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CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

newsletter

contents

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CIBMTR WORKING COMMITTEES IN THE SPOTLIGHT

We continue our series focusing on the Working Committees of the CIBMTR, which have increased in number from 17 to 19 since the December 2007 newsletter. The Working Committees provide scientific oversight for the use of CIBMTR data and statistical resources.

Working Committee responsibilities include 1) designing and conducting studies that involve CIBMTR data, statistical resources, networks, and/or centers; 2) reviewing proposals that will use CIBMTR data; 3) periodically assessing and revising relevant sections of CIBMTR data collection forms; and 4) planning and conducting workshops at CIBMTR meetings. Additionally, the Working Committees set priorities for observational studies that use the CIBMTR's large clinical databases. These observational studies are a core activity of the CIBMTR. For a full listing of the 19 Working Committees and their leadership, visit http://www.cibmtr.org/COMMITTEES/working_committees_idx.html.

In this issue, we highlight the Pediatric Cancer and Immunobiology Working Committees.

Pediatric Cancer Working Committee

At the 2008 BMT Tandem meetings, outgoing Pediatric Cancer Working Committee (PCWC) co-chair Bruce Camitta (Medical College of Wisconsin) was recognized for his significant contributions to the committee over the past 10+ years. His wit and wisdom and ability to coordinate studies with the pediatric cooperative groups have been invaluable. We look forward to his continued participation as both a committee member and investigator. The remaining co-chairs, Stephan Grupp (Children's Hospital of Philadelphia) and Stella Davies (Cincinnati Children's Hospital) are delighted to welcome Paul Carpenter (Fred Hutchinson Cancer Research Center) as a new co-chair; we are confident that Paul will continue to help move the committee's agenda forward. The committee co-chairs are assisted by the extraordinarily hard-working and talented scientific director, Mary Eapen, MD, MS and committee statisticians, Vincent He, MS and Mei-Jie Zhang, PhD.

The PCWC endorses studies assessing allogeneic and autologous transplantation for a variety of malignant pediatric diseases. The working committee is a lively, controversial, and interactive group that

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Immunobiology Working Committee

The Immunobiology Working Committee (IBWC) is the largest committee of the CIBMTR. Its 3 co-chairs—David Miklos, MD, PhD (Stanford University); Effie Petersdorf, MD (Fred Hutchinson Cancer Research Center); Machteld Oudshoorn, PhD (Europdonor)—are assisted by scientific directors Stephanie Lee, MD, MPH and Stephen Spellman, MBS, and statisticians John Klein, PhD; Tao Wang, PhD; Fiona Kan, MS, and Michael Haagenson, MS.

The IBWC addresses scientific questions about the association between genetic factors and successful transplantation outcomes. The committee endorses studies that assess genes and gene products of the major histocompatibility complex, natural killer cell repertoire, cytokine/proinflammatory cytokine and immune-response determinants, minor histocompatibility loci, and other genetic factors. The committee's studies also include comparisons of clinical outcomes from different donor types (eg, mismatched-related versus unrelated donors).

The long-standing requirement of the National Marrow Donor Program (NMDP) for centers to submit initial and outcome data on all donors and recipients of NMDP

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Stem Cell Therapeutic Outcomes Database (SCTOD)/FormsNet™ 2.0 Update

by Carol Doleysh, BS, CPA

FormsNet™ 2.0, the CIBMTR's new electronic data collection system, was successfully launched on December 3, 2007. As of May 31, 2008, all identified domestic centers and 125 international centers have access to FormsNet™ 2.0. Monthly version releases have corrected program "bugs," made error messages more user-friendly, and introduced new forms and features, such as audit trails. Since the March version release, feedback suggests that the new FormsNet™ 2.0 features are beneficial to data entry staff and data entry time is being reduced by up to 50%.

Critical technical difficulties encountered early in the launch process were identified and addressed and continue to be monitored. The National Marrow Donor Program (NMDP) Bioinformatics staff, with whom the CIBMTR subcontracts, has worked tirelessly to prioritize and correct system issues, giving highest priority to network, data entry, and issues that affect communication between the centers and the CIBMTR liaisons. Monthly version releases will continue to offer solutions for problems identified and other program enhancements.

The FormsNet™ 2.0 "Forms Due" feature was activated on January 8, 2008. The comprehensive "Forms Due Report" will assist centers and CIBMTR staff in prioritizing submission of forms required for quality monitoring. Although useful, the current "Forms Due" reports require additional revisions so that future reports will combine data from all cases submitted to the NMDP or CIBMTR using prior forms as well as all new cases submitted using FormsNet™ 2.0 since December 3, 2007.

Reimbursement for submitted forms will be processed on a quarterly basis starting in April for the period beginning on December 3, 2007 and ending on March 31, 2008. **A center must have a signed Data Transmission Agreement before reimbursement may be made.**

Some helpful resources for FormsNet™ 2.0 users include:

- Frequently Asked Questions: http://www.cibmtr.org/DATA/FAQ/1st_Draft_FAQ_Final_.pdf
- FormsNet™ 2.0 News Group Forum: http://groups.google.com/group/formsnet. We encourage at least 1 system user from each center to sign up for this forum to share and/or receive information about the system and related changes.
- Your Center Liaison (contact cibmtr@mcw.edu regarding center liaison assignments if necessary). Please reference your 5-digit CIBMTR center ID number in any communications with your liaison.

Continuous Process Improvement and Onsite Audit Program

The onsite audit programs of the NMDP and CIBMTR have been combined into a single audit system. The audit process has been streamlined and covers all types of transplants. The first audits were performed in January 2008; 13 centers were audited by the end of May 2008. The goal of the CIBMTR is to complete the first 25% of US and selected Canadian team audits by the end of 2008, which will represent the first of a four-year cycle.

Over the next year, the Continuous Process Improvement (CPI) program for related and autologous transplantation data will be implemented, with a target compliance rate of 90% by April of 2009; the unrelated transplant data compliance expectation of 90% will remain unchanged.

CIBMTR is mindful that a fully functional "Forms Due Report" is essential for executing the CPI process and is taking this into consideration as CPI is implemented during this transition period.

AGNIS

A Growable Network Information System (AGNIS) is a point-to-point communications system currently being developed that will allow transplant centers to electronically submit patient outcomes data directly from their database. The electronically transferred data will then be validated and stored in FormsNet™ 2.0. AGNIS "translates" center data into a common standardized language (the National Institutes of Health's Cancer Data Standards Repository or caDSR) so that it may be shared with other centers, registries, and networks that link to AGNIS.

The goal of AGNIS is to enable an "enter once, use often" capability, reducing each center's submission burden.

As an open-source, peer-to-peer messaging system, AGNIS will require resources, equipment, and Information Technology (IT) support at centers. We are actively seeking ways that the CIBMTR may help centers to acquire the necessary resources, equipment, and support.

Helpful resources for AGNIS users include:

- Development website: http://agnis.net/
- IT News Group Forum: http://groups.google.com/group/agnis

Systems Training

Numerous training opportunities have been available to CIBMTR and transplant center staff. In addition to online training, the ASBMT and CIBMTR cosponsored an Information Technology (IT) Summit in January 2008, which provided system training and information to data managers and IT professionals. Topics included the value of AGNIS, IT implementation (for centers to become an AGNIS node for data sharing), and software demonstrations. The meeting was well received and future IT Summits are planned. A 3-day Data Managers' Conference, held at the BMT Tandem meetings in February 2008, incorporated a hands-on FormsNet™ 2.0 lab and an open question-and-answer session.

Slides from these presentations are available online:

- IT Summit: http://www.asbmt.org/News/IT+Visuals.htm
- Data Managers' Conference: http://cibmtr.org/MEETINGS/DOCS/CRP-DM_Handouts.pdf

Public Website

The CIBMTR has collaborated with the Office of Patient Advocacy (OPA) in their single point of access contract requirement to develop a public Web site: http://bloodcell.transplant.hrsa.gov/. The Web site has been "live" for several months and features basic transplant, cord blood, and donor information, as well as the C. W. Bill Young Cell Transplantation Program description and contractor information. Future updates will include a search feature for SCTOD survival and outcomes data (after a minimum of 1-year of data collection), research repository information, and a visitor feedback survey. Also available are frequently asked questions for the Health Resources and Services Administration (HRSA) Knowledge-base [http://answers.hrsa.gov/].

In Memoriam

Charles Daniel "Dan" Calloway 2/28/75 – 11/16/07

The CIBMTR would like to extend our deepest condolences to the partner, family, friends, and coworkers of Charles Daniel "Dan" Calloway. Dan worked as a cancer clinical research associate at Legacy Good Samaritan Hospital in Portland, Oregon and was instrumental in submitting transplant data to the CIBMTR for many years. Dan is fondly remembered for his warmth and humor.

perspectives

Hello and Goodbye

By Stella M. Davies, MBBS, PhD, MRCP

Chair, CIBMTR Advisory Committee
Professor of Pediatrics, Cincinnati Children's Hospital Medical Center

Dear Friends,

I take up my position as incoming chair of the CIBMTR Advisory Committee with excitement for the challenge ahead and the burgeoning opportunities the CIBMTR offers. I also recognize that I am being asked to fill 2 very big shoes. Sergio Giralt, the outgoing chair, brought to the position his vast knowledge of transplantation, hard work and perseverance, and considerable diplomatic skills, all of which have served the registry well during a time of unprecedented growth and change. The CIBMTR will always be grateful to Sergio for his past contributions—my guess is, we will find new ways for him to contribute in the future, some that he may not yet have imagined!

I am pleased to report that the BMT Tandem meetings in San Diego in February 2008 were an unprecedented success. More than 2,500 attendees enjoyed an outstanding program of scientific presentations, workshops, and working committee meetings. Since the first combined IBMTR and ASBMT meeting in 1995, the BMT Tandem meetings have increased steadily in size and quality of work presented. I believe that the BMT Tandem meetings are now considered a leading international venue for presenting clinical and scientific transplantation data, perhaps exceeding the importance of those presented at more general meetings, such as ASH and ASCO. The CIBMTR recognizes the crucial importance of promptly sharing new data with the transplant community, who faithfully supplies the high-quality data used in registry analyses. Reporting the results of key transplant trials at the Tandem meetings is an important method of facilitating rapid incorporation of novel findings into clinical practice. We will continue to seek ways to improve data sharing in timely, informative, and enjoyable formats at the meeting.

The Working Committee meetings held during the BMT Tandem meetings are an important component of the meeting. At these meetings, the progress and interim results of ongoing studies are reviewed and discussed. New studies are proposed, discussed, and modified by attendees, all of whom are considered as committee members. Proposing a CIBMTR study is an adventure that provides young investigators with an excellent opportunity for meeting and interacting with more seasoned investigators and world-class statisticians. It is important that investigators appreciate both the strengths and limitations of using registry datasets for proposed studies. Registry data offer the opportunity to study larger sample sizes than can be studied in single-institution studies and look at variations in practice patterns (eg, comparing outcomes from patients receiving T-cell depleted marrows with patients receiving non T-cell depleted marrows) that may not be offered by a given transplant center. In practice, the lack of homogeneity in registry data opens the door to answering some but not all clinical and/or scientific questions; some questions may be better addressed in a single-institution study. When we prioritize CIBMTR studies, we think: "Is this a question best answered with registry data?" and "Is this a question that can only be answered with registry data?" If the answer to both questions is yes, the study is likely to receive a high priority classification by and support from the CIBMTR. Young investigators should be aware that analyzing the results of studies is time consuming for statisticians, whose activities are prioritized by the working committees. Analysis of study results may not be forthcoming immediately. When the analysis is complete, however, publishing the study results becomes an immediate priority, so that the information is quickly distributed to those who are most likely to benefit from the data. Please encourage investigators at your center (young and not-so-young) to get involved in the Working Committees, propose a study, and/or participate in the studies of others. This work is crucial in moving clinical practice forward.

2008 BMT Tandem Meetings Breaks Attendance Record!

by D'Etta Waldoch Benson, CMP

Since 1995, the combined annual meetings of the Center for International Blood & Marrow Transplant Research (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, nurses, pharmacists, and clinical research associates.

2008 BMT Tandem Meetings

An all-time, record-breaking 2,501 attendees from 41 countries gathered in San Diego, California at the Manchester Grand Hyatt Hotel to learn about the latest developments in blood and marrow transplantation at the 2008 Blood and Marrow Transplantation (BMT) Tandem Meetings. The program agenda included 5 plenary sessions, 19 concurrent sessions, 78 oral abstract presentations, 2 poster sessions, and 11 satellite symposia.

Investigators from 31 countries submitted 509 abstracts, which are available online at www.cibmtr.org or in the February 2008 issue of *Biology of Blood and Marrow Transplantation* (volume 14, issue 2, supplement).

Audio CDs, synchronized audio/visual CDs, and MP3 downloads of the 2008 BMT Tandem sessions, including sessions from the peripheral conferences for nurses, clinical research professionals, BMT center administrators, and BMT pharmacists, are available for purchase online. Conference evaluation forms and continuing medical education (CME) transcripts for physicians and allied health professionals are also available online. If you have not evaluated the conference and/or printed a copy of your CME transcript, visit the CIBMTR Web site (www.cibmtr.org) and follow the instructions provided (registration ID required). Other questions about CME transcripts may be directed to info@condorregistration.com; alternatively, call 1.256.852.4490.

2009 BMT Tandem Meetings

Moving from the Western seaboard to the Eastern seabord, the 2009 BMT Tandem Meetings will be held at the Tampa Convention Center in Tampa, Florida from February 11–15. Drs. Mark Litzow (representing CIBMTR) and James Ferrara (representing ASBMT) are scientific program co-chairs for this meeting. Topics slated for presentation at the Tampa meetings are listed in the sidebar.

In addition to 5 days of core scientific and clinical sessions, several related peripheral meetings will be conducted, including the following:

- Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Steering Committee Meeting
- BMT CTN Coordinator and Investigator Sessions
- Foundation for the Accreditation of Cellular Therapy (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.

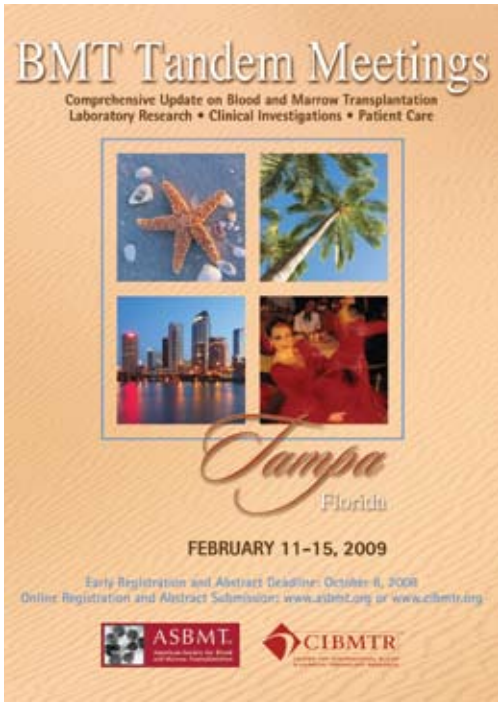
Sessions that specifically address transplantation for pediatric patients will be held on Thursday, February 12.

The CIBMTR (www.cibmtr.org) and ASBMT (www.asbmt.org) Web sites will provide regular updates regarding meeting topics, dates, and times for the core and peripheral conferences.

Online conference registration, hotel reservations, and abstract submission instructions (abstract submission deadline is October 8, 2008) will be available in August 2008.

For general conference-related information, please contact D'Etta Waldoch Benson, Certified Meeting Planner, by e-mail at bmttandem@cs.com or by phone at 414.805.0679.

Questions regarding sponsorship opportunities should be directed to Sherry Fisher at slfisher@mcw.edu or 414.805.0687.



2009 Topics

- Acute Leukemia
- B Cells
- Clinical Trial Design
- CLL: Biology and Treatment
- CML/Myeloproliferative Disorders
- Genomics/Proteomics
- GVHD
- Bacterial and Viral Infections
- Inflammation
- Innate Immunity
- Long-Term Care
- Multiple Myeloma
- Umbilical Cord Blood Transplantation
- Regenerative Medicine
- Regulation of the Immune Response
- Center-Specific Outcomes
- The Vulnerable Transplant Patient

Report on State of the Art in Blood and Marrow Transplantation

These summary slides are an annual report of the data submitted to the Center for International Blood and Marrow Transplant Research (CIBMTR). The first part, published in the December 2007 newsletter, focused on trends in the use of hematopoietic stem cell transplantation (HCT) according to donor type, graft source, patient age, and transplant regimen. Early outcomes, such as day 100 post-HCT mortality rates and causes of death, were also included in part 1.

Reference for the CIBMTR summary slides is: Pasquini MC, Wang Z. **Current use and outcome of hematopoietic stem cell transplantation: part II- CIBMTR summary slides, 2007.** *CIBMTR Newsletter* [serial online]. 2008;14(1):6-13. Available at: http://www.cibmtr.org/PUBLICATIONS/Newsletter/index.html. Accessed (insert date here).

This second part of the CIBMTR summary slides describes the probabilities of survival in patients with diseases most commonly treated with HCT. The data were derived from patients transplanted between 1998 and 2006 and reported to the CIBMTR. Survival curves are stratified by several factors: recipient age, donor type (ie, autologous, human leukocyte antigen [HLA]-identical sibling, or matched-unrelated donor transplant), time from diagnosis to HCT, disease status or chemosensitivity at time of transplantation, and conditioning regimen intensity. However, all comparisons are univariate and do not adjust for other potentially important factors. Consequently, differences in survival between curves should be interpreted cautiously.

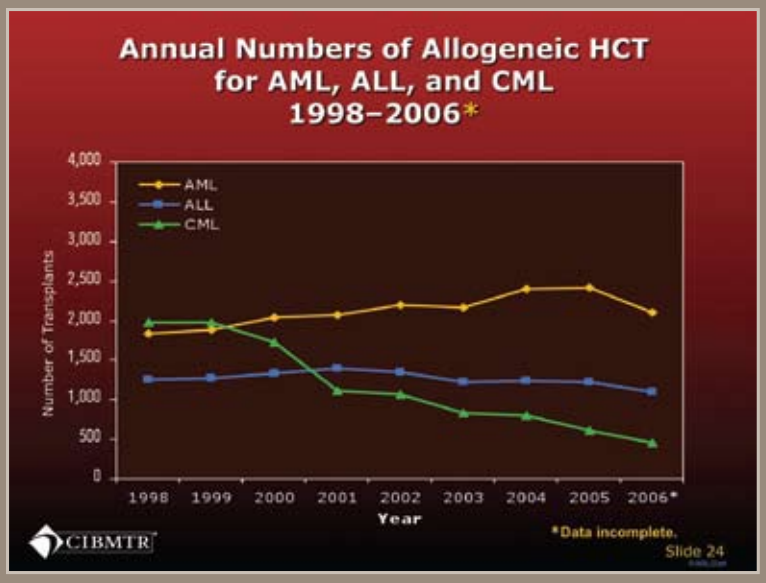
Acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), and chronic myelogenous leukemia (CML) are classified as early (ie, first complete remission [CR1] or first chronic phase [CP1]), intermediate (ie, second or subsequent CR or CP or accelerated phase [AP]), and advanced (ie, primary induction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

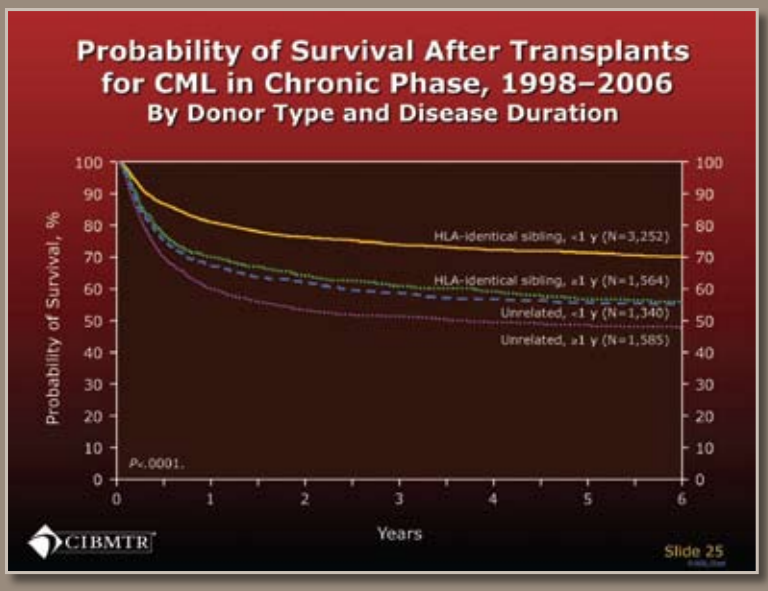
Preparatory regimen intensities are classified as myeloablative or reduced-intensity regimens, as reported by the transplant center. The CIBMTR uses the following operational definitions for regimen intensity:

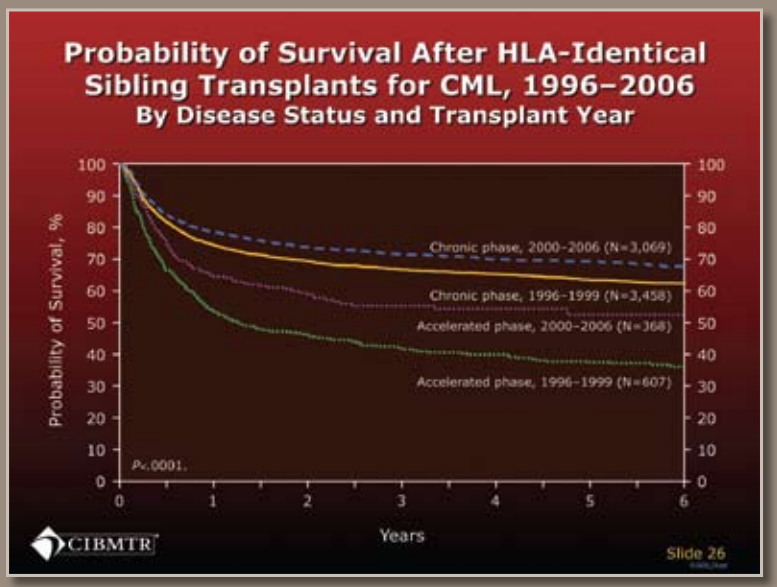
- Myeloablative conditioning regimen: regimens with total body irradiation (TBI) doses of ≥500 cGY, single fractionated doses of ≥800 cGY, busulfan doses of >9mg/kg, or melphalan doses of >150 mg/m^2 given as single agents or in combination with other drugs
- Reduced-intensity conditioning regimen: regimens with lower doses of TBI, fractionated radiation therapy, busulfan, and melphalan than those used to define a myeloablative conditioning regimen (above)

These operational definitions were applied to a subset of patients with available comprehensive data.

Part II
CIBMTR Summary Slides, 2007







Slides 24, 25, and 26: Annual numbers of patients undergoing allotransplantation for the most common indications have changed over the past decade. While allotransplantation for AML and ALL have steadily increased, allotransplantation for CML has decreased. Imatinib mesylate or another *bcr/abl*-specific tyrosine kinase inhibitor is the first treatment option for patients with newly diagnosed CML; allotransplantation is reserved for patients who fail such therapy. The CIBMTR has data for 7,741 CML patients in CP1 receiving an HLA-matched sibling donor (n=4,816) or unrelated donor (n=2,925) HCT between 1998 and 2006. Among patients receiving an HLA-matched sibling donor HCT <1 year after diagnosis, the 3-year probability of survival was 74% ± 1%. Among those receiving an HLA-matched donor HCT ≥1 year after diagnosis, the probability of survival was 61% ± 1%. The corresponding 3-year survival probabilities after unrelated donor HCT were 59% ± 1% and 51% ± 1%, respectively. Outcomes after allotransplantation have improved since the *bcr/abl*-specific tyrosine kinase inhibitors became commercially available in 2000. Three-year survival probabilities for patients transplanted in CP or AP before 2000 were 67% ± 1% and 42% ± 2%, respectively. The corresponding probabilities of survival in more recent years were 72% ± 1% and 55% ± 3%.

by Marcelo Pasquini, MD, MS[a] and Zhiwei Wang, MS[b]

[a]Assistant Scientific Director, [b]Masters Level Statistician
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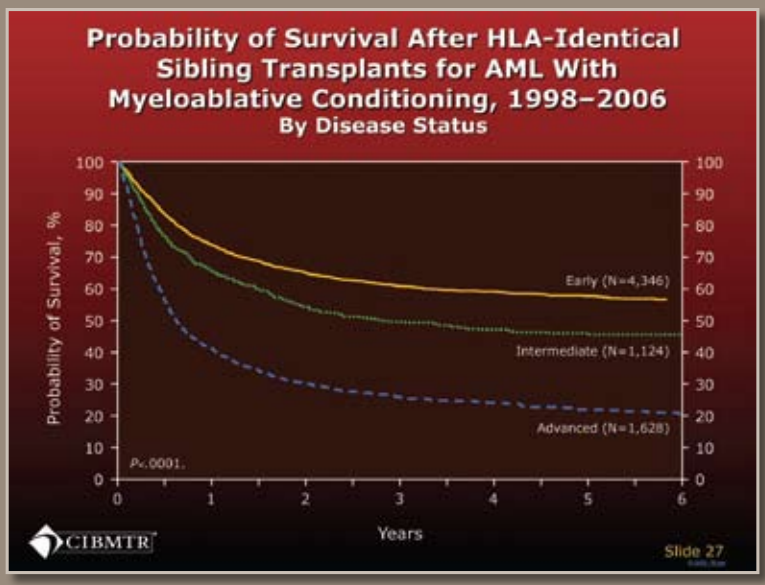
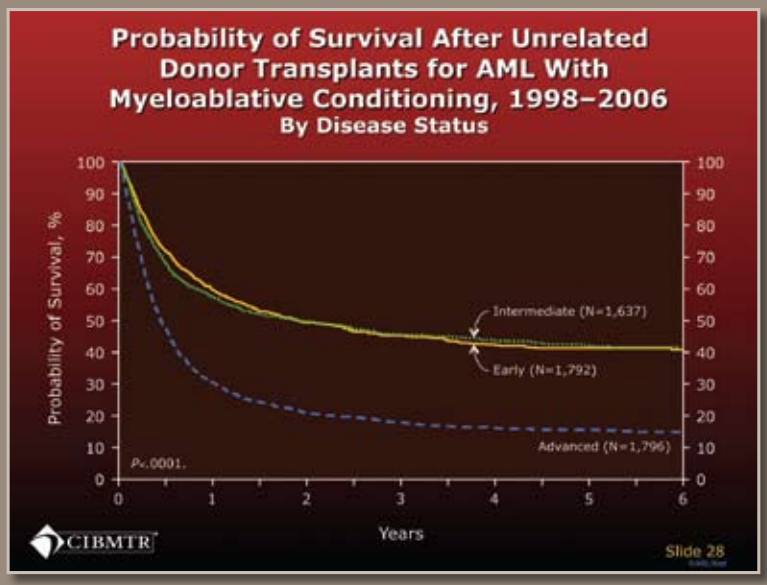
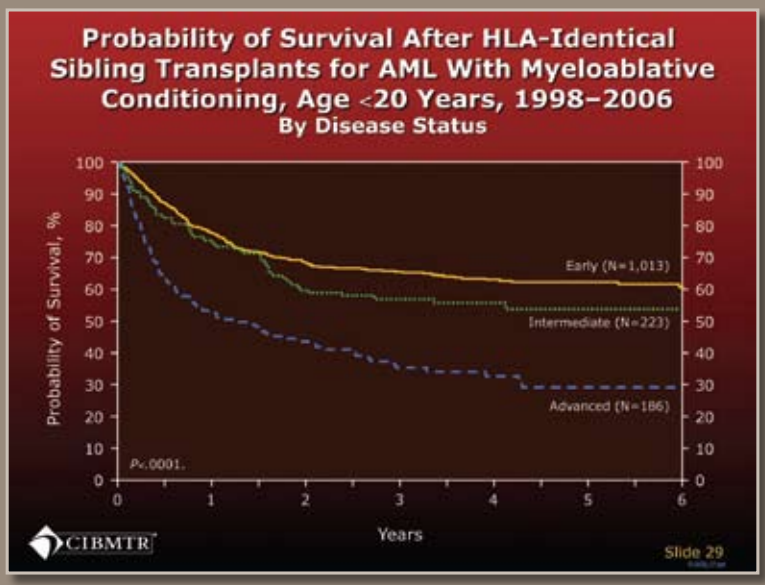
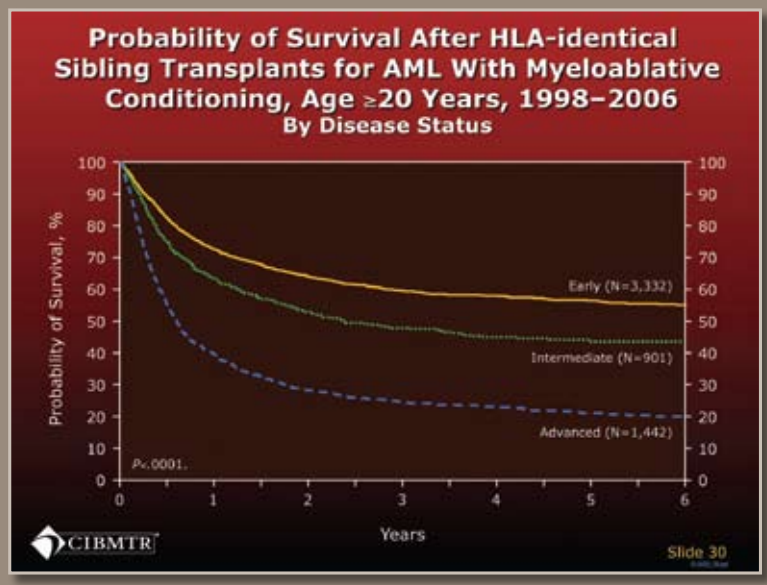


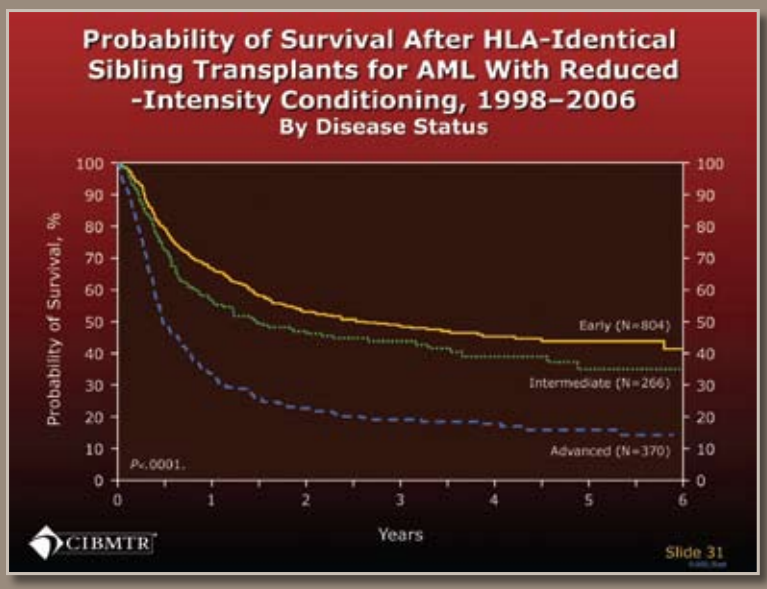


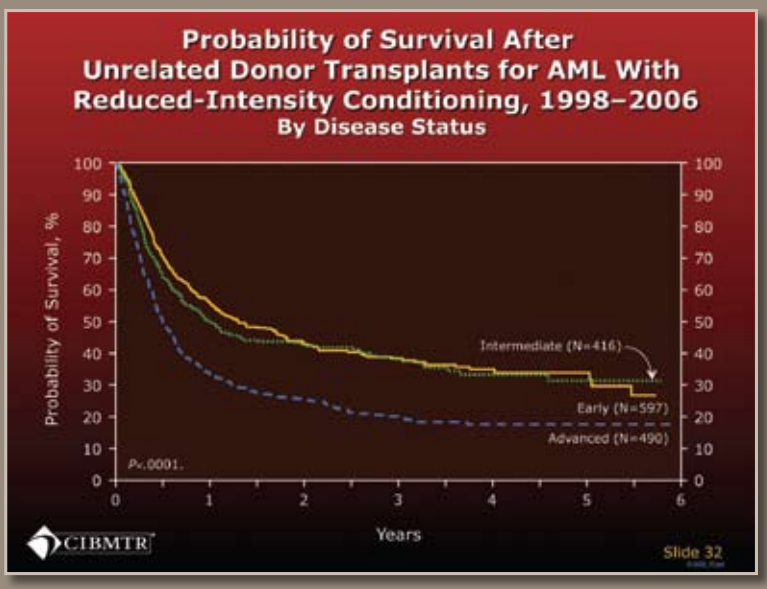
Slides 27 and 28: The CIBMTR has data for 12,323 patients receiving HLA-matched sibling (n=7,098) or unrelated donor (n=5,225) HCT for AML using myeloablative conditioning regimens between 1998 and 2006. Disease status at the time of HCT and donor type are the major predictors of posttransplant survival. The 3-year probabilities of survival after HLA-matched sibling HCT in this cohort are 61% ± 1%, 50% ± 2%, and 26% ± 1% for patients with early, intermediate, and advanced disease, respectively. The probabilities of survival after unrelated donor HCT are 46% ± 1% for patients with early and intermediate disease and 18% ± 1% for patients with advanced disease.



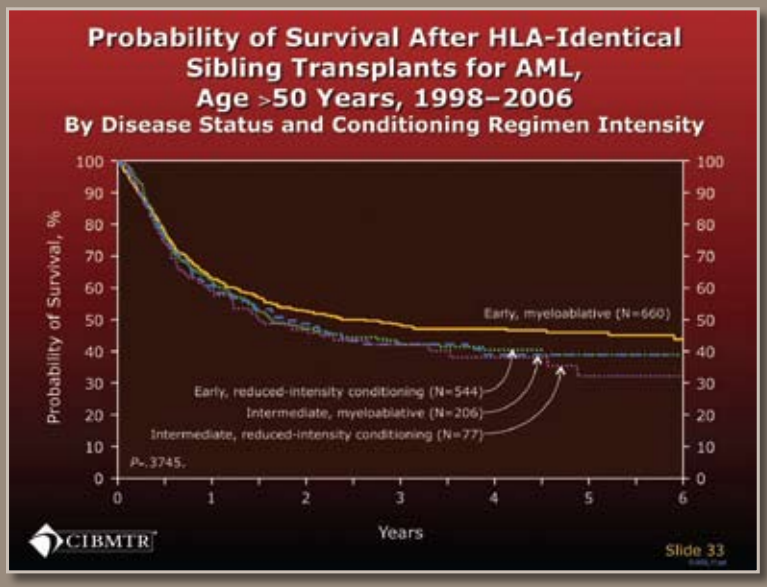


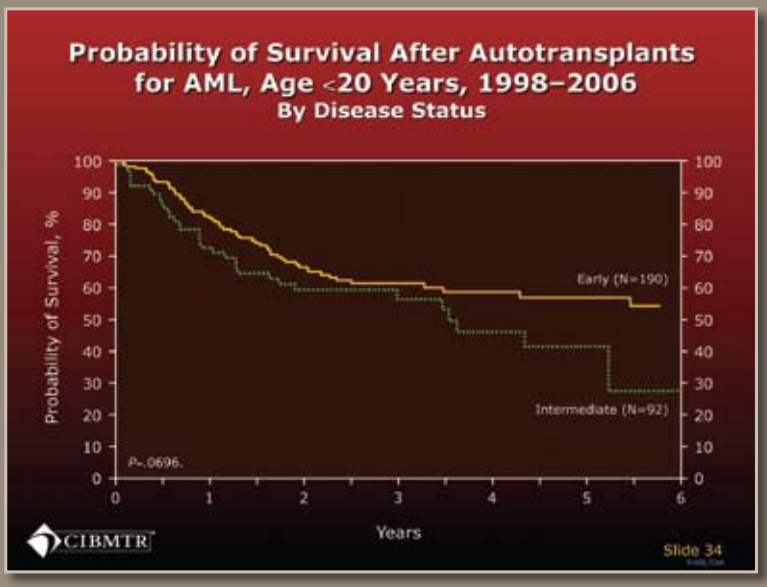
Slides 29 and 30: Among AML patients younger than 20 years, the 3-year probabilities of survival following HCT for patients with early, intermediate, and advanced disease are 65% ± 2%, 57% ± 4%, and 35% ± 4%, respectively. The corresponding probabilities of survival for patients 20 years or older are 60% ± 1%, 48% ± 2%, and 25% ± 1%.





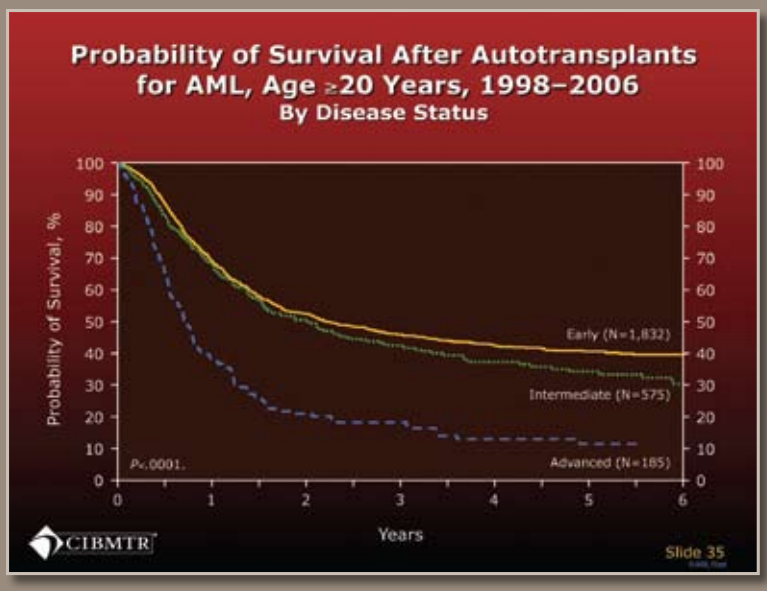
Slides 31 and 32: The 3-year probabilities of survival for the 1,440 patients with AML who received a reduced-intensity conditioning regimen and transplant from an HLA-sibling donor are 49% ± 2%, 44% ± 4%, and 19% ± 3% for patients with early, intermediate, and advanced disease, respectively. The probabilities of survival for the 1,503 recipients of unrelated donor allografts are 38% ± 3% for patients with early and intermediate disease and 20% ± 2% for patients with advanced disease.

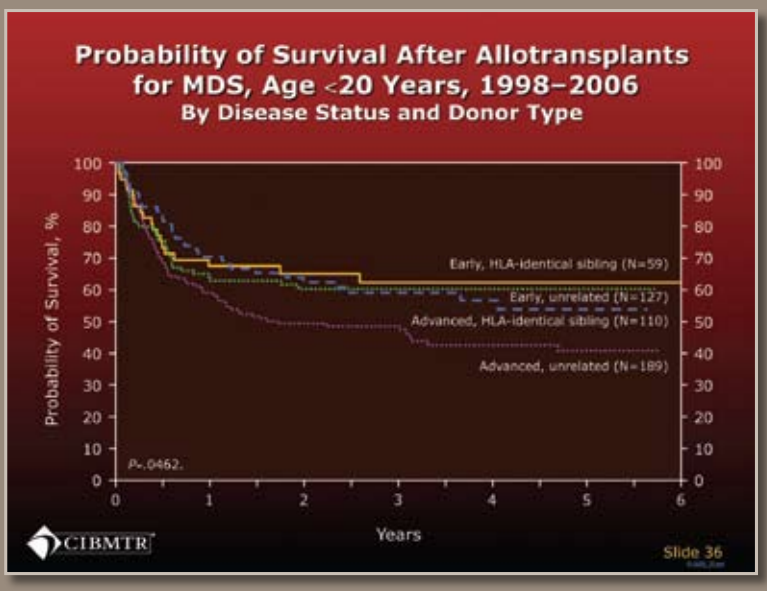




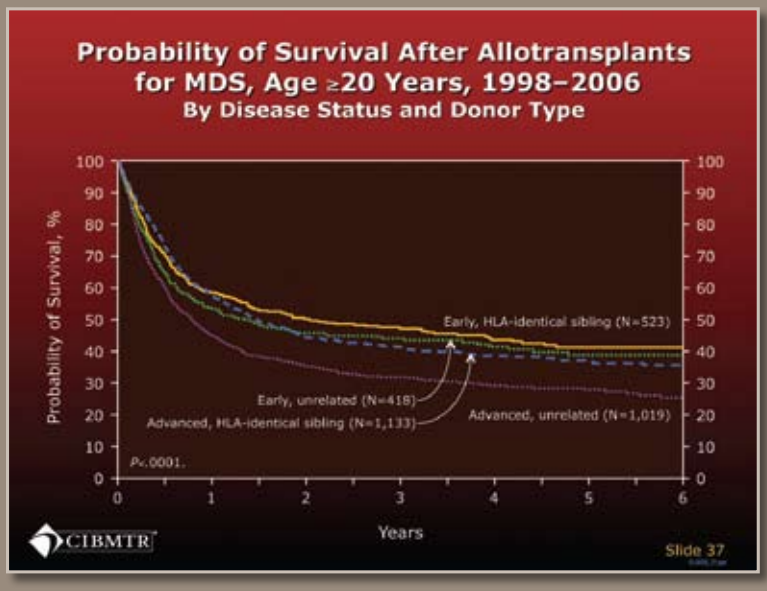
Slide 33: Reduced-intensity conditioning regimens are frequently used in patients older than 50 years of age. Among AML patients older than 50 years who received an HLA-matched sibling HCT, the 3-year probability of survival for patients who received a reduced-intensity conditioning regimen was 43%. Among patients who received a myeloablative conditioning regimen, the probability of survival was 49% ± 3% in patients transplanted in CR1 and 43% for those transplanted in subsequent remission.

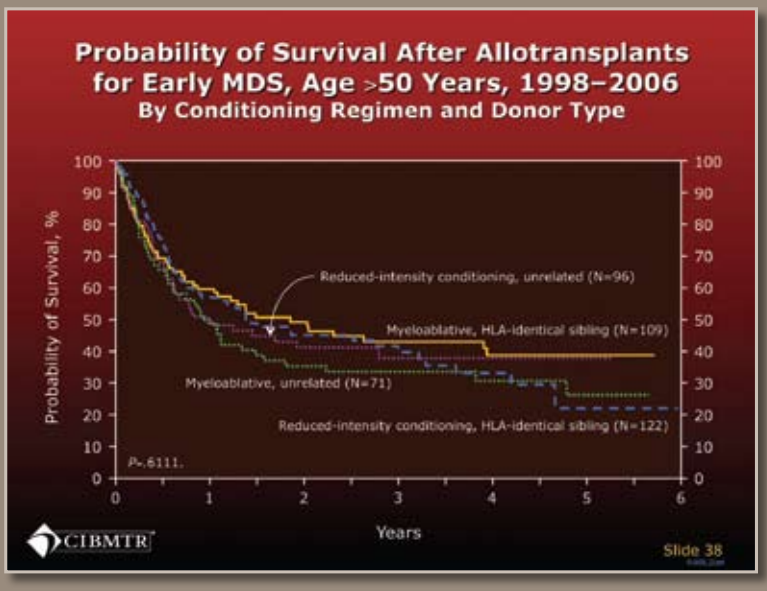
Slides 34 and 35: The CIBMTR has data for 2,865 autotransplants performed for AML between 1998 and 2006: 282 in patients younger than 20 years and 2,583 in patients 20 years of age or older. The 3-year probabilities of survival for early-disease patients <20 years and ≥20 years were 62% ± 4% and 46% ± 1%, respectively. Corresponding probabilities of survival for patients with intermediate disease were 57% ± 6% and 43% ± 2%, respectively. Autotransplants were rarely performed in young AML patients who were not in remission. Among patients ≥20 years old with advanced AML, the 3-year probability of survival after receiving an autotransplant was 18% ± 3%.



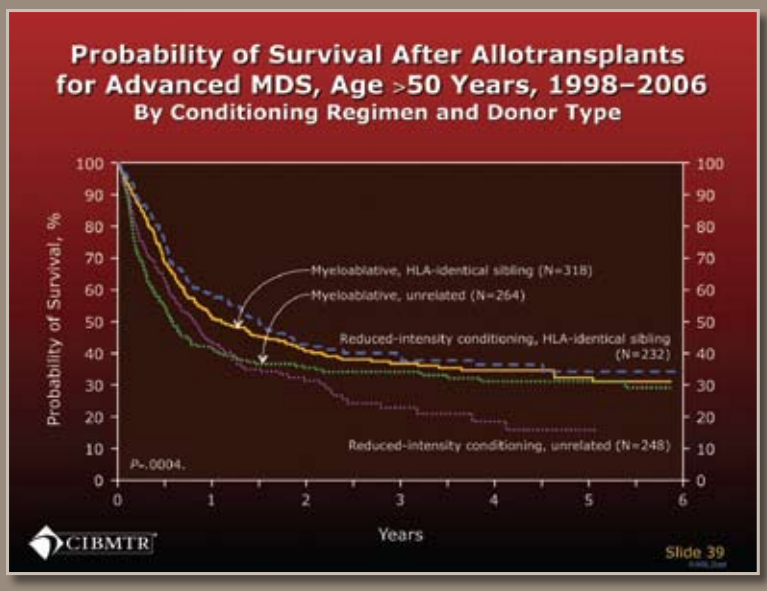


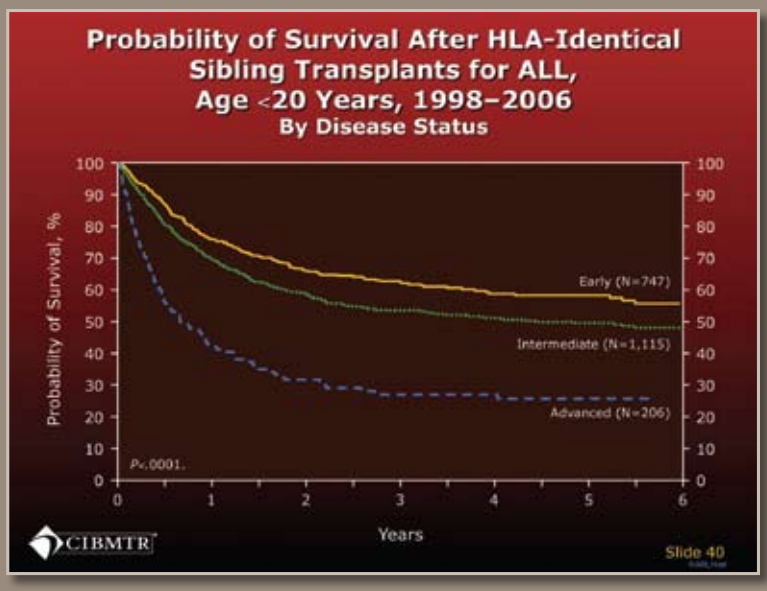
Slides 36 and 37: Allogeneic HCT is a potentially curative treatment for MDS. Outcomes differ according to the recipient's age, donor type, and disease status at transplant. Among 169 recipients of HLA-matched allogeneic HCT younger than 20 years of age, the 3-year probabilities of survival were 62% ± 7% and 59% ± 5% for patients with early and advanced disease, respectively. The corresponding probabilities of survival in the 316 recipients receiving an unrelated donor HCT were 60% ± 5% and 48% ± 4%. Among the 1,656 patients ≥20 years receiving HLA-matched sibling HCT, the 3-year probabilities of survival were 47% ± 2% and 41% ± 2% for early and advanced MDS, respectively. The corresponding probabilities in the 1,437 older patients receiving unrelated donor HCT were 44% ± 3% and 32% ± 2%.



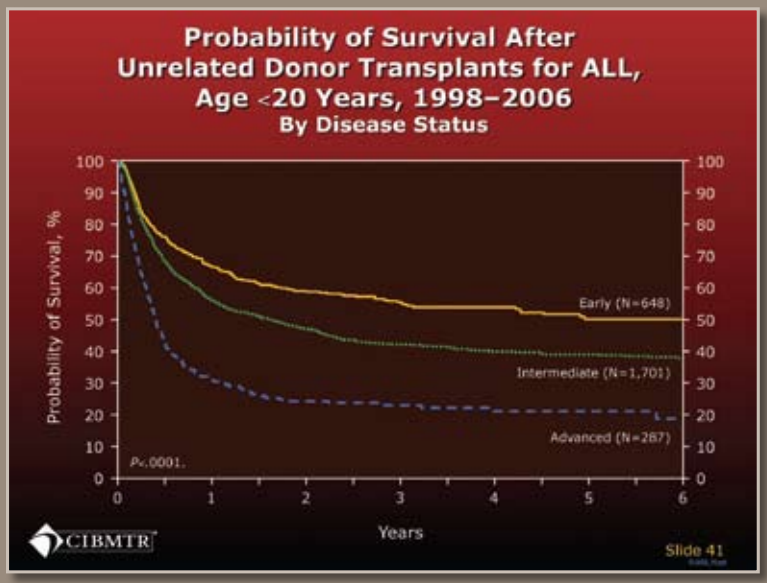


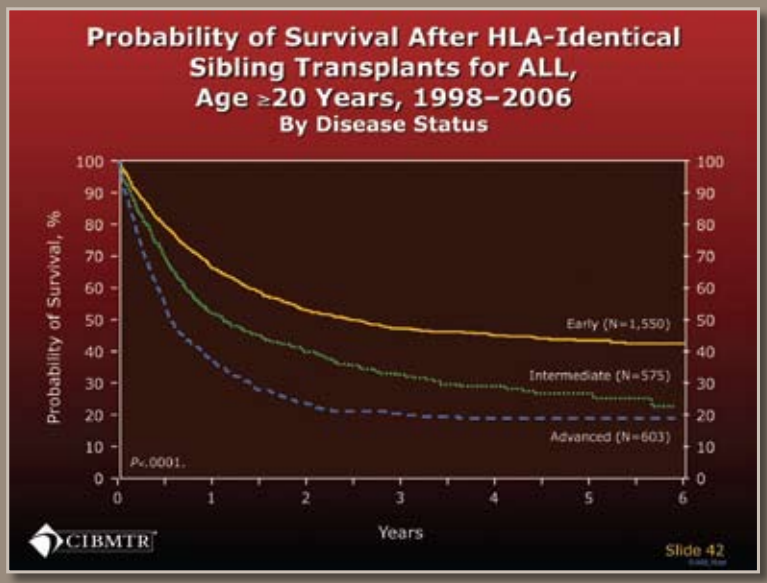
Slides 38 and 39: The median age of patients with MDS at diagnosis is 70 years, limiting the use of myeloablative conditioning regimens for most patients with this disease. Reduced-intensity conditioning regimens are increasingly used for allogeneic transplantation in older patients not previously considered candidates for transplantation. Among 231 patients >50 years who underwent HLA-matched donor HCT for early MDS, the 3-year probabilities of survival were 43% ± 5% and 40% ± 5% for patients receiving myeloablative and reduced-intensity conditioning regimens, respectively. The corresponding probabilities of survival in the 167 patients receiving unrelated donor HCT for early MDS were 34% ± 6% and 38% ± 6%. Among the 550 patients >50 years who underwent HLA-matched donor HCT for advanced MDS, the 3-year probabilities of survival were 37% ± 3% and 39% ± 4% for patients receiving myeloablative and reduced-intensity conditioning regimens, respectively. The corresponding probabilities of survival in the 512 patients receiving unrelated donor HCT for advanced MDS were 34% ± 3% and 23% ± 4%.



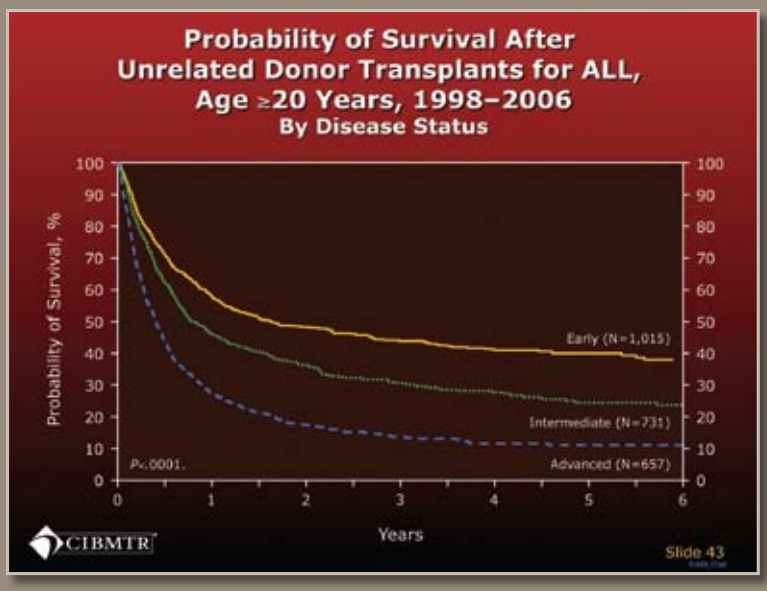


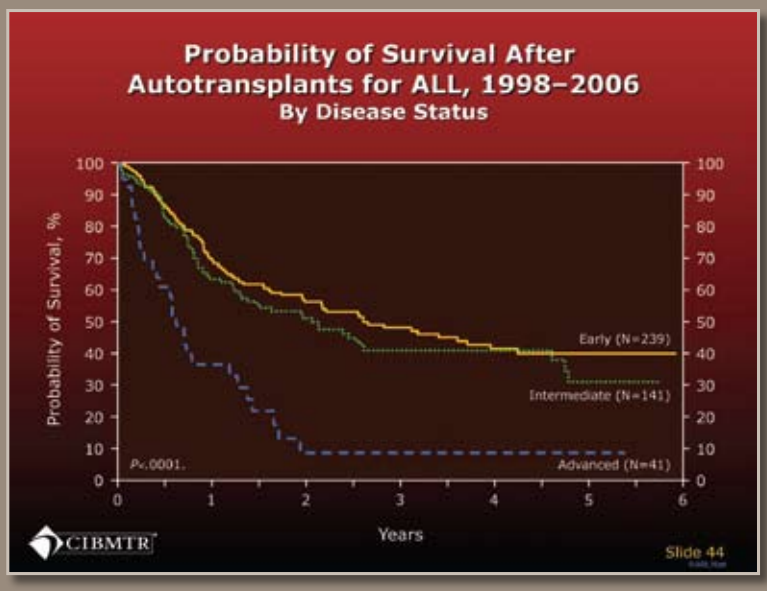
Slides 40 and 41: Among young patients with ALL, for whom chemotherapy has a high success rate, allogeneic transplantation is generally reserved for patients with high-risk disease (ie, high leukocyte count at diagnosis and presence of poor-risk cytogenetic markers), who fail to achieve remission, or who relapse after chemotherapy. Among the 2,068 patients younger than 20 years of age receiving HLA-matched sibling HCT, the 3-year probabilities of survival were 62% ± 2%, 54% ± 2 %, and 27% ± 4% for patients with early, intermediate, and advanced disease, respectively. The corresponding probabilities of survival among the 2,636 recipients of unrelated donor HCT were 56% ± 2%, 42% ± 2%, and 23% ± 3%.



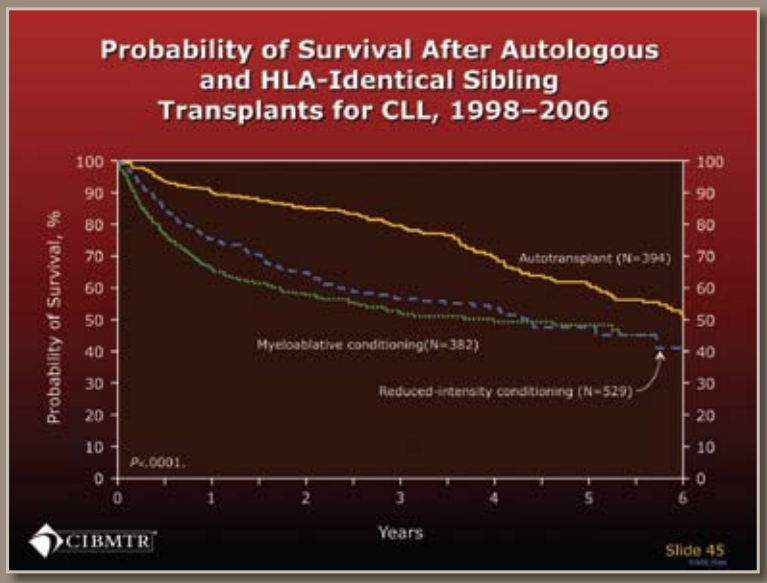


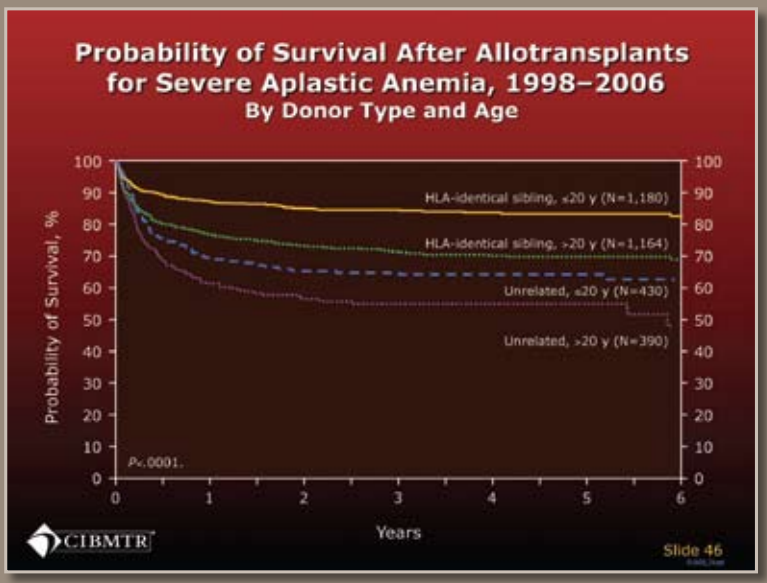
Slides 42 and 43: Older age at disease onset is a high-risk feature in ALL. Consequently, a larger proportion of ALL patients 20 years of age or older undergo allogeneic HCT for early disease. Among 2,728 patients ≥20 years of age receiving HLA-matched sibling HCT, the 3-year survival probabilities were 47% ± 2%, 33% ± 2%, and 21% ± 2% for patients with early, intermediate, and advanced disease, respectively. Corresponding probabilities among the 2,403 recipients of unrelated donor HCT were 44% ± 2%, 31% ± 2%, and 14% ± 2%.





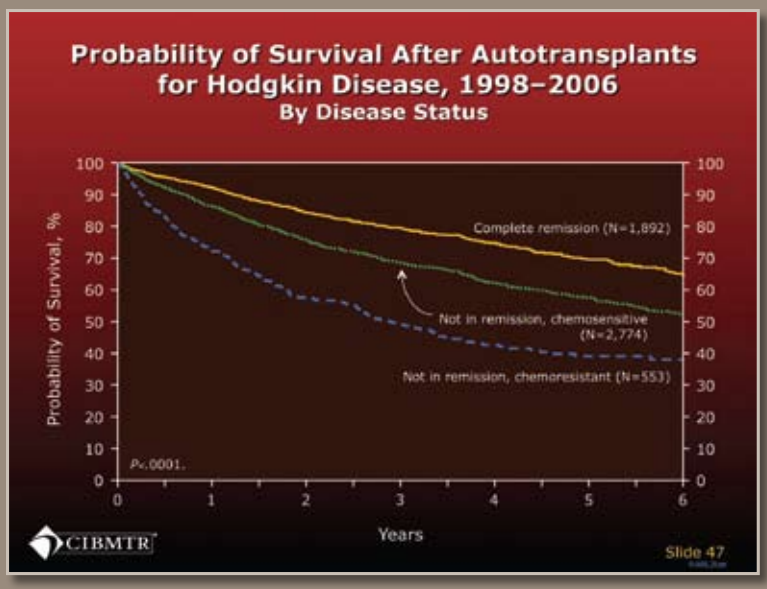
Slide 44: Autotransplants are performed in relatively few patients with ALL; most ALL patients who receive autotransplants are in complete remission at the time of transplantation. Among the 421 patients receiving autotransplants for ALL, the 3-year probabilities of survival were 48% ± 4%, 41% ± 5%, and 9% ± 6% for patients with early, intermediate, and advanced disease, respectively.



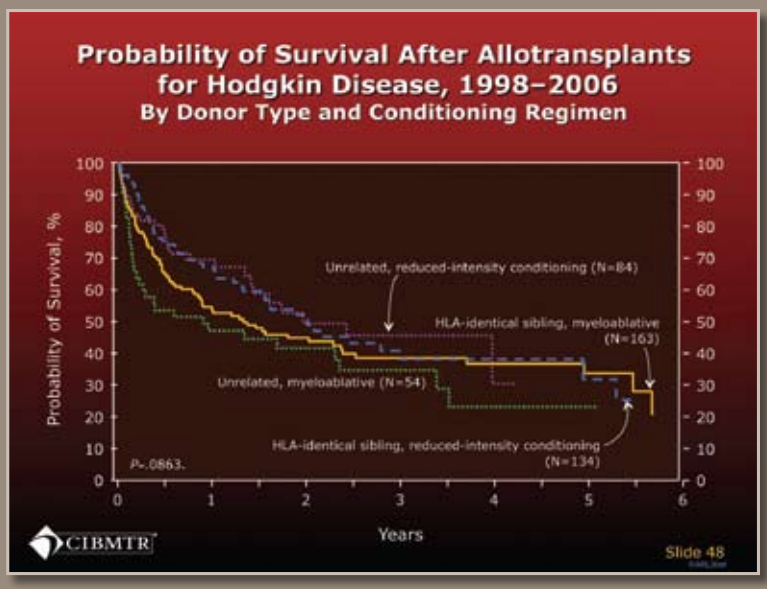


Slide 45: Both autologous and allogeneic HCT are treatment options for CLL patients who fail standard chemotherapy or have high-risk features (eg, cytogenetic abnormalities). The use of reduced-intensity conditioning regimens for allogeneic HCT continues to increase in this population. Among the 1,305 patients who underwent HCT for CLL, the 3-year probabilities of survival were 80% ± 2% after autotransplants, 52% ± 3% after HLA-matched sibling HCT with a myeloablative conditioning regimen, and 57% ± 3% after HLA-matched sibling HCT with a reduced-intensity conditioning regimen.

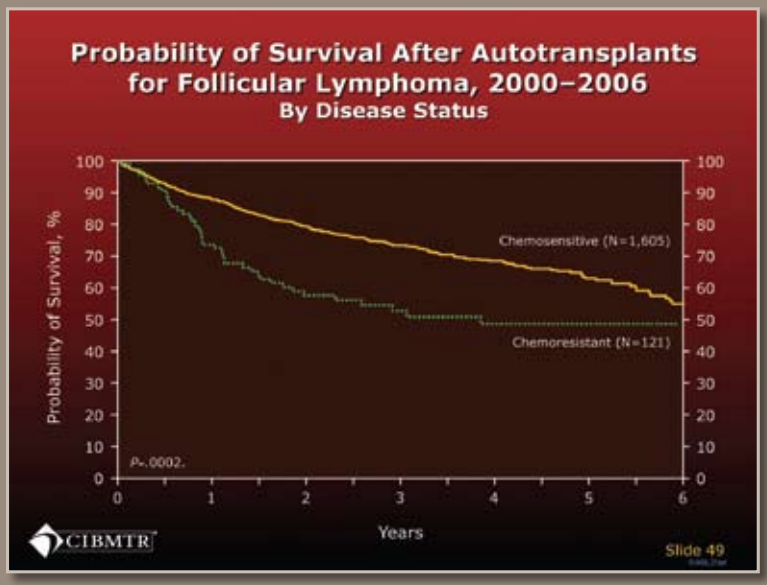
Slide 46: Allogeneic HCT is the treatment of choice for young patients with severe aplastic anemia and an HLA-matched sibling donor.
Among the 1,344 patients receiving HLA-matched HCT for aplastic anemia between 1998 and 2006, the 3-year probabilities of survival were 85% ±1% for those younger than 20 years and 71% ± 1% for those 20 years of age or older. Among the 820 recipients of unrelated donor HCT, the corresponding probabilities of survival were 65% ± 2% and 55% ± 3%.

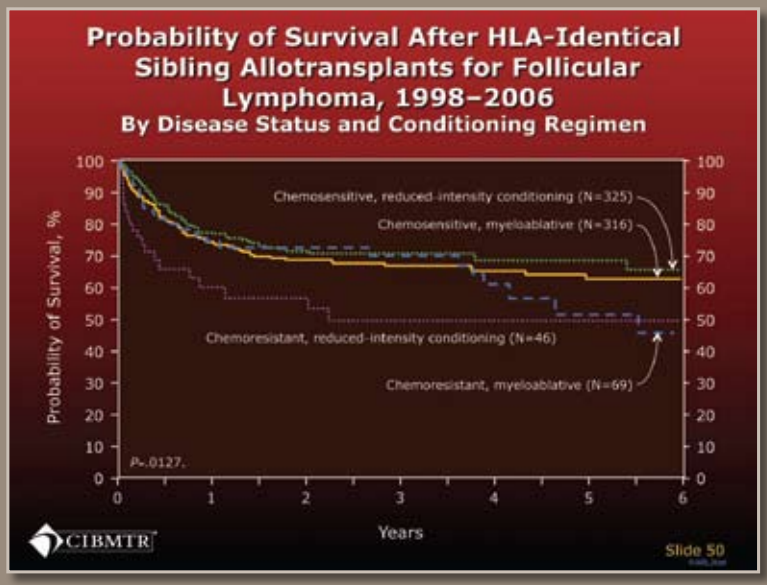


Slide 47: Transplantation for Hodgkin Disease (HD) is indicated in patients who have failed initial chemotherapy or radiation therapy. Survival after HCT for HD depends on disease response to previous salvage therapy. Among the 5,219 patients receiving autotransplants for HD between 1998 and 2006, the 3-year probabilities of survival were 78% ± 1%, 69% ± 1%, and 49% ± 3% for patients in complete remission, in partial remission, and with chemoresistant disease, respectively.

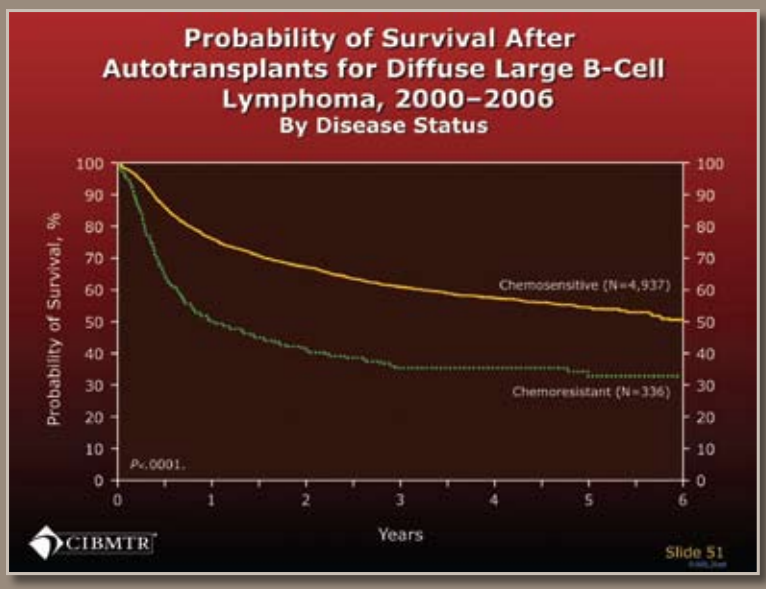


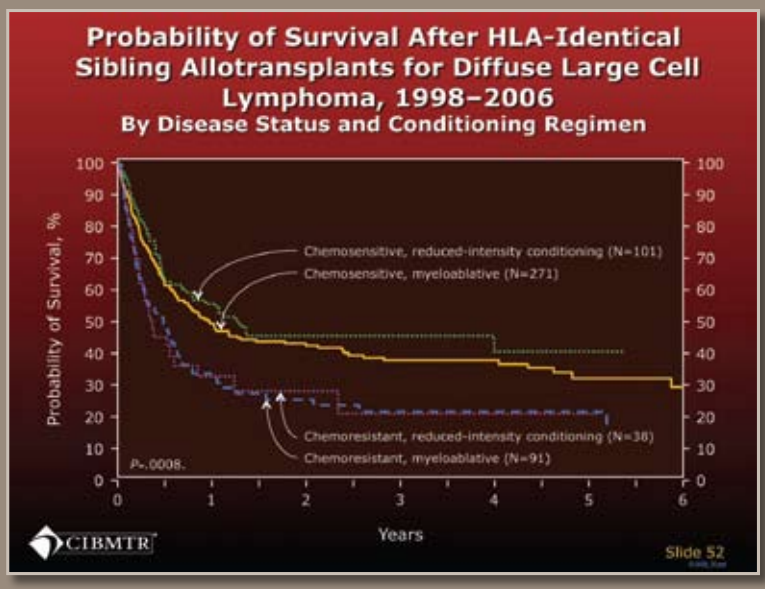
Slide 48: Allogeneic HCT for HD is generally performed in patients who experience disease relapse after receiving multiple lines of therapy or who have refractory disease and an available HLA-matched donor. The use of reduced-intensity conditioning regimens in these heavily pretreated patients allows for a graft-versus-lymphoma effect with less regimen-related toxicity. Among 297 patients receiving HLA-matched HCT for HD between 1998 and 2006, the 3-year probabilities of survival were 39% ± 5% with myeloablative conditioning regimens and 38% ± 5% with reduced-intensity conditioning regimens. The corresponding probabilities of survival in the 138 recipients of unrelated donor HCT were 35% ± 7% and 46% ± 8%.



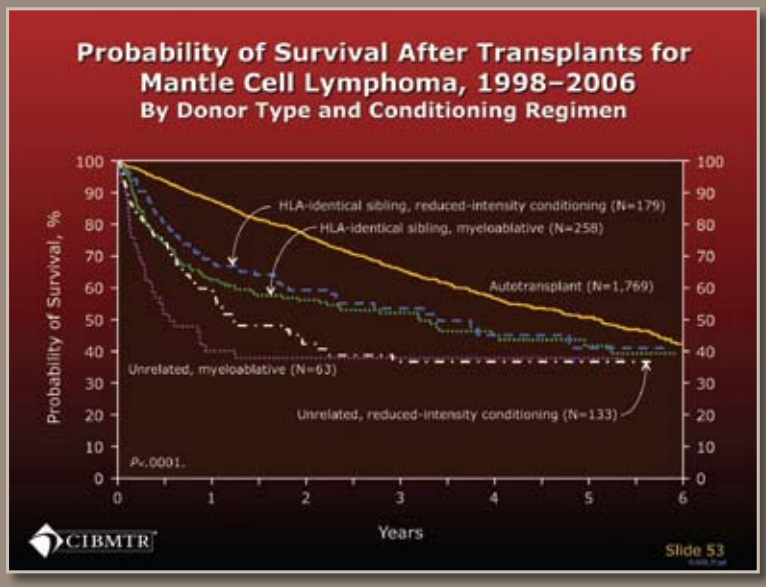


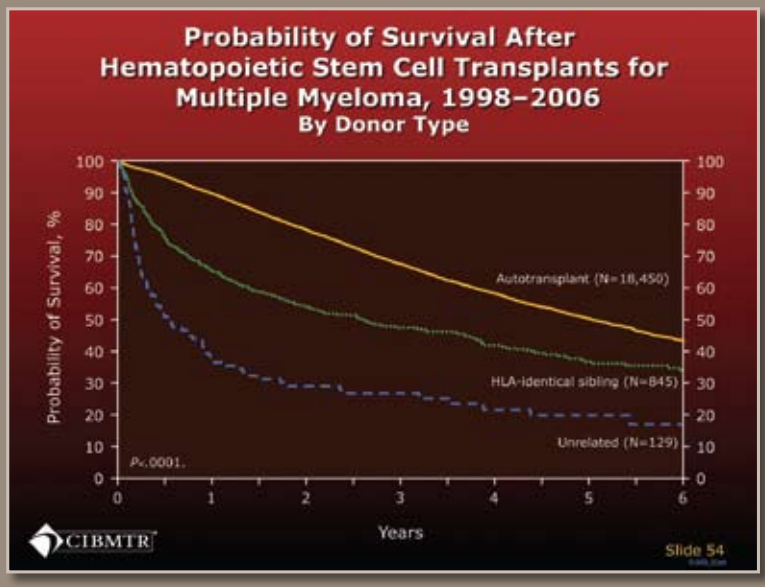
Slides 49 and 50: Transplantation for follicular lymphoma (FL) is generally reserved for patients with recurrent or aggressive disease. Autotransplantation is the most common transplant approach in this disease. Among the 1,726 patients receiving an autotransplant for FL between 2000 and 2006, most had chemosensitive disease. The 3-year probabilities of survival were 73% ± 1% and 53% ± 5% for patients with chemosensitive and chemoresistant disease, respectively. Similar to CLL and HD, the use of reduced-intensity conditioning regimens is increasing for patients with FL. Among 641 patients with chemosensitive FL undergoing HLA-matched sibling HCT between 1998 and 2006, the 3-year probabilities of survival were 67% ± 3% and 71% ± 3% for those receiving myeloablative and reduced-intensity conditioning regimens, respectively. Corresponding probabilities in the 115 patients with chemoresistant FL were 70% ± 6% and 50% ± 8%.





Slides 51 and 52: Autotransplants are an accepted treatment indication for diffuse large B-cell lymphoma (DLBCL) and, similar to FL, most autotransplants are performed in patients with chemosensitive disease. Among the 5,273 patients who received an autotransplant for DLBCL between 2000 and 2006, the 3-year probabilities of survival were 61% ± 1% and 36% ± 3% for patients with chemosensitive and chemoresistant disease, respectively. Allogeneic HCT for treatment of DLBCL is performed less frequently than for FL and is generally used only in patients with aggressive disease that has been resistant to previous therapies. Among the 362 patients with chemosensitive DLBCL undergoing HLA-matched sibling HCT, the 3-year probabilities of survival were 38% ± 3% and 46% ± 5% for patients receiving myeloablative and reduced-intensity conditioning regimens, respectively. The corresponding probabilities in the 129 patients with chemoresistant DLBCL were 22% ± 5% and 21% ± 9%.





Slide 53: The optimal timing of HCT for mantle cell lymphoma (MCL) is not well defined. As with other mature B-cell lymphoproliferative disorders, autotransplantation is the most common transplant approach. Among the 1,769 patients who received an autotransplant for MCL between 1998 and 2006, the 3-year probability of survival was 67% ± 1%. Three-year probabilities of survival for the 437 HLA-matched sibling and 196 unrelated donor transplants were 52% ± 4% and 38% ± 7%, respectively. Survival was similar regardless of conditioning regimen intensity.

Slide 54: Multiple myeloma (MM) is the most common indication for autologous HCT. Among 18,450 MM patients who received a single autotransplant between 1998 and 2006, the 3-year probability of survival was 68% ± 1%. Among the 974 patients who received an allogeneic HCT as the first transplant, the 3-year probabilities of survival were 48% ± 2% for the 845 recipients of HLA-matched sibling HCT and 27% ± 4% for the 129 recipients of unrelated donor HCT.

» 'Pediatric Cancer Working Committee' article continued from Page 1

influences clinical practice patterns through the publication of important clinical study results.

A key achievement of the PCWC has been the completion and publication of 2 studies performed collaboratively with the Children's Oncology Group. These studies compared the outcomes of acute lymphocytic leukemia (ALL) patients with both bone marrow and isolated CNS relapse, respectively, receiving transplantation with those receiving chemotherapy and have been remarkably valuable to clinicians selecting therapies for these types of patients.

Recent publications:

PC99-02 Gardner SL, Carreras J, Boudreau C, Camitta BM, Adams RH, Chen AR, Davies SM, Edwards JR, Grovas AC, Hale GA, Lazarus HM, Arora M, Stiff RJ, Eapen M. Myeloablative therapy with autologous stem cell rescue for patients with Ewing's sarcoma. *Bone Marrow Transplant.* [Epub ahead of print, February 4, 2008].

This study describes the disappointing outcomes of children receiving autologous transplants for relapsed Ewing's sarcoma. The authors recommend that transplantation be performed only as part of controlled clinical trials that critically assess treatment benefit.

PC03-05 Eapen M, Zhang MJ, Devidas M, Raetz E, Barredo J, Ritchey AK, Godder K, Grupp S, Lewis VA, Malloy K, Carroll WL, Davies SM, Camitta BM, for the Children's Oncology Group and the Center for International Blood and Marrow Transplant Research. Outcomes after HLA-matched sibling transplantation or chemotherapy in children with acute lymphoblastic leukemia in a second remission after an isolated central nervous system relapse: a collaborative study between the Children's Oncology Group and the Center for International Blood and Marrow Transplant Research. *Leukemia.* 2008;22(2):281-286.

This study showed no benefit for transplantation when compared with chemotherapy for isolated CNS relapse of ALL.

D01-59 Bunin NJ, Davies SM, Aplenc R, Camitta BM, Desantes KB, Goyal R, Kapoor N, Rosenthal J, Smith FO, Eapen M. Unrelated donor bone marrow transplants for children with acute myeloid leukemia beyond first remission or refractory to chemotherapy. *J Clin Oncol*. In press.

This paper reports survival rates of 45%, 20%, and 12% for children with AML transplanted in second remission, relapse, and primary induction failure, respectively.

PC05-01 Hale GA, He V, Termuhlen AM, Davies SM, Camitta BM, Cairo MS, Eapen M, Gross TG. Outcomes after hematopoietic stem cell transplantation for non-Hodgkin lymphoma in children and adolescents. Paper presented at: 2008 CIBMTR BMT Tandem meetings: February, 2008; San Diego, CA.

This paper reports great heterogeneity in diagnosis and treatment but similar overall survival rates after autologous and allogeneic transplantation.

Studies Currently Accruing Patients:

PC05-02 Nemecek ER. Outcome of unrelated hematopoietic stem cell transplantation for children with advanced acute lymphoblastic leukemia.

This study will describe survival after transplantation in children with ALL in third remission or beyond. A previous committee paper showed that children with late relapse (CR1 > 36 mo) can achieve acceptable outcomes with chemotherapy (Eapen M, et al. *Blood.* 2006;107(12):4961-4967). Determining whether children who relapse after CR3 will respond to transplantation is important information for clinicians and parents making treatment decisions. A protocol has been finalized and data collection is underway.

R02-34 Frangoul H. Unrelated donor transplantation for children with Philadelphia chromosome–positive (Ph-+) acute lymphoblastic leukemia (ALL).

The incorporation of imatinib mesylate into chemotherapy regimens for Ph-+ ALL has the potential to transform the use of transplantation for this disease. This study will provide data that will serve as a baseline for comparing outcomes of transplantation with chemotherapy in this patient population.

An additional study was discussed and classified as **high priority** at the February 2008 PCWC meeting.

PROP 1207-32 Verneris M. The outcome of pediatric patients with acute lymphoblastic leukemia following reduced-intensity conditioning transplant.

The effectiveness of using a reduced-intensity conditioning regimen for a disease as rapid and aggressive as childhood ALL is unknown. Outcomes of 49 nonablative reduced-intensity transplants and 99 reduced-intensity ablative transplants have been reported to the registry and will be used to determine whether or not this is an effective clinical strategy for children who are unlikely to tolerate a fully ablative preparative regimen.

» 'Immunobiology Working Committee' article continued from Page 1

products, cells, and DNA has aided IBWC research. Additionally, the NMDP Research Sample Repository provides a unique resource for investigators conducting retrospective analyses of immune-response determinants and transplant outcome. Currently, samples from more than 12,500 unrelated donor-recipient pairs for whom complete clinical data have been collected and validated are available. Nearly 70% of the paired samples have complete high-resolution data for HLA-A, B, C; DRB1/3/4/5; DQ; and DP loci. For investigations that examine the clinical role of the immune system in transplantation and do not require complete high-resolution HLA typing data and/or samples, the CIBMTR can provide clinical data on more than 36,500 HLA-identical sibling, 3,400 other-related, and 18,500 unrelated donor transplants.

The IBWC currently lists 42 studies in progress. Because the committee is so active, it may seem that additional proposals would be unwelcome. However, the exact opposite is true; the success of the committee depends on vibrant scientific interactions, new ideas and testable hypotheses, and

participation by individuals with different perspectives and scientific backgrounds. The IBWC encourages all investigators with expertise in the basic biological sciences (ie, immunology, immunobiology, and human genetics) to become actively involved with this committee. Working committee meetings convene annually at the BMT Tandem Meetings, although other venues for interaction are also available. Please contact one of the chairs or a member of the scientific staff to learn more or to discuss your research ideas and proposals. We look forward to chatting with you and seeing you at our meetings!

Recent publications:

D98-125 Wade JA, Hurley CK, Takemoto SK, Thompson J, Davies SM, Fuller TC, Rodey G, Confer DL, Noreen H, Haagenson M, Kan F, Klein J, Eapen M, Spellman S, Kollman C. HLA mismatching within or outside of cross-reactive groups (CREGs) is associated with similar outcomes after unrelated hematopoietic stem cell transplantation. *Blood.* 2007;109:4064-4070.

R03-73s Hou LH, Steiner NK, Chen M, Belle I, Ng J, Hurley CK. KIR2DL1 allelic diversity: four new alleles characterized in a bone marrow transplant population and three families. *Tissue Antigens.* 2007;69:250-254.

R03-57s Shulse C, Steiner NK, Hurley CK. Allelic diversity in KIR2DL4 in a bone marrow transplant population: description of three novel alleles. *Tissue Antigens.* 2007;70:157-159.

R03-57s Gedil MA, Steiner NK, Hurley CK. KIR3DL2: diversity in a hematopoietic stem cell transplant population. *Tissue Antigens.* 2007;70:228-232.

R03-57s Hou L, Chen M, Steiner NK, Belle I, Turino C, Ng J, Hurley CK. Seventeen novel alleles add to the already extensive KIR3DL3 diversity. *Tissue Antigens.* 2007;70:449-454.

R04-75s Malkki M, Gooley T, Dubois V, Horowitz M, Petersdorf EW. Immune response gene polymorphisms in unrelated donor hematopoietic cell transplantation. *Tissue Antigens.* 2007;69(suppl 1):50-53.

R04-76s Malkki M, Gooley T, Horowitz M, Petersdorf EW; IHWG HCT Component. MHC class I, II, and III microsatellite marker matching and survival in unrelated donor hematopoietic cell transplantation. *Tissue Antigens.* 2007;69(suppl 1):46-49.

R04-76s Malkki M, Gooley T, Horowitz MM, Absi L, Christiansen FT, Cornelissen JJ, Dormoy A, Dubois V, Gagne K, Gluckman E, Haagenson MD, Oudshoorn M, Spellman S, Petersdorf EW; International Histocompatibility Working Group in Transplantation. Mapping MHC-resident transplantation determinants. *Biol Blood Marrow Transplant.* 2007;13(8):986-995.

R02-33s Mehta PA, Eapen M, Klein JP, Gandham S, Elliott J, Zamzow T, Combs M, Aplenc R, MacMillan ML, Weisdorf DJ, Petersdorf E, Davies SM. Interleukin-1 alpha genotype and outcome of unrelated donor hematopoietic stem cell transplantation for chronic myeloid leukemia. *Br J Haematol.* 2007;137:152-157.

R04-91 Miller JS, Cooley S, Parham P, Farag SS, Verneris MR, McQueen KL, Guethlein LA, Trachtenberg EA, Haagenson M, Horowitz MM, Klein JP, Weisdorf D. Missing KIR ligands are associated with less relapse and increased graft-versus-host disease (GVHD) following unrelated donor allogeneic HCT. *Blood.* 2007;109:5058-5061.

R04-97 Lee SJ, Klein J, Haagenson M, Baxter-Lowe LA, Confer DL, Eapen M, Fernandez-Vina M, Flomenberg N, Horowitz M, Hurley CK, Noreen H, Oudshoorn M, Petersdorf E, Setterholm M, Spellman S, Weisdorf D, Williams TM, Anasetti C. High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation. *Blood.* 2007;110:4576-4583.

CIBMTR Data Entry Forms FormsNet™2.0 Update

by Diane J. Knutson, BS

On December 3, 2007, the long-awaited, revised CIBMTR data entry forms were released. The revised forms represent the diligent and collaborative input of many data managers, physicians, cell-processing directors, and several international organizations. The new forms replaced the previously separate CIBMTR and NMDP forms and were designed to harmonize with those from the European Group for Blood and Marrow Transplantation.

Centers from around the world were invited to access and evaluate the new Web-based data entry application for the revised forms, known as FormsNet™2.0 (FN™2). Feedback from end users has resulted in monthly software upgrades. Training for the FN™2 and its applications were offered at the February 2008 BMT Tandem Meetings. Additionally, a Transplant Essential Data (TED) Manual and Frequently Asked Questions section were developed and are available at the CIBMTR Web site (www.cibmtr.org). An instruction manual for the comprehensive report forms application is under development.

For FN™2 questions not addressed by the online resources described above, individuals should contact their center liaison at CIBMTR. Users with unanswered queries regarding the FN™2 forms and electronic applications may also call the help desk at 1.800.526.7809x8123 or send an e-mail to helpdesk@nmdp.org.

The CIBMTR is currently developing a transplant center survey to assess internal center organization and infrastructure as well as CIBMTR reporting practices. The survey will help identify ways that the CIBMTR can assist centers in the reporting process. We encourage you to participate in this survey so we can better meet your needs. Additional forms training will be provided at the Clinical Research Professionals/Data Management Conference, which will be held in conjunction with the NMDP Council Meeting in November 2008, as well as the BMT Tandem Meetings in Tampa in February 2009. Details will be posted on the CIBMTR Web site (www.cibmtr.org) when available.

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 Disease; the Office of Naval Research; the Health Resources and Services Administration (HRSA), and the generosity of the supporters listed below.

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