CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Newsletter

Volume 13 Issue 2 December 2007

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CIBMTR Working Committees in the Spotlight

We continue our series focusing on the work of the 17 Working Committees of the CIBMTR. The Working Committees provide scientific oversight for the use of CIBMTR data and statistical resources.

Their responsibilities include designing and conducting studies relevant to their subject area and involving CIBMTR data, statistical resources, networks and/or centers; considering proposals to use CIBMTR data for studies pertinent to their subject area; periodically assessing and revising relevant sections of CIBMTR data collection forms; planning and conducting workshops at CIBMTR meetings.

Working Committees have responsibility for setting priorities for observational studies using CIBMTR's large clinical databases. These observational studies are a core activity of the CIBMTR. For a full listing of the 17 Working Committees and their leadership, point your browser to **http://www.cibmtr.org/COMMITTEES/working_committees_idx.html**.

In this issue, we highlight the work of the Lymphoma and Graft versus Host Disease Working Committees.

Lymphoma Working Committee

Autologous and allogeneic hematopoietic stem cell transplantation (HCT) has been used to treat lymphoma for more than 10 years, much of that time in the context of clinical trials but now much more as standard of care. The Lymphoma Working Committee (LYWC), one of the first established within the CIBMTR, focuses on cellular therapy for these diseases and has conducted numerous studies addressing a wide range of issues in the field of HCT for patients with Hodgkin Disease and non-Hodgkin lymphoma.

The LYWC is led by 3 co-chairs: Koen van Besien, MD (University of Chicago); Hillard M. Lazarus, MD (University Hospitals of Cleveland); Julie M. Vose, MD (University of Nebraska). The Committee's CIBMTR Scientific Director is Parameswaran Hari, MD. The CIBMTR statisticians are Mei-Jie Zhang, PhD, and Jeanette Carreras, MPH. The co-chairs are responsible for promoting and developing the scientific agenda, establishing priorities after obtaining input from the Working Committee members, and ensuring the progress of the research studies and publications. They meet on a regular basis with CIBMTR staff.

From 2006 to present, the LYWC had the following studies either published/submitted or presented at international meetings:

LY01-02 Navarro WH, Loberiza Jr FR, Bajorunaite R, Armitage JO, Ballen K, Bashey A, Bredeson CN, Carreras J, Freytes CO, Gibson J, Hale GA, Horowitz MM, Lazarus HM, LeMaistre CF, Lister J, Marks D,

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Graft Versus Host Disease Working Committee

The Graft Versus Host Disease Working Committee is headed by 3 co-chairs: Olle Ringdén, MD, PhD (Huddinge University); Claudio Anasetti, MD (H. Lee Moffitt Cancer Center and Research Institute); Steven Pavletic, MD (National Cancer Institute). Additional CIBMTR personnel for the committee include statisticians Tao Wang, PhD, and Dan Wang, MS, and CIBMTR Scientific Director Mukta Arora, MD, MS.

The working committee is committed to designing and conducting clinical research in the field of graft versus host disease. Observational research using the large clinical database of the CIBMTR is the core activity of the committee. In addition, the committee reviews and evaluates new proposals submitted to the committee, reviews relevant sections of the data collection forms and conducts workshops at the CIBMTR meetings.

The incidence and clinical spectrum of graft versus host disease appears to be changing with newer strategies of hematopoietic stem cell transplant being currently used. Our mission is to study and evaluate clinical presentation and outcomes of the disease in different donor sources (related donor, unrelated donor, cord blood) and transplant strategies (myeloablative, non-myeloablative) being used and to identify high risk groups through observational studies using our large database. The committee has contributed significantly to scientific research as is documented by the submission of 4 abstracts to the American Society of Hematology this year. Two manuscripts are prepared and ready for submission and 3 more are in preparation. Its major

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Lymphoma Working Committee – continued from page 1

Martino R, Maziarz RT, Pavlovsky S, Schiller G, Schouten HC, Stadtmauer E, van Besien K, Vose JM, Rizzo JD. **Impact of body mass index on mortality of patients with lymphoma undergoing autologous hematopoietic cell transplantation.** *Biol Blood Marrow Transplant 12:541-551, 2006*.

LY02-01 Hari P, Carreras J, Zhang M-J, Rizzo JD, Gale RP, Armitage JO, Bashey A, Bolwell BJ, Bredeson CN, Bujan-Boza WA, Burns LJ, Cairo MS, Freytes CO, Gibson J, Goldstein SC, Hale GA, Herzig RH, Inwards DJ, Keating A, LeMaistre CF, Maharaj D, Marks DI, Mason JR, Maziarz RT, McCarthy PL, Miller AM, Shouten HC, Slavin S, Urbano-Ispizua A, Wiernik PH, Vose JM, Lazarus HM, van Besien K. **Reduced-Intensity versus Myeloablative HLA-Matched Sibling Transplants in Follicular Lymphoma.** *Submitted*.

LY04-02 Hayes-Lattin B, Carreras J, Zhang M-J, van Besien K, Vose JM, Lazarus HM, Rizzo JD, Hari P. **Superior Survival after Autologous vs. Allogeneic Hematopoietic Stem Cell Transplantation for Diffuse Large B-Cell Lymphoma Not Explained By Differences in Chemosensitivity.** *Presented at the 48th Annual Meeting of the American Society of Hematology, Orlando, FL, 2006. Manuscript in progress.*

LY05-02 Smith SM, van Besien K, Carreras J, Vose JM, Lazarus HM, Hari P. **Clinical Outcome of a Second Autologous Hematopoietic Stem Cell Transplant for Non-Hodgkin and Hodgkin Lymphoma Relapsing After a First Autotransplant.** *Presented at the 48th Annual Meeting of the American Society of Hematology, Orlando, FL, 2006. Manuscript in progress.*

LY05-03 Devetten M, Hari P, Carreras J, Logan B, van Besien K, Vose JM, Lazarus HM, Anderlini P. **Unrelated Donor Non-meloablative/Reduced Intensity Hematopoietic Stem Cell Transplantation for Patients with Relapsed and Refractory Hodgkin's Lymphoma.** *Presented at the 48th Annual Meeting of the American Society of Hematology, Orlando, FL, 2006. Manuscript in progress.*

The following section summarizes additional LYWC studies with manuscripts in preparation:

D98-10 Unrelated Allogeneic Bone Marrow Transplantation for Non-Hodgkin's Lymphoma (Study Chair: Philip Bierman, MD, University of Nebraska Medical Center, Omaha, NE). This project describes the results of unrelated allogeneic bone marrow transplants for NHL that have been facilitated by the National Marrow Donor Program.

LY01-01 Outcomes of Autologous Transplants for Lymphoma in Patients 55 and Over (Study Chair: Hillard M. Lazarus, Case Western Reserve University, Cleveland, OH). This project compares the clinical outcomes of elderly (age > 55 years) versus younger (< 55 years) patients receiving autotransplant for NHL while adjusting for other patient-, disease-, and treatment-related factors.

The following section summarizes ongoing LYWC research studies:

LY03-01 Effects of Pre-transplant In-vivo Rituximab on the Outcomes of Autologous HCT in Patients with NHL (Study Chair: J. Vose, University of Nebraska Medical Center, Omaha, NE; ***Status:*** *Analysis*). This project compares clinical outcomes of autotransplants for diffuse large B-cell lymphoma in patients who received rituximab during the mobilization phase, preparative regimen or first year posttransplant versus those who did not receive rituximab.

LY04-01 Alternative Donor HCT for Children with NHL (Study Chair: G. Hale, St. Jude Children's Research Hospital, Memphis, TN; ***Status:*** *Protocol Development*). This project describes clinical outcomes after reduced intensity or non-myeloablative conditioning regimen in alternative donor HCT (unrelated donor or mismatched family members) in patients with NHL.

LY04-03 Outcomes of Autologous Versus Allogeneic HCT for Patients with NHL with Pre-existing Central Nervous System Involvement (Study Chair: R. Maziarz, Oregon Health & Science University, Portland, OR; ***Status:*** *Form Development*). This project compares the clinical outcomes between patients undergoing autologous transplantation for non-Hodgkin lymphoma with versus without pre-existing CNS involvement.

LY06-02 Non-myeloablative Allogeneic HCT in Patients Who Experience Relapse After Autologous Stem Cell

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New Forms Harmonization

By Diane J. Knutson, BS

What an exciting time to be involved in HCT research! Three years ago CIBMTR met with NMDP to revise the Research Report Forms and harmonize them into a single set of documents. Along the way we updated the TED Forms with EBMT (MED-A). Then, came along the caDSR and AGNIS projects drawing in more groups such as APBMTG (Asian Pacific BMT Group), COG (Children's Oncology Group) and others to develop common data elements. A little more than a year ago the U.S. government initiated the Stem Cell Therapeutic Outcomes Database (SCTOD).

Each project impacted the other hence it has been a long process weaving them all together. The collaboration and communication are exactly what the founders of these research organizations planned all along: the HCT world working together to find the answers to their research questions the quickest way possible. Training for data collectors is now being conducted in various formats such as international teleconferences (July 2007), live meetings (most recently at the NMDP Council Meeting in Minneapolis and upcoming at the BMT Tandem Meetings in San Diego, February 2008). The CIBMTR web site is hosting links to recorded versions of some of the sessions (http://www.cibmtr.org/MEETINGS/Meeting_Materials_Archive/index.html) accessible at your convenience. New manuals are available for the new Forms which will include Disease Insert Manuals produced with input from the CIBMTR Working Committees. If the answers to your data queries are not found in the Manuals, each center now has a specific Clinical Research Liason to contact, either in Milwaukee or Minneapolis, for personalized attention. The Unique ID system is going to minimize the risk of "duplicate" recipients in the database, as this number will follow the recipient no matter where in the world they receive their care. Forms submission now consists of a simple schedule to be followed for all transplant recipients (allo or auto, related donor or unrelated, bone marrow, peripheral blood stem cell or umbilical cord blood) and Donor Cellular Infusion data is now collected within the body of the main Forms. And all of this is done with a new, free, Web based data entry tool: FormsNet™ 2.0. Soon the AGNIS project will enable centers to transmit the data elements from their own database to meet the requirements of Forms submission and to be able to communicate with any other AGNIS node. But with all this technology, don't worry—humans are still needed to interpret the meaning of the results of the analyses. We look forward to seeing you in San Diego at the BMT Tandem Meetings!

Perspectives

By Sergio A. Giralt, MD

Chair, Advisory Committee CIBMTR, Professor of Medicine, University of Texas, M. D. Anderson Cancer Center, Houston, TX, USA

MORE THAN THE SUM OF ITS PARTS

How many times have we heard that a specific organization is worth more than the sum of its parts? Although this phrase is commonly used, one wonders how we can prove it, and in these days of corporate takeovers and asset sell-offs, whether such statements are indeed true. As I culminate my tenure as Chair of the Advisory Committee of the CIBMTR, I have come to realize that our organization is a true example of how a human enterprise can become so synergistic that its true value is much more than the sum of its parts.

Take for example the medical director of a medium sized program in a specific country or region that decides to report to the CIBMTR. His fifty transplants a year by themselves hardly constitute a representative transplant experience, and if he or she were to try to publish their cumulative experience it would be unlikely to find its way into a widely read journal, unless they had done something highly innovative (unlikely with the modest transplant activity). However, by reporting the data to the registry, this medical director can now participate in the different working groups, and propose studies looking at ideas or issues that he or she has encountered during clinical practice. These ideas would find resonance and be refined within the peer-review process of the working committees and eventually lead to a protocol for an observational study. Moreover, through the protocol development process, this medical director or one of his staff members would have developed relationships and networks that could lead to an eventual collaboration in a prospective trial looking at ways to improve transplant outcomes.

On another dimension, continued participation in working committees and in protocol development allows us to identify leaders in the field outside of the large, well established transplant centers, and gives a venue for junior faculty to propose hypothesis generating or confirming projects. For many of these "emerging leaders" in our field this is the best opportunity to generate a "peer reviewed" publication early in the course of their careers and few things provide more encouragement to continue an academic career than seeing our work published in a journal of our peers.

In summary, as we think about the amount of time we spend sending data to the registry, as well as the frustrations in delays in getting projects through, let's remember we are the CIBMTR, we provide the data, we suggest the projects and we sit on the committees that make this wonderful organization work. Let's remember that when Mortimer Bortin started asking his colleagues to share their data he embarked on a visionary road that has led us to where we are today. The data that we have made available to the CIBMTR through our efforts has become a true mother lode of information; it has allowed us to demonstrate trends in our fields, generate and confirm hypotheses and design clinical trials. The CIBMTR has opened the world of transplant research to many junior faculty and currently established transplanters. All this has resulted in improved treatments for our patients and their families (the definitive mission statement for all of us). The network created through the CIBMTR has fostered an atmosphere of collaboration unknown in many other fields of research. In short, the CIBMTR is a true example of where the whole is much more than the sum of the parts. Our continued participation and involvement can only make it bigger and better. Thank you all for your efforts and I look forward to seeing you in San Diego.

Lymphoma Working Committee – continued from page 2

Transplantation for Lymphoma (Study Chair: C Freytes, University of Texas Health Science Center, San Antonio, TX; ***Status:*** *Protocol Development*). This project describes the clinical outcomes of patients undergoing non-myeloablative HCT for NHL relapsing after autologous transplantation.

LY06-03 HLA-identical Sibling HCT Versus HLA Matched Unrelated Donor HCT in Patients with Follicular Lymphoma (Study Chair: A Sureda, Hospital de la Santa Creu I Sant Pau, Barcelona, Spain; ***Status:*** *Data File Preparation*). This project compares the clinical outcomes between patients undergoing allogeneic transplantation from an HLA-identical sibling versus an HLA matched unrelated donor for follicular NHL. This is a joint study of the Lymphoma Working Party of the EBMT and the LYWC of the CIBMTR.

LY06-05 Comparison of Autologous Versus Allogeneic HCT for T-cell NHL (Study Chair: S Smith, University of Chicago, Chicago, IL; ***Status:*** *Protocol Development*). This project compares outcomes of autologous versus allogeneic hematopoietic stem cell transplantation for patients with T-cell non-Hodgkin lymphomas.

LY06-06 A Prognostic Model for Prolonged Event-free Survival After Autologous or Allogeneic HCT for Relapsed and Refractory Hodgkin Disease (Study Chair: P McCarthy, Roswell Park Cancer Institute, Buffalo, NY; ***Status:*** *Data File Preparation*). This project will validate a prognostic model for event-free survival for patients with Hodgkin Disease, based on factors measured at the time of HCT and will determine if other predictive models are superior.

LY07-01 T-depleted Allotransplantation for Lymphoma (Study Chair: Koen van Besien, University of Chicago, Chicago, IL; ***Status:*** *Protocol Development*). This project will compare the clinical outcomes of patients undergoing allogeneic stem cell transplantation using unmanipulated versus in vivo or in vitro T-cell depleted grafts.

LY07-02 Transplant Outcomes in Patients with Mycosis Fungoides and Sezary Syndrome (Study Chair: Mary Jo Lechowicz, Emory University, Atlanta, GA; ***Status:*** *Protocol Development*). This project will test the hypothesis that reduced intensity conditioning regimens followed by allogeneic transplantation confers equivalent or superior relapse-free survival to treatment with myeloablative conditioning regimens and allogeneic transplantation in patients with cutaneous T-cell lymphoma/Sezary syndrome.

LY07-03 Unrelated Donor Transplantation Versus Second Autotransplants for Autograft Failures (Study Chair: S. Smith, University of Chicago, Chicago, IL; ***Status:*** *Protocol Development*). This project will compare the clinical outcomes of non-myeloablative HCT versus the outcomes of second autologous HCT lymphoma relapsing after a first autologous stem cell transplant.

We encourage all members of the transplant community to actively participate in the Committee 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 LYWC meeting will be held in February 2008 at the BMT Tandem Meetings in San Diego, California.

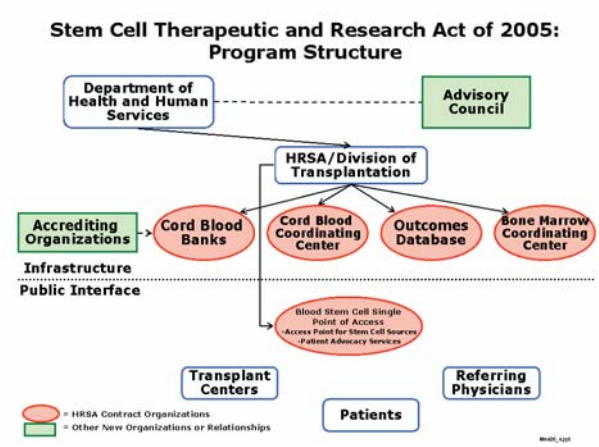
C.W. Bill Young Cell Transplantation Program Stem Cell Therapeutic Outcomes Database

By J. Douglas Rizzo, MD, MS & Paula Watry, RN, PA-C

Where are we now?

The Center for International Blood and Marrow Transplant Research (CIBMTR) has made considerable progress establishing the Stem Cell Therapeutic Outcomes Database (SCTOD) for the C.W. Bill Young Cell Transplantation Program (administered by the United States Health Resources and Services Administration (HRSA)). As this article goes to print, CIBMTR is in position to launch FormsNet™ 2.0 and the new data collection instruments pending approval from the Office of Management and Budget. With the launch of FormsNet™ 2.0, we will implement an innovative electronic data collection system and enhanced forms that represent the first major visible accomplishment to establish the SCTOD. This marks the beginning of an exciting new era for research in hematopoietic cell transplantation (HCT) as we believe these changes will result in substantial benefit to transplant centers.

Background:
In December 2005, the U.S. Stem Cell Therapeutic and Research Act of 2005 (Public Law 109-129) established the C.W. Bill Young Cell Transplantation Program (the Program). Figure 1 displays the overall schema of this Program. The 5 key components are: a Bone Marrow Coordinating Center (BMCC); a Cord Blood Coordinating Center (CBCC); an Office of Patient Advocacy and Single Point of Access for health care professionals and patients (OPA/SPA); and a Stem Cell Therapeutics Outcomes Database (SCTOD). The National Marrow Donor Program (NMDP) was awarded the contract for the first 3 components. Lastly, several cord blood banks received contracts to develop a National Cord Blood Inventory.



Data collection for the SCTOD will include collection of data for 1) allogeneic HCTs done in the U.S. using related or unrelated donors; 2) allogeneic HCTs done using US donors, whether the transplantation is done in the U.S. or elsewhere: and 3) use of allogeneic hematopoietic cells for emerging clinical applications other than hematopoietic reconstitution.

Highlights of recent accomplishments

Revised Forms, the first steps:
Implementation of the SCTOD presented significant challenges and opportunities for the CIBMTR and the HCT community. Beginning in October 2006, the CIBMTR collaborated with national and international partners to develop a standard HCT dataset for collection. During the process, consideration was given to meeting the needs of the program while maintaining awareness of the potential burden faced by transplant centers. At the recommendation of the ASBMT Quality Outcomes committee, data collection instruments now include a comorbidity index to allow for better case-mix adjustment to meet the needs of center-specific outcomes reporting. Consensus was reached in March 2007, allowing finalization of data elements and forms.

The following forms will be used to collect data for the SCTOD:
- Pre-TED
- Post-TED
- Infectious Disease Markers (IDM), HLA, Infusion Form

These forms may be viewed at: http://www.cibmtr.org/DATA/data_idx.html. Transplant centers will be required to use these new forms within 3 months of launching the new data collection systems. We urge teams to approach their hospital administrators seeking support for this new, mandatory cost of doing business.

Unrelated to the SCTOD, but equally important, the CIBMTR also finalized substantial revisions to Harmonized Research Forms to be used by Research Centers to submit comprehensive research data for selected sub-sets of patients. After release, these forms will be used for all research reporting to both the NMDP and CIBMTR, eliminating separate but overlapping research data fields. The new research forms, too, can be found at http://www.cibmtr.org/DATA/data_idx.html, and will follow the same implementation as the SCTOD instruments.

FormsNet™ 2.0, the new Electronic Data Collection System
The FormsNet™ 2.0 system was designed and implemented by the NMDP IT department under a sub-contract with the MCW to collect data for the Program. It is a web-based application for submission of outcomes data, both at the TED and Harmonized Research Form level. Some of the positive features of the system are:
- Web-based application with easy, secure access
- SecurID® RSA token, ID and PIN required
- Real time features
- Forms submission
- "Forms due" list
- Validation and error correction/override
- Incomplete form storage for completion later
- Query and reporting tools
- Data entry that does not require a mouse
- Completed form availability in PDF format

Initiation of FormsNet™ 2.0 at HCT centers will happen in stages, in order to provide adequate opportunity for program support to new users. We anticipate implementing FormsNet at centers over the course of a few months. Although we strongly encourage centers to adopt this electronic method of data reporting, for centers choosing to do so, paper forms may still be submitted for the near future.

AGNIS (A Growable Network Information System) is an electronic messaging system under development. At the time of this printing, the system is functional and capable of exchanging much of the data collected for the SCTOD. AGNIS will be used to exchange data between center's databases and the CIBMTR in each direction. Initially, centers who submit data to the SCTOD using Forms-

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Report on state of the art in blood and marrow transplantation –

The Summary Slides are an annual report of the data submitted to the CIBMTR. This first part focus on trends in the use of hematopoietic stem 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.

Reference for the CIBMTR summary slides is:

Pasquini, M.C.; Wang, Z.; Schneider, L. **Current use and outcome of hematopoietic stem cell transplantation: part I- CIBMTR Summary Slides, 2007.** CIBMTR Newsletter [serial online]. 2007, 13(2):5-9. Available at: http://www.cibmtr.org/PUBLICATIONS/Newsletter/index.html Accessed (insert date here).

Marcelo Pasquini, MD, MS[a]; Zhiwei Wang, MS[b]; Linda Schneider[c]

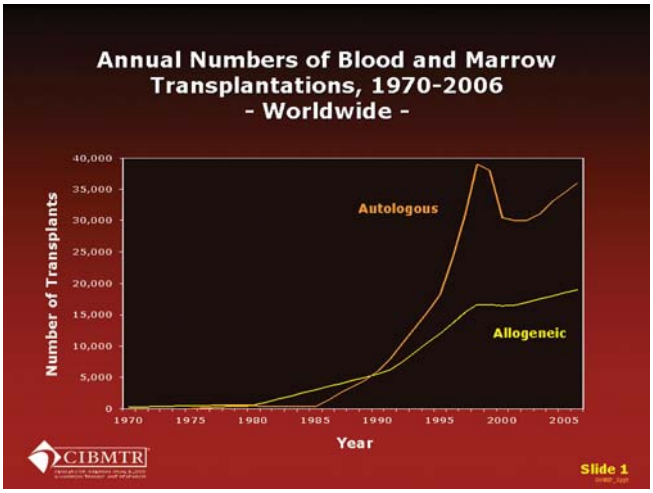
[a]Assistant Scientific Director, [b]Masters Level Statistician, [c]DTP Specialist.

Part I – CIBMTR Summary Slides, 2007

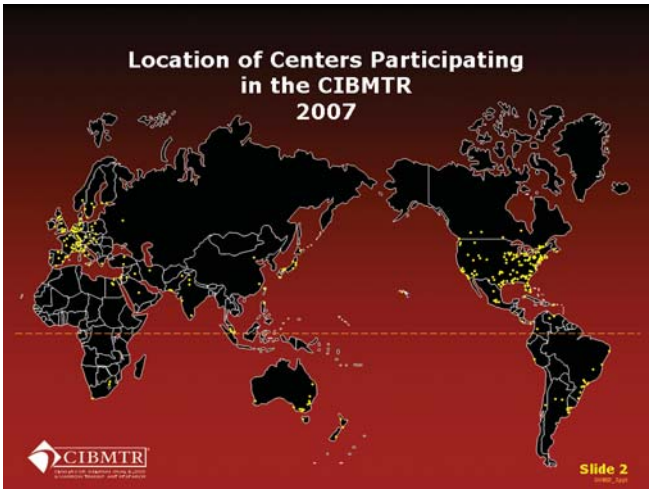
By Marcelo Pasquini, MD, MS; Zhiwei Wang, MS; Linda Schneider, DTP

CIBMTR, Medical College of Wisconsin, Milwaukee, WI, USA

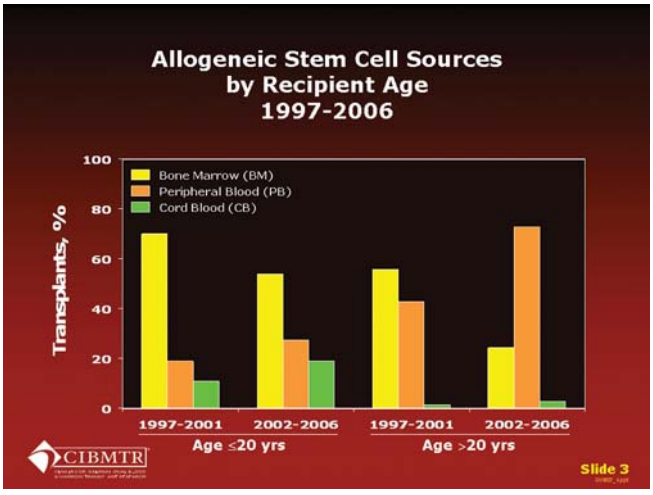
Slide 1: There are an estimated 50-60,000 hematopoietic stem cell transplants (HCTs) done annually worldwide. This slide reflects several notable events over the past decade. These include the initial enthusiasm and later disappointment about the use of autotransplants for breast cancer, the availability of targeted nontransplant therapy for chronic myelogenous leukemia (a leading indication for allogeneic HCT) and the increasing use of autologous and allogeneic HCT in older patients.

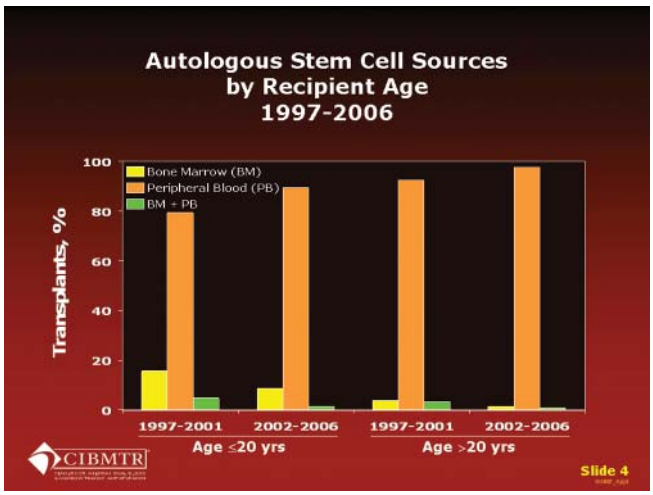


Slide 2: The CIBMTR database includes data reported by more than 500 centers in 54 countries worldwide.



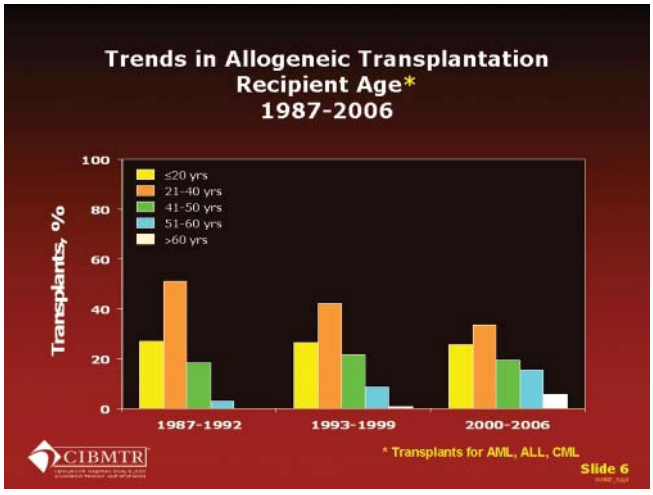
Slide 3: Bone marrow is the primary graft source for transplantation in children though use of peripheral blood and umbilical cord blood grafts are increasing. During the period 2002 to 2006, peripheral blood grafts accounted for 27% and cord blood accounted for 19% of allotransplants in patients younger than 20 years of age. Among adults older than 20 years, peripheral blood is the most common source of allogeneic grafts; very few adults receive cord blood transplants currently.





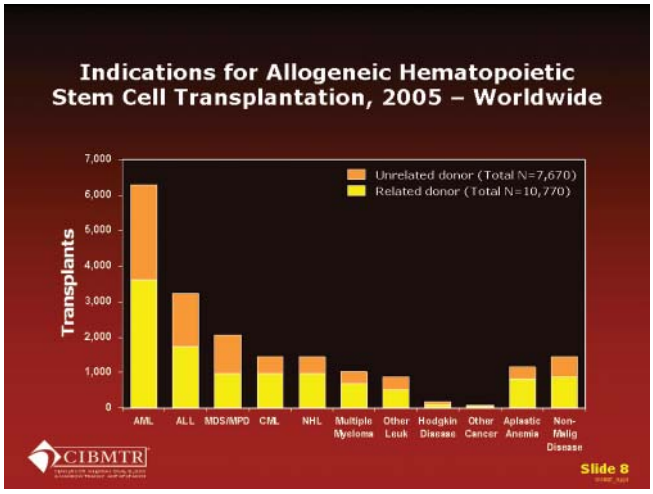
Slides 4: Peripheral blood is the main source of autologous grafts, accounting for 90% of autotransplants in children and >95% of autotransplants in adults.

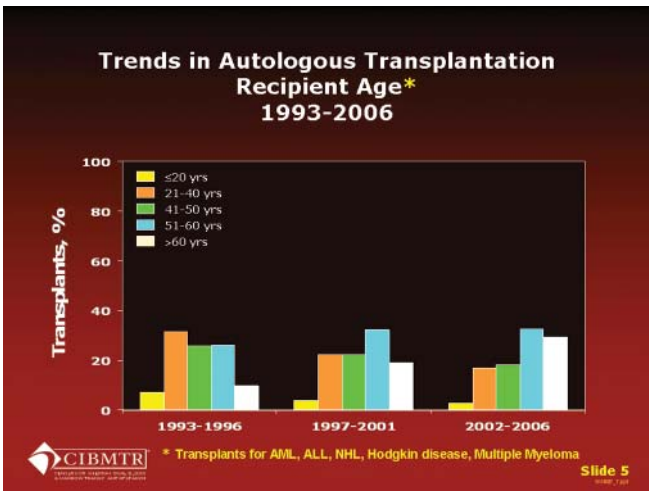
Slides 5 & 6: The numbers of autologous and allogeneic HCTs in patients older than 50 continue to increase. Sixty-two percent of



for autotransplantation and acute leukemia was the most common indication for allogeneic transplantation.

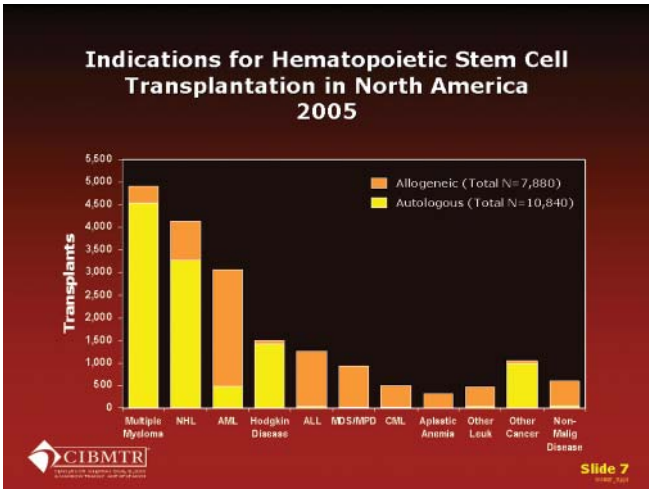
Slide 8: Approximately 40% of allotransplants are from unrelated donors. Indications are similar to those for related donor transplantation.



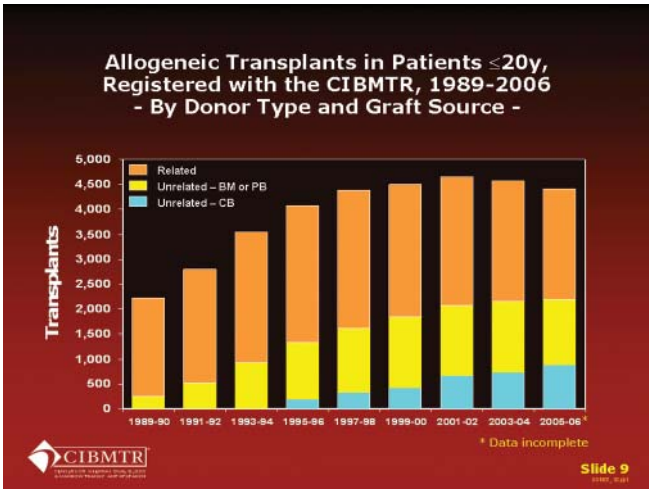


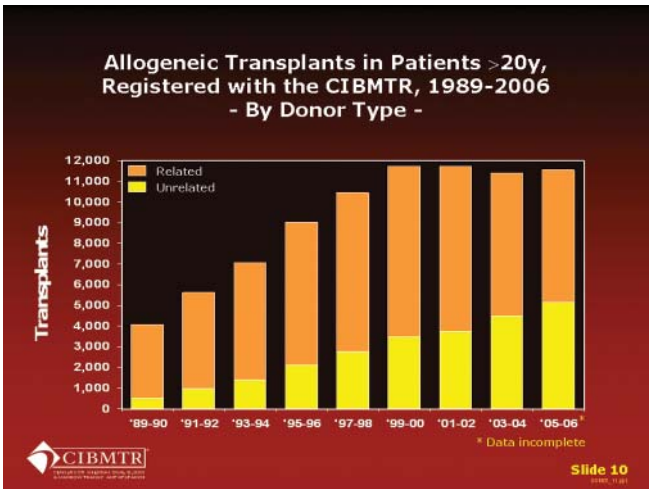
autograft recipients and 35% of allograft recipients in 2002-2006 were older than 50 years of age.

Slide 7: The most common indications for HCT in North America in 2005 were multiple myeloma and lymphoma, accounting for 56% of all HCTs. Multiple myeloma was the most common indication



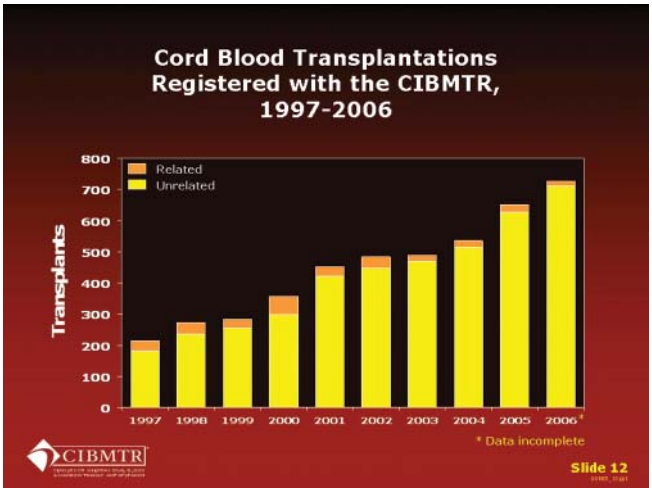
Slides 9 & 10: Among patients younger than 20 years of age, 50% of allogeneic transplants are from unrelated donors. Forty percent of the unrelated donor transplants in these patients use cord blood grafts. Among adults older than 20 years of age, 44% of transplants use unrelated donors in the period of 2005 to 2006.





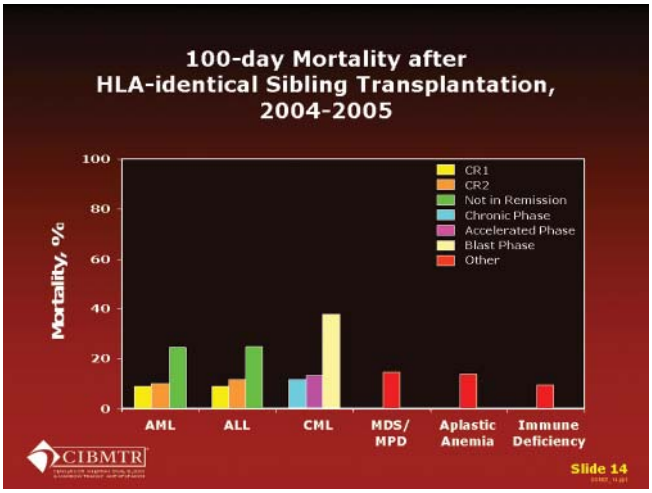
Few of these use cord blood grafts. Studies demonstrating similar outcomes with unrelated and related donor transplants (especially in children), increased availability of unrelated donors and cord blood grafts all contribute to these trends.

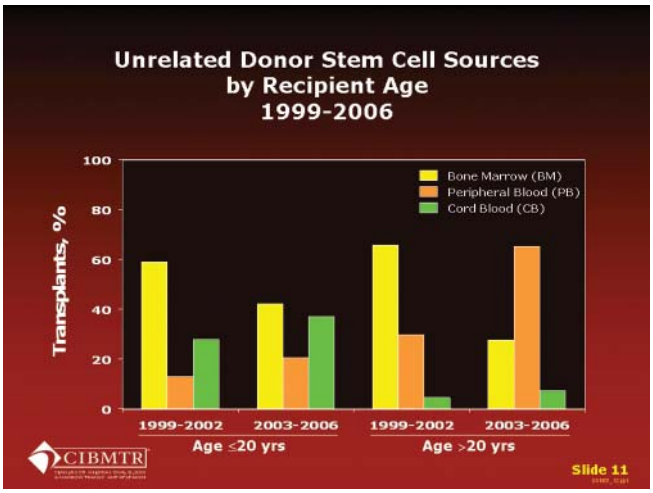
Slide 11: There has been a shift toward use of peripheral blood and cord blood rather than marrow for unrelated donor transplantation.



of umbilical cord blood transplantations, primarily from unrelated donors.

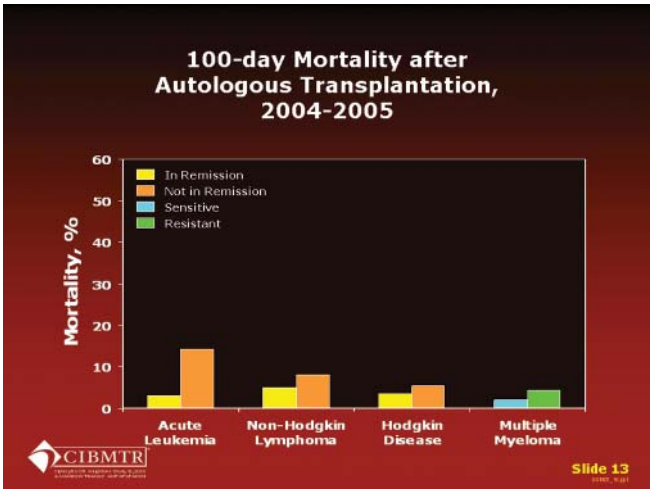
Slide 13: A 100-day mortality is an often-cited statistic to reflect toxicity. One-hundred day mortality rates are much lower after autologous than after allogeneic transplantation. Primary disease





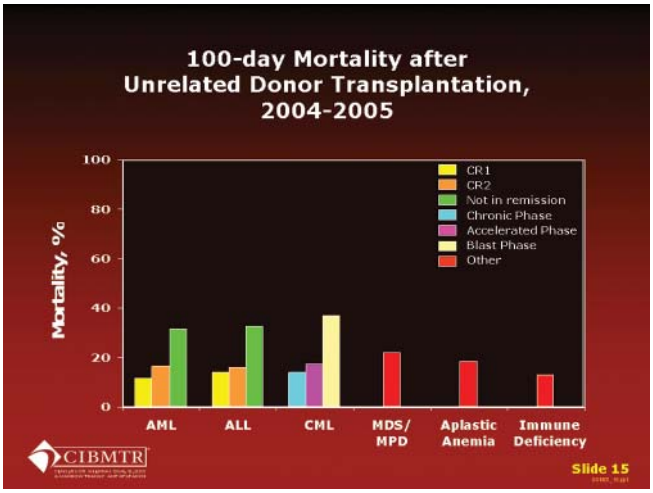
Among patients younger than 20 years, marrow was used for 42% of unrelated donor transplants in 2003-2006 compared to 59% in 1999-2002. Among adults older than 20 years, marrow accounted for 28% of unrelated donor transplants in 2003-2006 compared to 66% in 1999-2002.

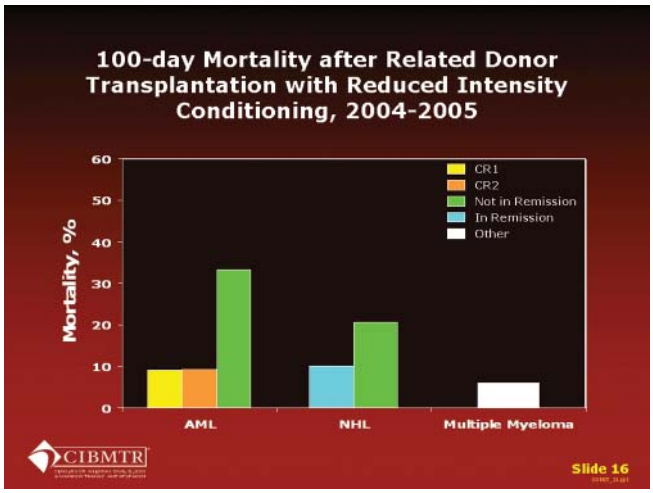
Slide 12: The past 10 years have seen a steady increase in the number of cord blood banks and, consequently, in the number



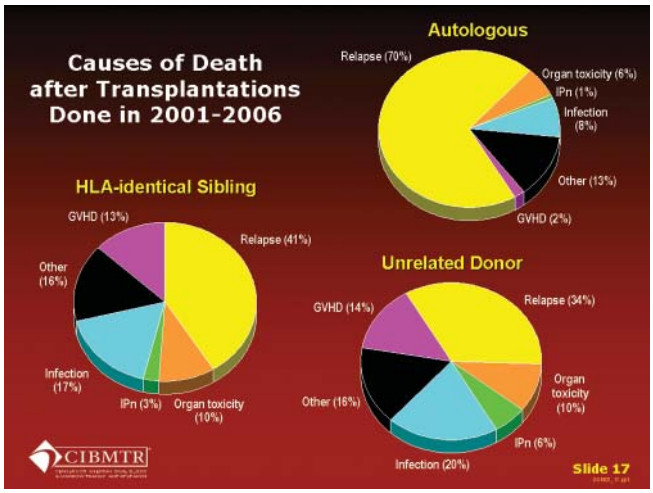
and disease status at time of transplantation also significantly affect early posttransplant mortality.

Slides 14 to 16: The effect of disease stage is even more apparent in the allotransplant setting. For instance, patients receiving HLA-

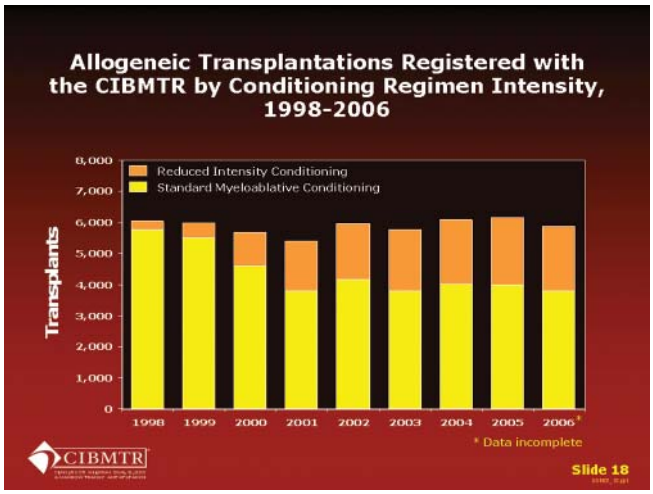




identical sibling transplants for acute myeloid leukemia in remission have a 100-day mortality rate of 8 to 10% compared to 22% for patients with active leukemia at time of transplantation. Early mortality after unrelated donor transplantation is higher than after HLA-identical sibling transplantation but also depends on disease and disease stage. The causes of death in the first 100 days posttransplant

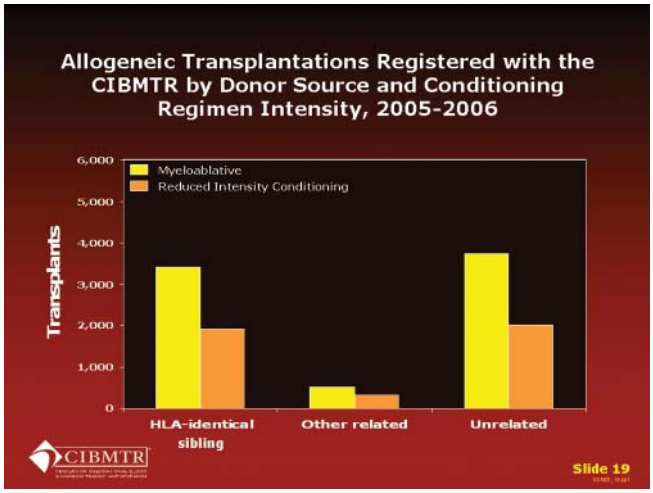


mainly relate to graft versus host disease, infection and end-organ damage. Patients with active disease at transplantation also have a higher risk of relapse. Early mortality in patients receiving allogeneic transplants after reduced intensity conditioning is generally lower. However, patients with active disease have 100-day mortality rates approaching those observed with more intensive conditioning because of high rates of recurrent malignancy.

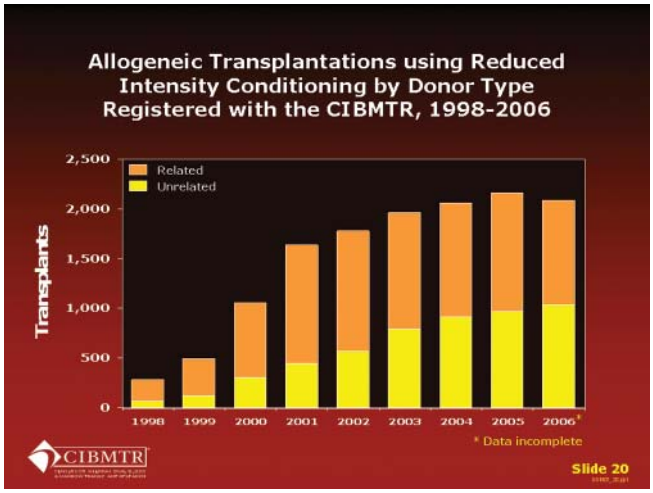


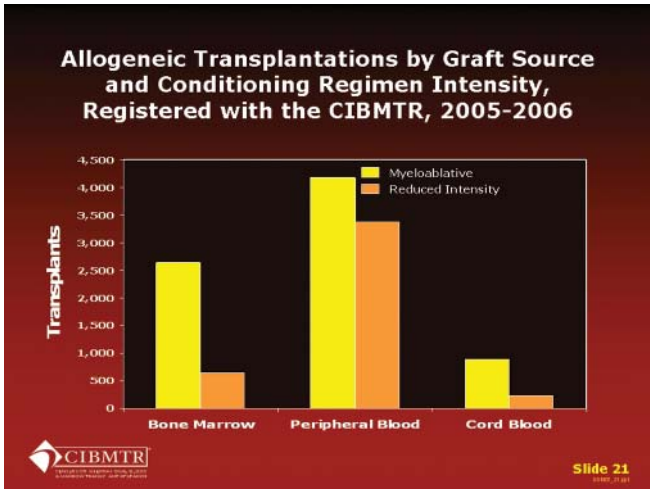
Slide 17: Relapse is the single most common cause of death after HCT; it accounts for 70% of deaths after autotransplantation. Graft-versus-host disease (GVHD), interstitial pneumonitis (IPn) and infection are major causes of death after allotransplantation.

Slides 18 to 21: The classification of conditioning regimen intensi-



ties 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 reduced intensity by the transplant center were classified as such. Cases without such information and with available data on chemotherapy agents, radiation and doses





2008 BMT Tandem Meetings – On the Sunny Side of the Street

By D'Etta Waldoch Benson, CMP

Plan to spend February 13-17 in sunny San Diego, California, at the Manchester Grand Hyatt for the 2008 BMT Tandem Meetings. More than 2,000 attendees representing 40+ countries are expected to attend the 2008 Meetings.

Detailed information about the 2008 BMT Tandem Meetings is continuously updated on the CIBMTR (www.cibmtr.org) or ASBMT (www.asbmt.org) Web sites. Online conference registration and hotel reservations are all running at full speed. Check back periodically for updates to the provisional agenda.

In addition to the Manchester Grand Hyatt, guest rooms are also available at reduced rates to BMT Tandem Meetings attendees at the San Diego Marriott Hotel & Marina (1 block from the Hyatt), Westin Horton Plaza (7 blocks away) and Courtyard by Marriott Downtown (10 blocks away). Check the web site regarding availability.

Scientific Program Chairs for 2008 are Drs. Stella Davies (for CIBMTR) and Marcel van den Brink (for ASBMT). The 2008 agenda includes 5 plenary sessions, 14 concurrent sessions, 78 oral abstract presentations, 2 poster sessions and 11 satellite symposia. Topics slated for presentation at the San Diego meetings are listed in the sidebar.

2008 TOPICS:

Aging
Amyloidosis
BMT CTN State of the Science
Cancer Stem Cells
Chronic GVHD
CIBMTR/EBMT Key Studies
Controversies in Transplant for Lymphoma
Genomics
Graft Failure
GVL
Hematopoietic Stem Cells
Immune Cell Therapies
Immune Reconstitution
Memory T Cells
NMDP – Cord Blood
Pediatric Cancer Symposium
Regenerative Medicine
Tolerance
Transplants for Acute Leukemia
Transplant-related Complications
Workshop on Mouse Modeling

In addition to 5 days of scientific and clinical meetings, related meetings include: BMT CTN Steering Committee – Feb 12; FACT Training Workshops – Feb 12; Clinical Research Professionals' Data Management Conference – Feb 12-14; CIBMTR Working Committee Meetings – Feb 13-16; BMT Center Administrative Directors Conference – Feb 13-14; BMT Pharmacists Conference – Feb 15-17; Transplant Nurses Conference – Feb 15-17; and the BMT Center Medical Directors Conference – Feb 16. Sessions focused primarily to pediatric cancer will be held Feb 14.

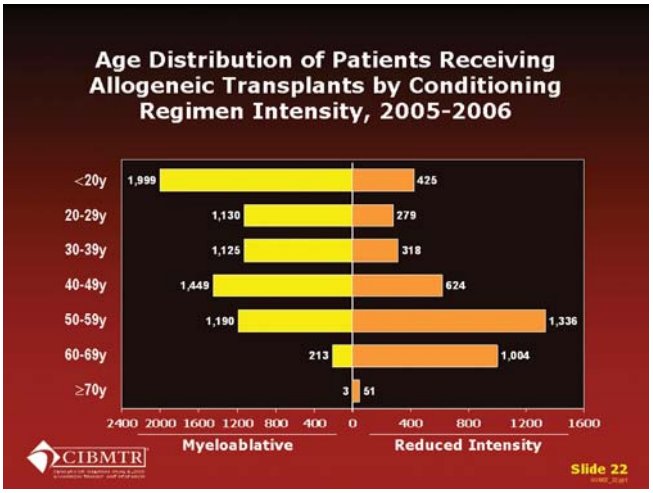
For general information, please e-mail D'Etta Waldoch Benson, CMP at the conference office at bmttandem@cs.com, or call 414-456-8377.

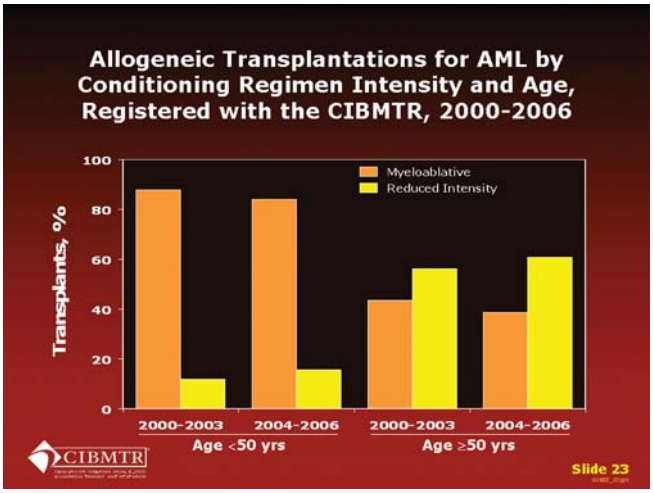
Questions regarding support opportunities at the 2008 BMT Tandem Meetings may be directed to Sherry Fisher at slfisher@mcw.edu or 414-456-8897.

The combined annual meetings of the Center for Blood and Marrow Transplant Research (CIBMTR) and the American Society for Blood and Marrow Transplantation (ASBMT) are 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.

were classified according to the CIBMTR operational definition of conditioning regimen intensity. Myeloablative regimens are defined as total body irradiation doses of ≥ 500cGy in a single dose or ≥ 800 cGy fractionated, busulfan > 9mg/kg or melphalan > 150mg/m^2 given as single agents or in combination with other drugs. About 40% of allogeneic transplantations now use reduced intensity regimens.

Slides 22 to 23: The use of reduced intensity regimens has contributed to the increased use of allogeneic transplantation in older (and sicker) patients. More than 50% of patients receiving reduced intensity conditioning are older than 50 years compared to fewer than 25% of those receiving standard high-intensity regimens.





GVHD Working Committee – continued from page 1

strengths include outstanding leadership and a dynamic membership roster consisting of investigators who actively participate on the writing committees providing critical insight and feedback on all studies. Access is possible to both the clinical database and blood sample repositories for conducting research in this area.

Publications:

GV02-01 Khoury HJ, Loberiza Jr FR, Ringdén O, Barrett AJ, Bolwell BJ, Cahn J-Y, Champlin RE, Gale RP, Hale GA, Urbano-Ispizua A, Martino R, McCarthy PL, Tiberghien P, Verdonck LF, Horowitz MM. **Impact of Posttransplant G-CSF on Outcomes of Allogeneic HCT.** *Blood, 2006;107(4):1712-6*.

D96-01 Davies SM, Wang D, Wang T, Arora M, Ringdén O, Anasetti C, Pavletic S, Casper J, MacMillan ML, Sanders J, Wall D, Kernan NA. **Recent Decrease in Acute GVHD and Increased Relapse in Children with Leukemia Receiving Unrelated Donor Bone Marrow Transplants.** *Submitted*.

GV99-03 Levine JE, Barrett AJ, Zhang M-J, Arora M, Pulsipher MA, Bunin N, Fort J, Loberiza Jr FR, Porter D, Giralt S, Drobyski W, Ringdén O, Horowitz MM, Collins R. **Donor Leukocyte Infusions to Treat Hematologic Malignancy Relapse Following Allogeneic Stem Cell Transplantation in a Pediatric Population.** *Submitted*.

Abstracts submitted to American Society of Hematology, 2007 (all with manuscripts submitted or in preparation):

D96-01 Davies SM, Wang D, Wang T, Arora M, Ringdén O, Anasetti C, Pavletic S, Casper J, MacMillan ML, Sanders J, Wall D, Kernan NA. **Recent Decrease in Acute GVHD and Increased Relapse in Children with Leukemia Receiving Unrelated Donor Bone Marrow Transplants.**

GV00-01 Hahn T, McCarthy PL, Wang D, Zhang M-J, Arora M, Pavletic S, Barrett AJ, Ringdén O. **Risk Factors for Acute Graft-versus-Host Disease (GvHD) after Related Donor HLA-Matched Myeloablative Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Adult Leukemia: Identification of Modifiable and Non-Modifiable Factors.**

D01-91 Ratanatharathorn V, Horowitz MM, Logan B, Arora M, Wang D, Uberti JP, Gale RP, Antin JH, Bornhaeuser M, Hale GA, Ringdén O, Cairo MS, Gupta V, Cutler C, Anasetti C, Pavletic SZ. **Prior Therapy with Rituximab Correlates with Less Acute Graft-versus-Host Disease and Better Survival in B-Cell Lymphoma Patients Who Received Allogeneic Peripheral Blood Stem Cell Transplantation.**

GV05-04 Arora M, Pavletic S, Anasetti C, Barrett AJ, Wang T, Antin JH, Di Bartolomeo P, Bolwell BJ, Bredeson CN, Cairo MS, Gale RP, Giralt S, Hahn T, Hale G, Halter J, Jagasia M, Litzow MR, Locatelli F, McCarthy PL, Mort C, Petersdorf EW, Russel J, Schiller G, Schouten HS, Tallman M, Verdonck LF, Wingard JR, Horowitz MM, Ringdén O. **Graft-Versus-Leukemia Effect is Equivalent in Recipients of Matched Sibling and Matched Unrelated Donor Conventional Hematopoietic Cell Transplant.**

Other Studies in Progress:

GV00-02 Risk Factors for Acute GVHD After HLA Matched Related HCT for Leukemia (Study Chairs: T. Hahn, Roswell Park Cancer Institute, Buffalo, NY; P.L. McCarthy, Roswell Park Cancer Institute, Buffalo, NY; Study Statisticians: K. Sobocinski, M-J Zhang). *Data analysis is complete and manuscript is being prepared.*

GV05-02 Study of Risk Factors and Outcome of Acute GVHD After Allogeneic HCT (Study Chairs: Madan Jagasia, MD, Vanderbilt University Medical Center; N. Chao, Duke University, Durham, NC; Shin Mineishi, MD, University of Michigan, Ann Arbor; Study Statistician: Dan Wang). *Protocol is being developed.*

GV05-05 Incidence, Risk Factors and Clinical Manifestations of Graft Versus-Host Disease Diagnosed After Donor Lymphocyte Infusion in Patients Receiving Reduced Intensity Hematopoietic Stem Cell Transplants (Study Chairs: Daniel R Couriel, MD and Rima Saliba, PhD, University of Texas MD Anderson Cancer Center, Houston; Ronald Sobecks, MD, Cleveland Clinic Foundation; Study Statistician: Dan Wang). *Protocol is being developed.*

GV06-04 Current Trends in Chronic Graft-Versus-Host Disease (Study Chair: Sally Arai, MD, Stanford University, Stanford; Study Statistician: Dan Wang). *Protocol is being developed.*

GV04-04 Risk Factors for Relapse and Mortality in Patients with Chronic Graft-Versus-Host-Disease (Study Chairs: David Jacobsohn MD, Children's Memorial Hospital; Steven Pavletic, MD, National Cancer Institute, Bethesda; Michael Boyiadzis MD, MHSc, UPMC Cancer Pavilion, Pittsburgh; Study Statistician: Dan Wang). *The data file is in preparation.*

We invite all members to participate in our committee and submit new proposals or provide input in the design, conduct and analysis of ongoing studies. Proposals can be submitted year long and will be reviewed by the committee at the next scheduled monthly conference call.

SCTOD update – continued from page 4

Net™ 2.0 will be able to receive their data back using an AGNIS system. As the system approaches full implementation (expected by mid 2008), centers will be able to electronically submit data from their own database for loading into FormsNet™ 2.0. Upon completion of the system, AGNIS will also allow other transplant networks and registries to share data across systems (e.g. ProMISe, inter-center collaborations).

Systems Training, two phases:

- Introductory training sessions for the SCTOD forms were held, via Webcast, during the summer. Audio-recorded forms training sessions designed for new data managers, those who missed the summer courses or those wanting a refresher are available at: http://www.cibmtr.org/DATA/HARMONIZED/harmonized_idx.html.

- FormsNet™ 2.0 training CDs are scheduled for release to all centers upon notification of launch for the program. Centers must complete the training session and receive their secureID cards before using FormsNet™ 2.0. Centers are encouraged to send at least one representative to in-person training sessions scheduled for November 2007 (NMDP Council meeting) and February 2008 (BMT Tandem meeting).

Transplant Center Team numbers, IRB protocols and data agreements:
The CIBMTR and NMDP have communicated with transplant center staff throughout the year via website messages/materials, ASBMT newsletters and frequent broadcast emails. A comprehensive list of transplant team participants has been generated to identify all known centers, assign new team ID numbers, and establish updated contact information for center representatives. Modified research protocols for local IRB approval and Data Transmission Agreements (DTA) have been circulated to all centers. Centers have been advised to continue using existing IRB approved protocols and DTAs until these processes have been executed locally (even if after the launch date); however, reimbursement for completed forms that use the new format is not possible until a signed agreement is received.

Continuous Process Improvement (CPI) and on-site Audit Program: *how to handle backlog*:
The NMDP's current CPI program to assess and maintain standards

continued on page 11

SCTOD Update – continued from page 10

for accurate completion and timely submission of required forms has been expanded to include all data collected by the CIBMTR. The CPI program remains the same for unrelated donor transplants and will continue uninterrupted. Effective January 1, 2008, we will begin to apply this program to related donor and autologous transplants, phasing the program in gradually over the ensuing 18 months. Forms submission will be tracked by center for the first 6 months and centers will be informed without consequence. Seventy percent compliance will be required within the next 3 months, 80% for the subsequent 3 months, and 90% compliance over the next 3 months and thereafter. Forms still due to the CIBMTR pre-dating launch of the new systems will be integrated into the CPI system.

The on-site audit program of the NMDP and CIBMTR has been combined into a single audit system. The audit process has been streamlined and covers all types of transplants. This new audit program will also be launched in the first quarter of 2008.

Related recipient/donor pair Repository
A related donor recipient research sample repository will be developed by the CIBMTR, expanding the previously established NMDP sample repository. A revised protocol for collection of research samples for banking has been approved by the NMDP and CIBMTR IRBs and made available to selected centers. A Pilot Program has been established using these centers experienced with the unrelated recipient/donor sample collection systems of the NMDP. Instructions have been distributed to these centers and collection of related recipient/donor pair samples will begin with FormsNet™ 2.0 launch. Over time, this feature will be extended to more transplant centers.

Public Website:
CIBMTR personnel have participated in the development of the public website (a contract requirement of the OPA/SPA). The website launched in mid August and is accessible to the public at http://bloodcell.transplant.hrsa.gov. Representatives from the CIBMTR Consumer Advocacy Committee provided significant input from the patient perspective. This covers basic transplant, cord blood and donor information as well as the new legislation, the Program and its contractors. Future plans for the website include further development of the following:

- SCTOD query tools (search feature for survival and outcomes data; glossary)
- Research Repository information
- FAQs for the HRSA Knowledgebase [http://answers.hrsa.gov]
- Visitor Feedback Survey

In appreciation:
Substantial progress has been made towards fulfilling the promise of the new program. Many other new aspects of the C.W. Bill Young Program are still to come. CIBMTR appreciates the tremendous assistance received from the HCT community to achieve the current status, and looks forward to further progress in the coming year.

We will continue to use the cibmtr.org website and other tools for dissemination of further information about the Stem Cell Therapeutic Outcomes Database.

Foundation and corporate support of the CIBMTR

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 Disease; Office of Naval Research; Health Resources and Services Administration (DHHS); Centers for Disease Control and Prevention; 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.

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