheral blood stem cells are the most common graft source for unrelated HCT in adults.

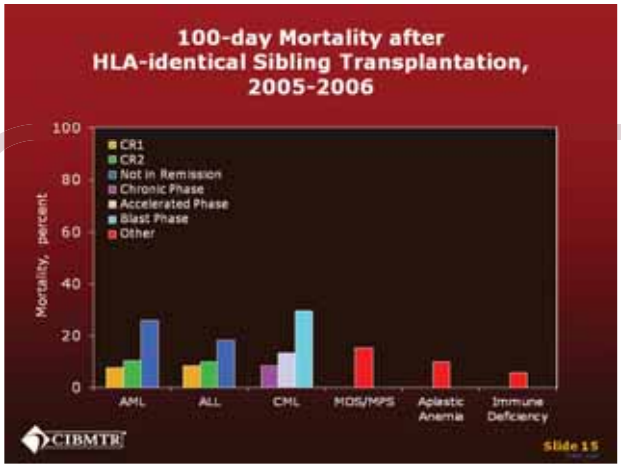


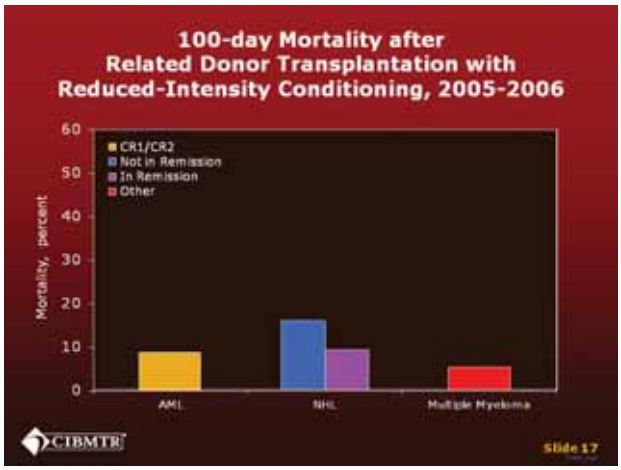
Slide 12: The past 10 years have seen a steady increase in the number of cord blood banks and consequently, in the number of umbilical cord blood transplantations. Although cord blood is most frequently an unrelated donor graft source, there are consistent small numbers of related donor cord blood transplants performed every year.

Slide 13: One-year survival rates after transplantation have generally improved in the last two decades. Outcomes of unrelated donor transplants are approaching those observed with related donors. Improvements in HLA-matching techniques, with consequently better donor selection, better overall patient selection for transplantation, and improvements in supportive care are the likely explanation for this trend.

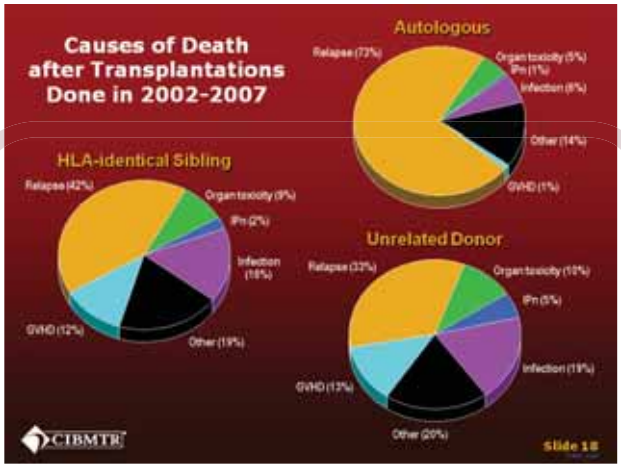


Slide 14: The 100-day mortality rate is often cited to reflect the toxicity of the transplantation process. Hundred-day mortality rates are much lower after an autologous than after an allogeneic transplant. The primary disease and disease status at the time of transplantation also significantly affect early post-transplant mortality.

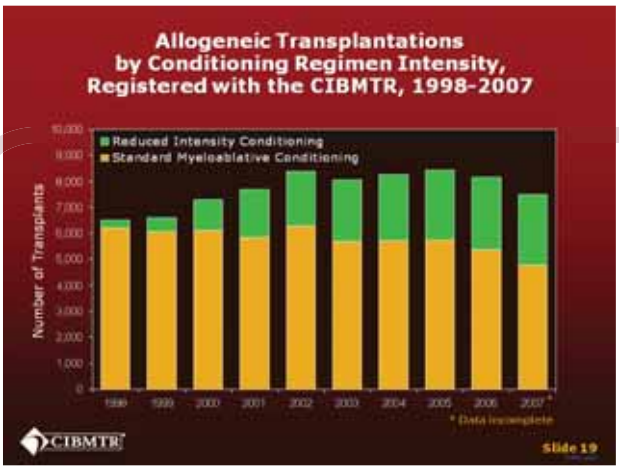


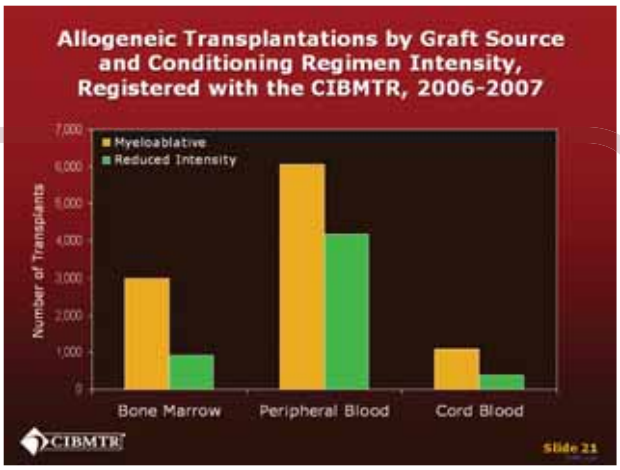


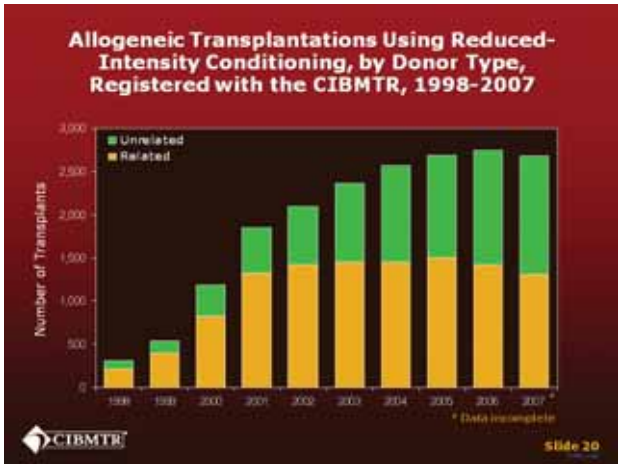
Slides 15 to 17: The effect of disease stage is even more apparent for allogeneic transplants. For instance, patients receiving HLA-identical sibling transplants for acute myeloid leukemia in remission have a 100-day mortality rate of 7 to 10% compared to 26% for patients with active leukemia at time of transplantation. Early mortality after an unrelated donor transplant is higher than after an HLA-identical sibling transplantation, but this also depends on disease and disease stage. The causes of death in the first 100 days post-transplant relate mainly to the primary disease, graft-versus-host disease, infection and end-organ damage. Early mortality in patients receiving allogeneic transplants after reduced-intensity conditioning is generally lower. However, patients with active disease have 100-day mortality rates approaching those observed with more intensive conditioning because of high rates of recurrent malignancy.

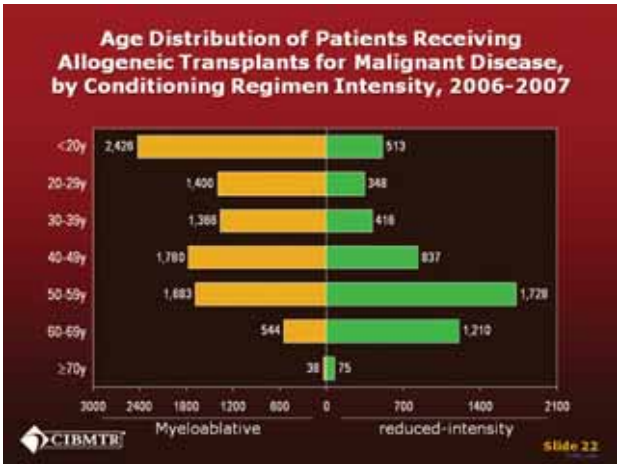


Slide 18: Relapse is the single most common cause of death after all transplant types, accounting for 73% of deaths after autologous HCT. Graft-versus-host disease (GVHD), interstitial pneumonitis (IPn) and infection are the major causes of death after allogeneic HCT.

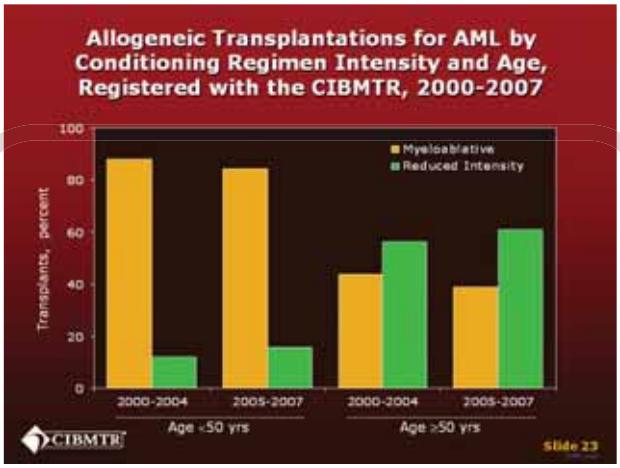








Slides 19 to 22: The numbers of allotransplants performed with reduced intensity conditioning have steadily increased since 1998, accounting for more than a third of transplants in the later periods. Unrelated donor transplants with reduced intensity conditioning follow the same trends observed with transplants with myeloablative conditioning, with a slight majority of unrelated over sibling donor transplants. Mobilized peripheral blood is the most common graft source for transplants with reduced intensity conditioning. The age distribution according to conditioning regimen intensity demonstrates the preferential use of conditioning regimens with lower intensity in patients older than 50 years. Sixty percent of reduced-intensity conditioning recipients are within this age group, compared to fewer than 25% of those receiving standard high-intensity regimens. Patients younger than 50 years who are ineligible to receive myeloablative conditioning because of co-morbidities may undergo an allogeneic transplant with reduced-intensity conditioning.



Slide 23: Acute myeloid leukemia (AML) is the most common indication for reduced-intensity conditioning allotransplant, and the proportion of these transplants compared to myeloablative regimens is increasing in older patients. Fifty-three percent of patients 50 years and above received an allotransplant with reduced intensity conditioning in 2005-2007. In younger patients, standard myeloablative intensity regimens remain the most common.

Our Supporters

Thanks to the many contributors who have joined our international collaboration for research in blood and marrow transplantation. We gratefully acknowledge the support of the Medical College of Wisconsin; the National Cancer Institute; the National Heart, Lung and Blood Institute; the National Institute of Allergy and Infectious Diseases; Office of Naval Research; Health Resources and Services Administration (HRSA/DHHS) and the generosity of the supporters listed below.

The views expressed in this newsletter do not reflect the official policy or position of the National Institute of Health, the Department of the Navy, the Department of Defense, or any other agency of the U.S. Government.

AABB
*Aetna
American Society for Blood and Marrow Transplantation
*Amgen, Inc.
Anonymous donation to the Medical College of Wisconsin
Astellas Pharma US, Inc.
Baxter International, Inc.
Bayer HealthCare Pharmaceuticals
Be the Match Foundation
Biogen IDEC
*BioMarin Pharmaceutical, Inc.
Biovitrum AB
BloodCenter of Wisconsin
*Blue Cross and Blue Shield Association
Bone Marrow Foundation
Canadian Blood and Marrow Transplant Group
CaridianBCT
*Celgene Corporation
CellGenix, GmbH
Centers for Disease Control and Prevention
Children's Leukemia Research Association
ClinImmune Labs
CTI Clinical Trial and Consulting Services
Cubist Pharmaceuticals
Cylex, Inc.
CytoTherm
DOR BioPharma, Inc.
Dynal Biotech, an Invitrogen Company
Eisai, Inc.
*Enzon Pharmaceuticals, Inc.
European Group for Blood and Marrow Transplantation
*Gamida Cell, Ltd.
GE Healthcare
Genentech, Inc.
*Genzyme Corporation
Histogenetics, Inc.
HKS Medical Information Systems
Hospira, Inc.
Infectious Diseases Society of America
Kiadis Pharma
Kirin Brewery Co., Ltd.
The Leukemia & Lymphoma Society
Merck & Company
Medical College of Wisconsin
MGI Pharma, Inc.
Michigan Community Blood Centers
*Millennium Pharmaceuticals
Miller Pharmacal Group
*Milliman USA, Inc.
*Miltenyi Biotec, Inc.
National Marrow Donor Program
Nature Publishing Group
New York Blood Center
Novartis Oncology
Oncology Nursing Society
*Osiris Therapeutics, Inc.
*Otsuka America Pharmaceutical, Inc.
Pall Life Sciences
Pfizer Inc
Saladax Biomedical, Inc.
*Schering Corporation
Society for Healthcare Epidemiology of America
StemCyte, Inc.
StemSoft Software, Inc.
Sysmex America, Inc.
*Teva Pharmaceutical Industries
*THERAKOS, Inc.
Thermogenesis Corporation
Vidacare Corporation
Vion Pharmaceuticals, Inc.
ViraCor Laboratories
*ViroPharma, Inc.
*Wellpoint, Inc.

*** Corporate Member**

CIBMTR Advisory Committee Members

Please address correspondence to:

CIBMTR® Milwaukee Campus
Medical College of Wisconsin

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

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

Website: www.cibmtr.org
Email: cibmtr@mcw.edu

Please contact the CIBMTR Statistical Center with address updates or to add a colleague to the CIBMTR Newsletter mailing list. We welcome your suggestions and comments.

This newsletter has been published for and on behalf of the CIBMTR by:

The SCAN Group Inc.
From concept to success.

W222 N625 Cheaney Drive
Waukesha, WI 53186

(262) 521-1365

www.scangroup.net

CIBMTR® Minneapolis Campus
National Marrow Donor Program

3001 Broadway Street N.E. Ste. 110
Minneapolis, MN 55413-1753 USA

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

Website: www.cibmtr.org
E-mail: cibmtr-contact@nmdp.org