CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Newsletter

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CIBMTR Awarded HRSA Contract to Administer the C.W. Bill Young Cell Transplantation Program Outcomes Database

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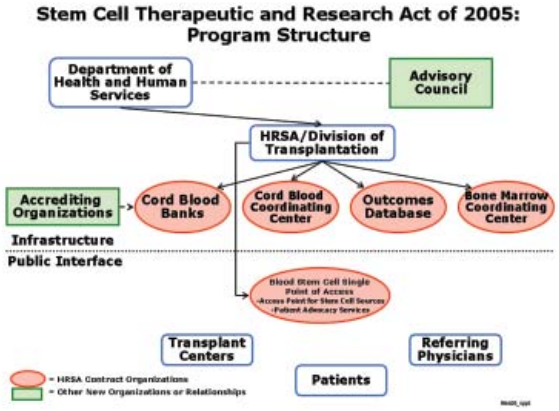
The Center for International Blood and Marrow Transplant Research (CIBMTR) is pleased to be the recipient of the contract (administered by the United States Health Resources and Services Administration (HRSA)) to establish and maintain the Stem Cell Therapeutic Outcomes Database (SCTOD) for the C.W. Bill Young Cell Transplantation Program. This is the beginning of an exciting new era for research in hematopoietic cell transplantation (HCT).

The C.W. Bill Young Cell Transplantation Program (the Program) builds on the infrastructure for donor procurement and outcomes analysis developed by the National Marrow Donor Program (NMDP), which has held the U.S. contract to maintain a National Bone Marrow Donor Registry (NBMDR) for unrelated donor transplantation since its inception in 1987. 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 to succeed (and enhance) the NBMDR. The Program is named after C.W. Bill Young, a recently re-elected 36 year veteran Congressman from Florida who has been a strong advocate of biomedical research and who was instrumental in the founding of the U.S. donor registry. The Program will include five key components: 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). Several cord blood banks will also receive contracts to develop a National Cord Blood Inventory. See Figure 1.

Working with its NMDP partner, the CIBMTR submitted the winning proposal to administer the SCTOD. The NMDP also was awarded the BMCC, CBCC and the OPA/SPA contracts. Although the landscape of HCT will change because of this legislation, the contract awards to CIBMTR and NMDP represent a substantial benefit to transplant centers, who have become accustomed to collaborating with these organizations. Current, long-standing relationships will not be disrupted as the NMDP and CIBMTR work to implement new and modified requirements of the Program. The CIBMTR and NMDP will use their substantial experience and adapt proven, in-place methods and systems to ensure a successful transition to the new Program.

Implementation of the new Program will present new challenges and opportunities for the HCT community. Important aspects of the program are: development of new systems to collect HCT data electronically, enhanced efforts to develop a standard dataset of HCT data, new requirements for U.S. centers to report outcomes data for all allogeneic transplantations, development of a related donor-recipient research sample repository, systems to make more data publicly available, broadened reporting of U.S. transplant center-specific survival rates, and data collection on uses of stem cells for new therapeutic applications (e.g.,



Data collection for the SCTOD component of the Program will include collection of data for: allogeneic HCTs done in the U.S. using related or unrelated donors; allogeneic HCTs done using cells obtained through the Program, whether the transplantation is done in the U.S. or elsewhere: and use of allogeneic hematopoietic cells for emerging clinical

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applications other than HCT. In order to minimize the burden of data collection and assure that the most relevant data is collected, CIBMTR has begun discussions with U.S. authorities, the American Society of Blood and Marrow Transplantation (ASBMT), the European Blood and Marrow Transplant Group (EBMT), the Foundation for Accreditation of Cellular Therapy, the World Marrow Donor Association, cord blood banks and others in the international HCT community arrive at consensus on a reasonable set of common data elements to be collected for all patients. The current Transplant Essential Data form (corresponding to the EBMT Med-A form) will serve as a starting point (http://cibmtr.org/DATA/registering_centers.html). [Of note, centers participating as Research Centers in the CIBMTR will still be asked to complete comprehensive Report Forms on a subset of these patients; in a separate initiative the NMDP and CIBMTR have been working to harmonize the forms used for related and unrelated donor transplants.] The CIBMTR and NMDP are adapting established electronic data collection systems to collect these data under the HRSA contract. It is anticipated that these electronic systems will also allow centers to access their own HCT data as one of the benefits of participation. CIBMTR will work with consultants from PACT (Production Assistance for Cellular Therapies) and the SCCT (Specialized Centers for Cell-Based Therapy) and others to develop an approach to collect and analyze data on the use of hematopoietic cells for clinical applications other than HCT. Finally, CIBMTR and NMDP will work to expand the current unrelated donor-recipient specimen repository to include specimens obtained from related donor-recipient pairs. The databases and specimen repository created by these additional requirements of the C.W. Bill Young Program will serve as a resource for HCT investigators to address important research questions.

The new Program will also require publication of an annual report of Transplant center-specific outcomes similar to the report currently generated by the NMDP for unrelated HCT. CIBMTR strongly believes in the importance of adjusting for difference in “case-mix” of patients across transplant centers using parameters for disease status and comorbidities at the time of HCT. The experience held by the NMDP will facilitate generation of these reports, and CIBMTR will work closely with the ASBMT Quality Outcomes Committee, the CIBMTR Consumer Advocacy Committee, transplant center director representatives and HRSA to prepare a fair report that is useful for the transplant community and understandable to the general public.

Although change is often difficult, and will certainly require patience as new systems are implemented, the transition to the C.W. Bill Young Cell Transplantation Program promises to offer an enhanced platform from which to conduct clinical investigation into the outcomes of HCT for traditional and emerging indications.

The C.W. Bill Young Cell Transplantation Program and the NMDP

By Dennis L. Confer, MD

Chief Medical Officer, National Marrow Donor Program, Minneapolis, MN, USA

The National Marrow Donor Program (NMDP) is a non-profit corporation that since 1987 has held a series of government contracts to operate the “National Bone Marrow Donor Registry”. In this role NMDP has facilitated more than 25,000 unrelated donor transplants for patients with blood disorders, such as leukemia and aplastic anemia, as well as immune system and genetic disorders. Currently more than 6.1 million adult donors and 52,000 cord blood units are listed on NMDP’s registry. New adult donors are recruited at about 280,000 annually. Cord blood unit numbers will grow significantly as a result of the Stem Cell Therapeutic and Research Act of 2005.

The new act created the C.W. Bill Young Cell Transplantation Program, a totally revamped system for delivering hematopoietic stem cell transplantation options to the U.S. public. This legislation is sweeping in its scope, but emphasizes a federal commitment to development of umbilical/placental cord blood. The legislation creates a National Cord Blood Inventory (NCBI), established by contracts awarded to individual cord blood banks that are charged with responsibility to begin collection of 150,000 new, high-quality cord blood units (CBU). The CBU inventories (both NCBI and non-NCBI units) of these contracted banks, as well as the inventories of other qualified member banks, will be listed, searched and distributed through the National Cord Blood Coordinating Center (CBCC). An analogous National Bone Marrow Coordinating Center (BMCC) will oversee adult donor recruitment, donor search, product collection and product distribution activities of the adult donor registry. The public interface to these coordinating centers will be provided through another contract awarded to establish an Office of Patient Advocacy/ Single Point of Access (OPA/SPA) function.

Six cord blood banks are charter members of the NCBI. They are: Carolinas Cord Blood Bank at Duke University Medical Center, MD Anderson Cord Blood Bank, Milstein National Cord Blood Bank Program at the New York Blood Center, Puget Sound Blood Center, StemCyte, Inc., and the University of Colorado Cord Blood Bank. As described elsewhere in this issue, a contract for the outcomes database was awarded to CIBMTR. Contracts to operate the CBCC, BMCC and OPA/SPA were awarded to the NMDP. Because NMDP received these latter three contracts, much of the complexity inherent in the Program will be shielded from the public and from the transplant community.

Federal oversight of the Program rests with the Department of Transplantation in the Health Resources and Services Administration (HRSA). HRSA is a federal agency dedicated to improving health care access in the U.S. In HRSA’s own words, “HRSA is the nation’s access agency – improving health and saving lives by making sure the right services are available in the right places at the right time.” Accordingly, the new contracts with NMDP include many requirements related to improving access to transplantation therapies. Some of the most interesting requirements relate to enhancing the information supplied to patients, their families and the public. For example, NMDP must develop software that allows patients, families, and the public at large, to conduct searches of the adult donor and CBU registries. This is envisioned as a public web site where any individual with HLA data can obtain information about the potential for matching adult donors and CBU. While this service clearly provides patients with

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Perspectives

By Sergio A. Giralt, MD

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

Hematopoietic Progenitor Cell Transplantation in 2006 – New Challenges and New Opportunities for the Center of Interntional Blood and Marrow Transplant Research

This year we celebrate the 50th anniversary of the publication of the seminal paper by Barnes and Loutit which demonstrated for the first time in a mouse model the existence of a graft versus leukaemia effect mediated by donor cells (1). This paper was the first seed in the development of our field. This seed bore its first fruits almost 20 years later when Dr Thomas reported the transplant outcomes of the first 100 patients in Seattle receiving high dose chemo-radiotherapy and allogeneic transplantation as treatment for refractory leukaemia (2). The concepts of dose intensity as a strategy to overcome cancer cell resistance, hematopoietic progenitor cell rescue as a tool to deliver supralethal chemo-radiotherapy and finally the existence of an immune mediated graft versus tumor effect are still the basis of our field today.

As I begin my term as Chair of the Advisory Committee of the Center for International Blood and Marrow Transplant Research (CIBMTR), certain challenges to the future development of our field are apparent and should be considered as opportunities to move our field forward and improve the outcomes of the patients we serve. The most pressing of these challenges as I see them are:

1. Access To Hematopoietic Progenitor or Stem Cell Transplantation (HCT). Despite strong evidence demonstrating the benefits of allografting and autografting in patients with a variety of hematologic disorders, the rates of transplantation for many diseases remain low. The obvious barriers of donor availability and patients' medical conditions are being addressed by developing alternative donor and graft strategies and less toxic conditioning regimens. Other barriers of access to transplant specialists such as regional distribution of transplant centers, referral bias, and insurance coverage, will require concerted efforts from us as transplant specialists and our professional societies

2. Displacement Of HCT By Alternative Therapies. Chronic myelogenous leukemia has shown us how quickly HCT can be replaced by alternative therapies perceived to be superior. The results with imatinib undoubtedly justify its use as frontline therapy, reserving allografting for second line therapy. However in some patients (children or those with syngeneic donors) early HCT may still be appropriate. Studies addressing the appropriate timing of HCT in the imatinib era are needed. With the approval of new agents for multiple myeloma, lymphoma and myelodysplastic syndromes, many disease experts are reconsidering the role of autografting and allografting in these disorders. Determining the role of transplantation and other therapies must be addressed by well designed clinical trials which we as a community should be helping to develop, implement and analyze through organizations such as the CIBMTR, the BMT Clinical Trials Network, and the American Society for Blood and Marrow Transplantation (ASBMT) in collaboration with other cooperative groups, and disease specific research organizations and advocacy groups such as the Multiple Myeloma Research Foundation, the International Myeloma Foundation and the Leukemia and Lymphoma Society among others.

3. Increasing Burden of Reporting and Regulatory Obligations: With the recent legislation establishing the C.W. Bill Young Cell Transplant Program, outcomes reporting for all allogeneic HCT will soon become the "law of the land". Although such an initiative is appropriate, a large unfunded mandate for reporting may result in the closure of some small to medium-sized transplant units who will be unable to cope with the added data management demands. We need to work together to seek informatics solutions that will minimize the burden on transplant centers, such as the AGNIS (A Growable Network Informration System) project being developed by CIBMTR and the National Marrow Donor Program with input from ASBMT, the European Group for Blood and Marrow Transplantation and other international partners.

4. Replacement of Trained Personnel. The care of patients undergoing HCT becomes increasingly more complex, as we transplant older patients, use alternative stem cell sources, and explore graft engineering and other cellular therapies. Although the Foundation for Accreditation of Cellular Therapies and the ASBMT have developed criteria the HCT specialists should have, no formal curriculum exists, nor is there a certification program approved. Additionally, we must define what the potential need for HCT will be so we can effectively recruit and train our successors.

These challenges are also opportunities for the future. The number of patients undergoing autologous and allogeneic HCT continues to increase, the potential indications promise to expand and the possibility of improving treatment outcomes by incorporating many recently introduced agents is tantalizing. Prospective evaluation of transplant outcome with mandatory reporting could potentially improve our abilities to demonstrate the efficacy of HCT and serve as a catalyst for the eventual development of HCT as a sub-specialty with specific credentialing requirements which may provide incentive for physicians in training to pursue this career. I am proud to say that the CIBMTR has, and continues to, play a major role in addressing these challenges, making them into opportunities. Some examples include:

a) Development of the Health Services Subcommittee to address issues of access.

b) Initiation of a Working Committee for International Studies

c) Partnering with the NMDP and the EMMES corporation to become the Data Coordinating Center for the BMT Clinical Trials Network.

d) Performing the first studies looking at center characteristics affecting outcomes .

e) Harmonizing data reporting forms with the NMDP and developing AGNIS.

f) Partnering with the NMDP, and the ASBMT to respond to the recent solicitation from HRSA for proposals to develop a national transplant outcomes database for related and unrelated donor HCT

Thus I continue to encourage all of members of the HCT community to actively participate in all activities concerning the CIBMTR, from data reporting to study proposals. In as much as we are participants in these activities, the CIBMTR will represent our needs and together we can improve the field of HCT to the benefit of the patients we see and serve everyday.

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2007 BMT Tandem Meetings – February 8-12 in Keystone, CO

By D'Etta Waldoch, CMP

Interest in the BMT Tandem Meetings at Keystone Conference Center in Colorado is booming once again! The deadline for Early Registration and Abstract Submission for the 2007 Meetings was October 9. At that time almost 1000 attendees had registered for the conference, which represents a 34% increase over registration figures last time we met in Keystone in 2005. The total number of abstracts submitted for the 2007 meeting is 457; up 31% over those submitted in 2005.

BMT Tandem Meetings, 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.

In case you are among the few who haven't visited our web site yet, conference registration, housing reservations, ground transportation options, the provisional agenda and more! are available online at www.cibmtr.org. The deadline for housing requests is January 5, 2007, after which accommodations will be on a space-available basis.

In addition to five days of scientific and clinical meetings there are seven related events, mostly preceding the BMT Tandem Meetings this year: Clinical Research Professionals' Data Management Conference - February 5-7; Transplant Nurses Conference - February 5-7; BMT Pharmacists Conference - February 6-8; Pediatric BMT – February 7; FACT Training Workshops - February 7; BMT Center Administrators Conference - February 8-9; and the BMT Center Medical Directors Conference - February 11.

Plan to combine educational sessions and committee meetings with time for rest and recreation in breathtaking Summit County. Those who enjoy winter activities will be delighted to learn that the 2006/2007 Ski Season at Keystone opened a week earlier than planned. Local residents report that the snow-making machines have been roaring and Mother Nature has been providing a great deal of snow to create a great base for us to enjoy in the mountains in February!

Be sure to keep an eye on the cibmtr.org web site for updates about the 2007 BMT Tandem Meetings in Keystone.

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

Mark Your Calendars

Blood and Marrow Transplant Clinical Trials Network (BMT CTN)

State of the Science Symposium

June 7th & 8th, 2007

Ann Arbor, MI

HRSA Contract and NMDP...*continued*

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greater access to health-related information, it also creates obligations to ensure that the information is accurate, properly represented and accompanied with important disclaimers. For example, the public search report cannot fully anticipate the transplant center's eligibility rules or HLA matching requirements.

The new contracts also require that patients are periodically updated about the status of their donor/CBU search that is being managed by a transplant center. If the search is interrupted or cancelled, the contractor must notify the patient. These requirements will be difficult to implement in a "fool-proof" manner, but will work best with solid collaboration between NMDP and the transplant centers. Additional contract requirements relate to increasing transplantation activity, improving efficiency and developing performance measures. These and other requirements will challenge NMDP, CIBMTR and their partners to create a working environment for innovation and collaboration.

The C.W. Bill Young Cell Transplantation Program has created a vision for the future of transplantation therapies in the U.S. Implementation of this vision has been entrusted to two well-known organizations, CIBMTR and NMDP, working in collaboration with federal officials and the transplant community. The demands are numerous, but rewards for our transplant community and the patients we serve are innumerable.

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

Introduction – Explanation of Data Set and Terms

This second part of the CIBMTR summary slides describes posttransplant survival in patients with the most common indications for hematopoietic stem cell transplantation (HCT). Data derived from patients transplanted in 1998-2004 and reported to the CIBMTR. Curves are stratified by several factors that impact outcomes: recipient age, donor type (autologous, HLA-identical sibling and unrelated), 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 (first complete remission [CR1] or first chronic phase [CP1]), intermediate (second or subsequent CR or CP or accelerated phase [AP]) and advanced (primary induction failure, relapse or blast phase). Myelodysplasia (MDS) is divided into early (refractory anemia [RA] or refractory anemia with ringed sideroblasts [RARS]) and advanced (refractory anemia with excess blasts [RAEB], refractory anemia with excess blasts in transformation [RAEB-t] or chronic myelomonocytic leukemia [CMML]). Lymphoma is classified according to sensitivity to prior therapy: chemo-sensitive and chemo-resistant.

Preparatory regimen intensities are classified as myeloablative or reduced intensity as reported by the transplant center. The CIBMTR operational definition for regimen intensity designates as myeloablative those regimens including total body irradiation (TBI) doses of ≥500 cGY single dose or ≥800 cGY fractionated, busulfan > 9mg/kg and melphalan > 150 mg/m2 given as single agents or in combination with other drugs. Reduced intensity regimens are those with lower doses of TBI, busulfan and melphalan.

Reference for the CIBMTR summary slides is:
Pasquini, M. C.; He, V.; Perez, W. Current use and outcome of hematopoietic stem cell transplantation: part II - CIBMTR Summary Slides, 2005. CIBMTR Newsletter [serial online]. 2006;12(2): 5-10. Available at: http://www.cibmtr.org/ABOUT/NEWS/2006DEC.pdf. Accessed (insert date here).

For Power Point presentations:
CIBMTR Newsletter, Volume 12, Issue, 2, December 2006.

If data are used in an oral presentation, please send us the name, place and date of the meeting where the data are presented, and the title of your presentation to cibmtr@mcw.edu.

Part II – CIBMTR Summary Slides

By Marcelo C. Pasquini, MD, MS[a], Vincent He, MS[b], and Waleska S. Pérez, MPH[c]

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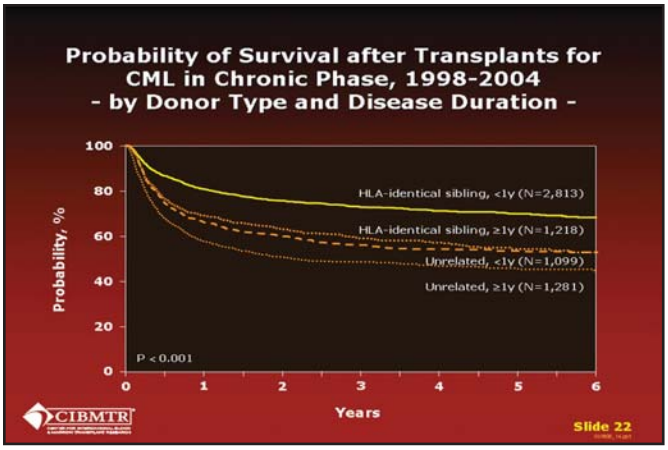
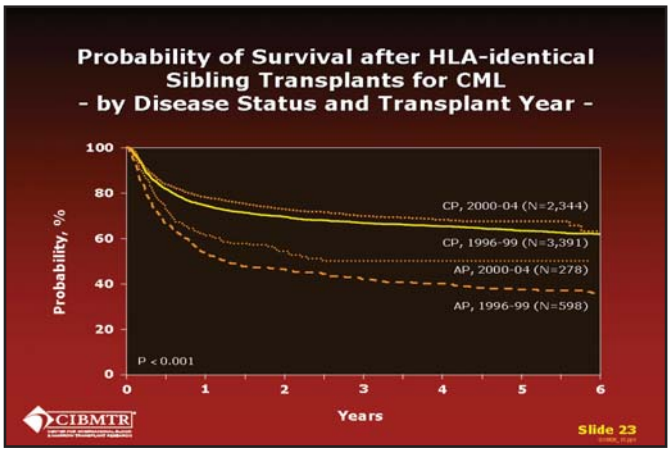
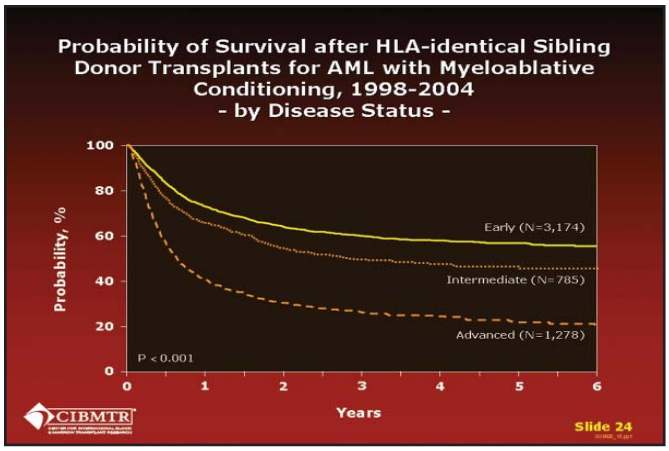
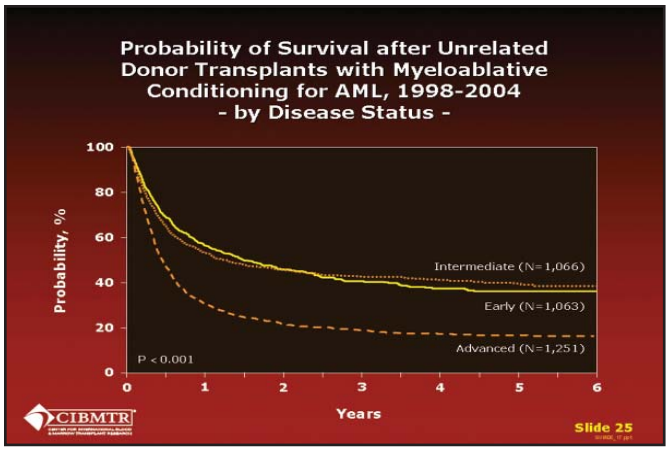


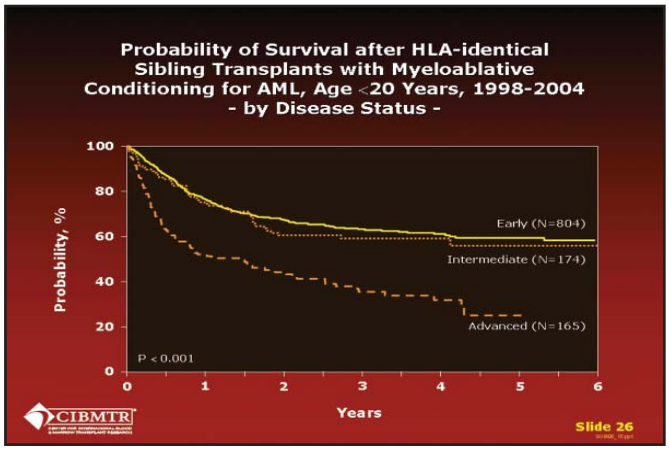


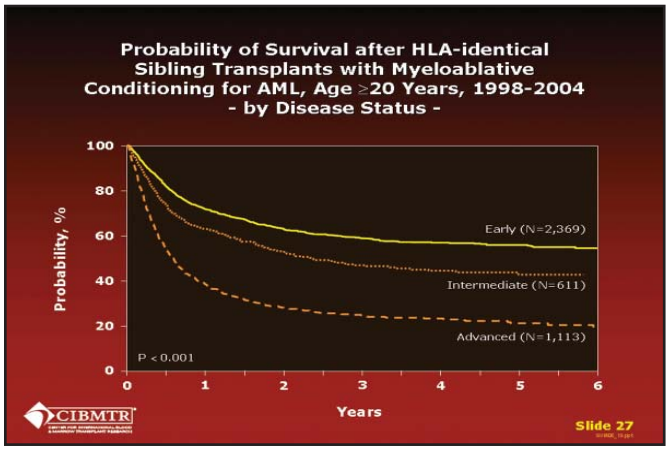
Slides 22 and 23: The CIBMTR has data for 6,411 patients receiving HLA-identical sibling (n=4,031) or unrelated donor (n=2,380) transplants for CML in chronic phase in 1998-2004. Among patients receiving HLA-identical sibling HCT < 1 year after diagnosis, the 3-year probability of survival was 73% ± 1%. Among those receiving HLA-identical sibling HCT ≥ 1 year after diagnosis, the probability was 59% ± 2%. Corresponding 3-year survival probabilities after unrelated donor HCT were 56% ± 2% and 48% ± 1%. The introduction of imatinib for the treatment of CML led to substantial decreases in numbers of HCT performed for this disease. Outcomes before and after availability of this therapy are shown in ***Slide 23***. Three-year probabilities of survival for patients in CP and AP prior to 2000 were 67% ± 1% and 42% ± 2%, respectively. Corresponding probabilities in the post-imatinib era are 70% ±1% and 50% ± 4%.

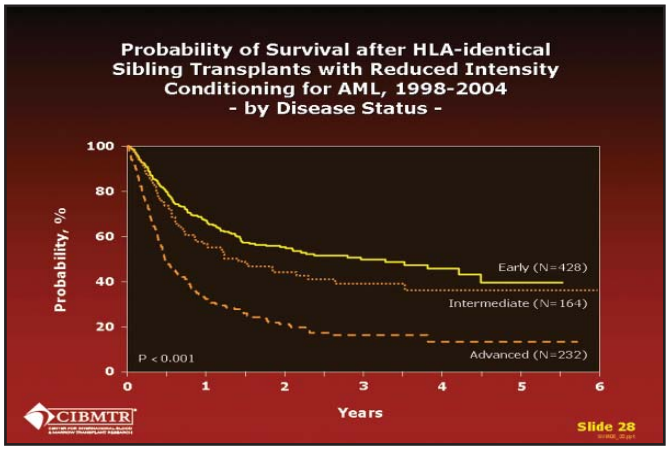


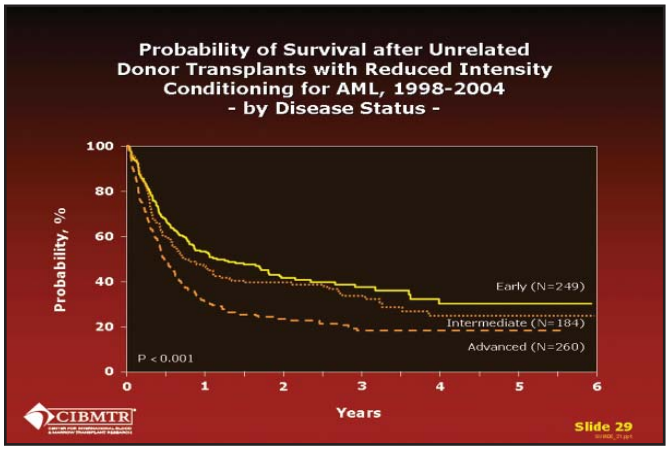


Slides 24-27: The CIBMTR has data for 8,617 patients receiving HLA-identical sibling (n=5,237) or unrelated donor (n=3,380) HCT for AML using myeloablative conditioning in 1998-2004. Disease status at time of HCT and donor type were major predictors of posttransplant survival. Three-year probabilities of survival after HLA-identical sibling HCT were 60% ± 1%, 50% ± 2% and 26% ± 1% for patients with early, intermediate and advanced disease, respectively. Corresponding probabilities after unrelated donor HCT were 41% ± 2%, 42% ± 2% and 19% ± 1%. ***Slides 26 and 27*** show survival probabilities in patients < 20 years of age and in those ≥ 20 years, respectively. Among patients < 20, 3-year probabilities of survival were 63% ± 2%, 59% ± 4% and 35% ± 4% after HCT for early, intermediate and advanced disease, respectively. Corresponding probabilities for patients ≥ 20 years of age were 59% ±1%, 47% ± 2% and 25% ±1%.

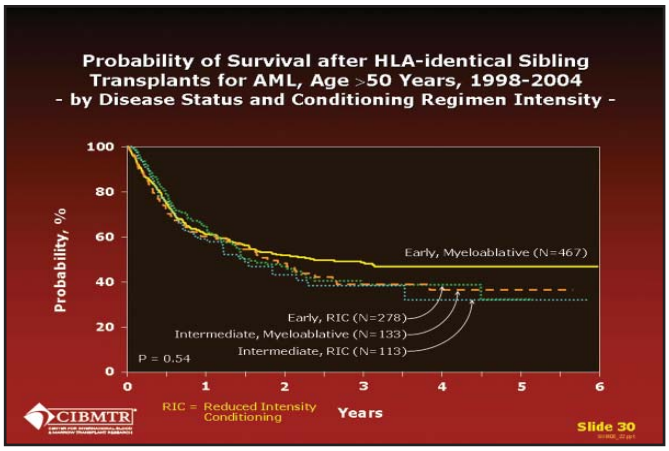




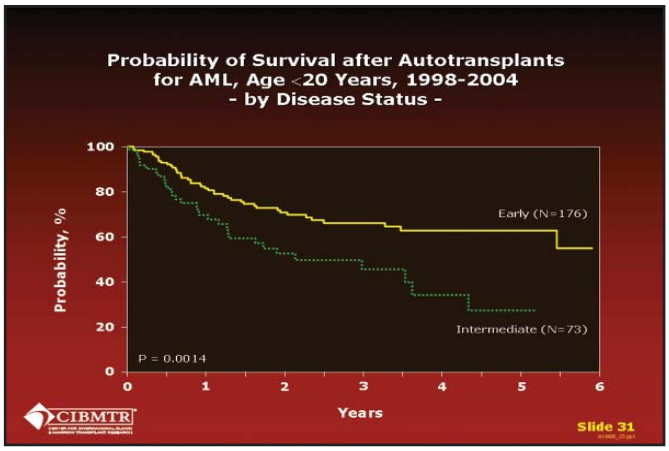


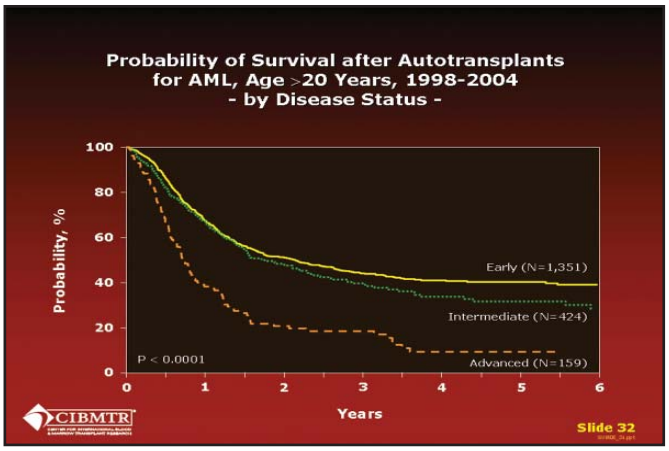


Slides 28 and 29: The use of reduced intensity conditioning for HCT in AML is increasing. The 3-year survival probabilities of 824 patients with AML who underwent HCT with reduced intensity conditioning were 50% ± 3%, 39% ± 5% and 16% ± 3% for those with early, intermediate and advanced disease, respectively. Corresponding probabilities for 693 recipients of unrelated donor HCT were 38% ± 4%, 34% ± 4% and 18% ± 3%.

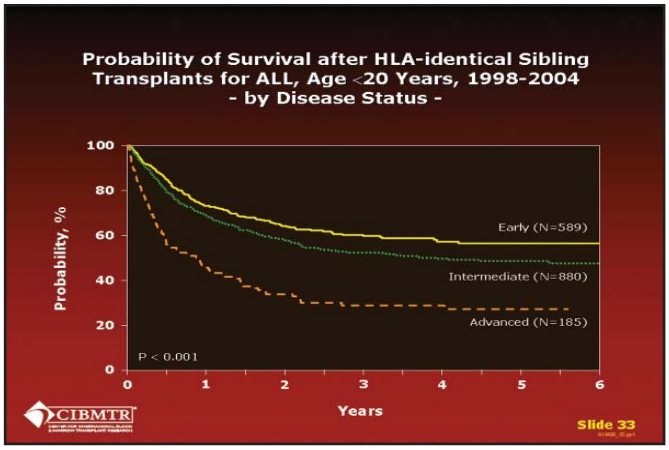


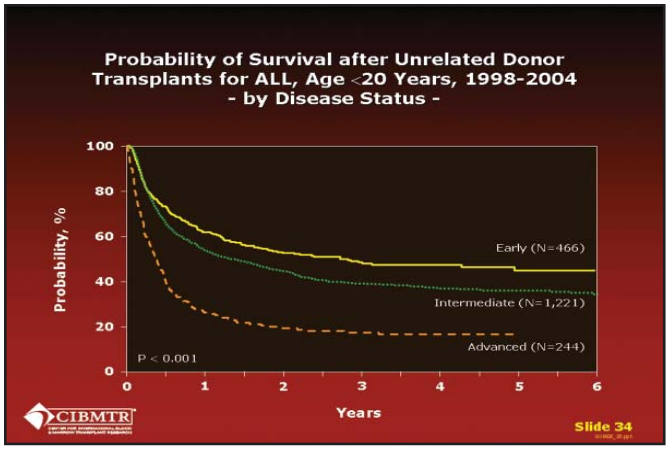
Slide 30: Reduced intensity conditioning regimens are most commonly used in patients older than 50 years. Among patients older than 50, the 3-year probability of survival after HCT for early disease was 49% ± 3% with myeloablative conditioning and 39% ± 4% with reduced intensity conditioning. Among those with intermediate disease, the corresponding probabilities were 39% ± 5% and 38% ± 6%.



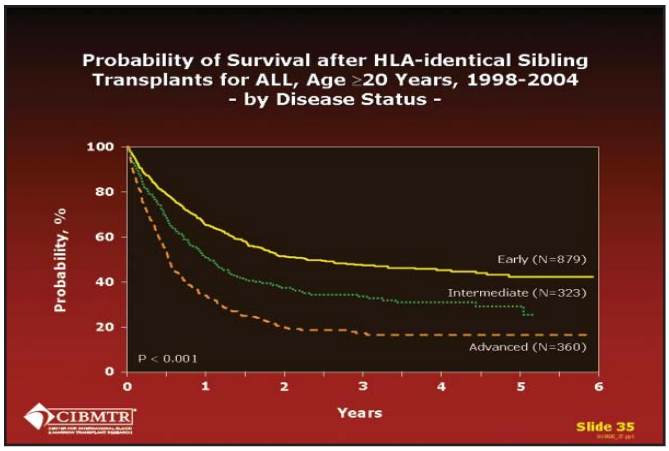


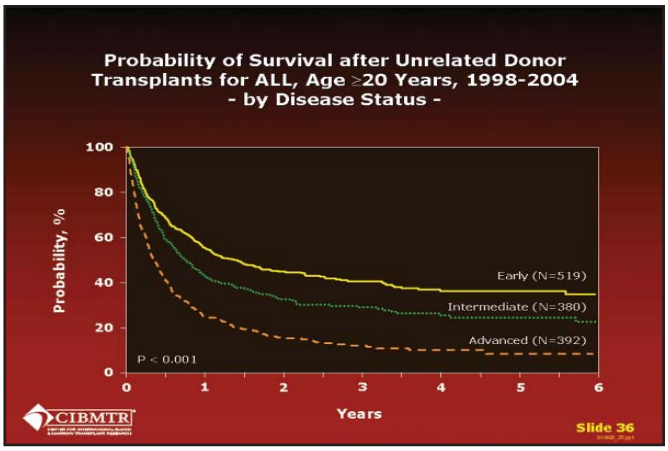
Slides 31 and 32: The CIBMTR has data for 2,184 autotransplants for AML done in 1998-2004, 250 in patients < 20 and 1934 in patients ≥ 20 years old. Three-year survival probabilities for patients with early disease were 66% ± 4% in patients younger than 20 years and 44% ± 2% for older patients. Corresponding probabilities for patients with intermediate disease were 45% ± 8% and 40% ± 3%. Autotransplants were only rarely performed in young patients not in remission. Among patients older than 20 years with advanced AML, the 3-year probability of survival after receiving an autotransplant was 18% ± 4%.



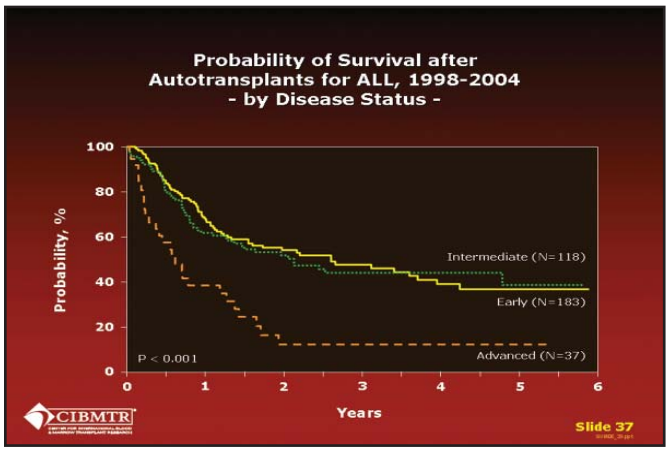


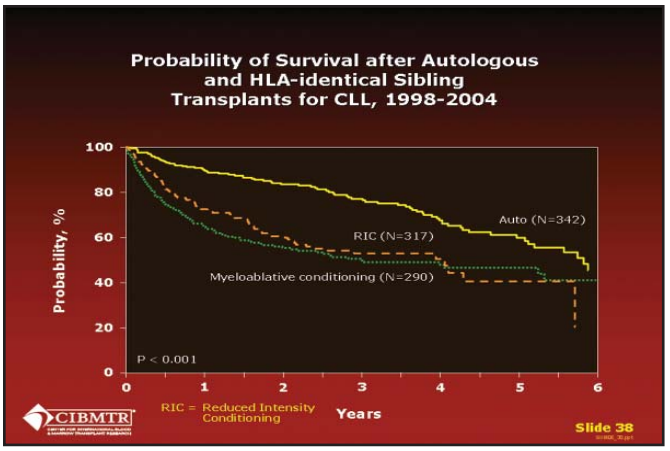
Slides 33 and 34: Among young patients with ALL, for whom conventional chemotherapy has a high success rate, allogeneic HCT is generally reserved for those with high risk disease (high leukocyte count at diagnosis, presence of poor risk cytogenetic markers), those failing to achieve remission or relapsing after chemotherapy. Among 1,654 patients < 20 years of age receiving HLA-identical sibling HCT, 3-year probabilities of survival were 60% ± 2.5%, 52% ± 2% and 29% ± 4% for patients with early, intermediate and advanced disease, respectively. Corresponding probabilities among 1,941 recipients of unrelated donor HCT were 48% ± 3%, 39% ± 1.5% and 17% ± 3%.





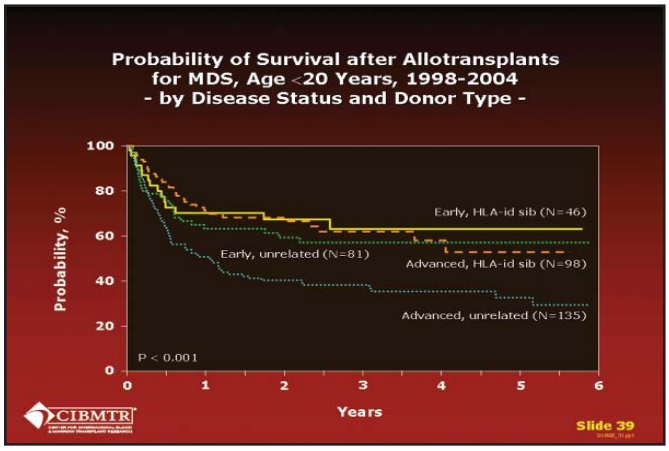
Slides 35 and 36: Older age at onset is itself a high risk feature in ALL. Consequently, a larger proportion of ALL patients older than 20 years undergo allogeneic HCT for early disease. Among 1,564 patients > 20 years of age receiving HLA-identical sibling HCT, 3-year probabilities of survival were 47% ± 2%, 34% ± 3% and 17% ± 2% for patients with early, intermediate and advanced disease, respectively. Corresponding probabilities among 1,291 recipients of unrelated donor HCT were 41% ± 2.5%, 29% ± 3% and 12% ± 2%.

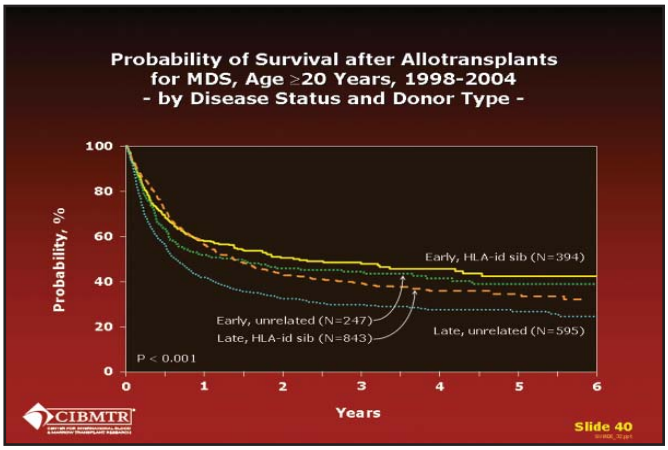




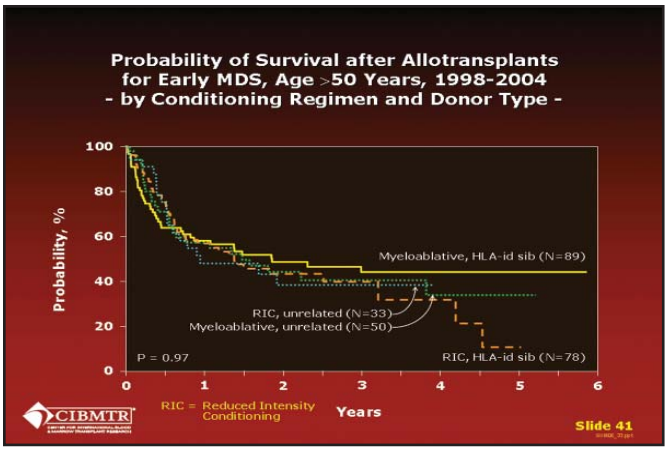
Slide 37: Autotransplants are done in few patients with ALL, most are in complete remission. Among 338 patients receiving autotransplants for ALL, 3-year probabilities of survival were 47% ± 5%, 44% ± 6% and 12% ± 6% for patients with early, intermediate and advanced disease, respectively.

Slide 38: Both autologous and allogeneic HCT are increasingly considered for patients with aggressive chronic lymphocytic leukemia (CLL) that fails standard chemotherapy. There has been an increase in use of reduced intensity conditioning for allografting, likely because of the older age of this population. Among 949 patients who underwent HCT for CLL, 3-year probabilities of survival were 77% ± 3% after autotransplants, 50% ± 3% after HLA-identical sibling HCT with myeloablative conditioning and 53% ± 4% after HLA-identical sibling HCT with reduced intensity conditioning.

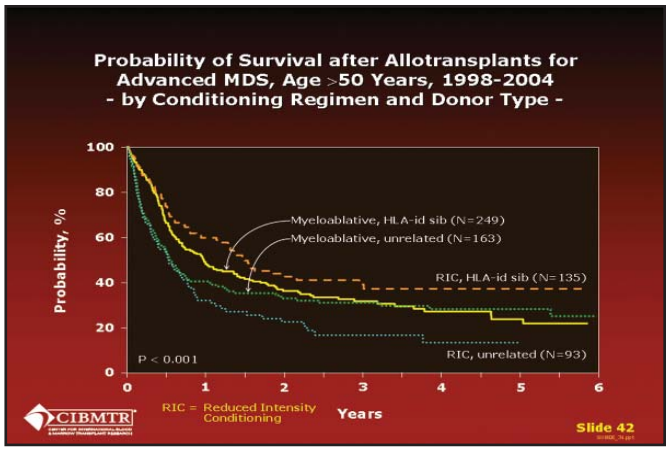




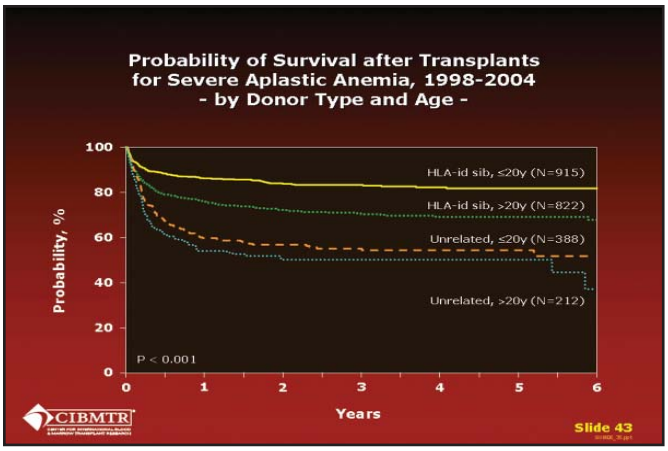
Slides 39 and 40: Allogeneic HCT can cure some patients with MDS. Outcomes differ according to recipient age, donor type and disease status at transplantation. Among 144 patients < 20 years of age, 3-year probabilities of survival were 63% ± 8% and 62% ± 6% for those with early and advanced MDS, respectively. Corresponding probabilities in 216 recipients of unrelated donor transplants were 57% ± 6% and 38% ± 4%. Among 1,237 patients > 20 years of age receiving HLA-identical sibling HCT for MDS, 3-year probabilities of survival were 47% ± 3% and 40% ± 2% for early and advanced MDS, respectively. Corresponding probabilities in 842 older patients receiving unrelated donor transplants were 44% ± 3% and 30% ± 2%.



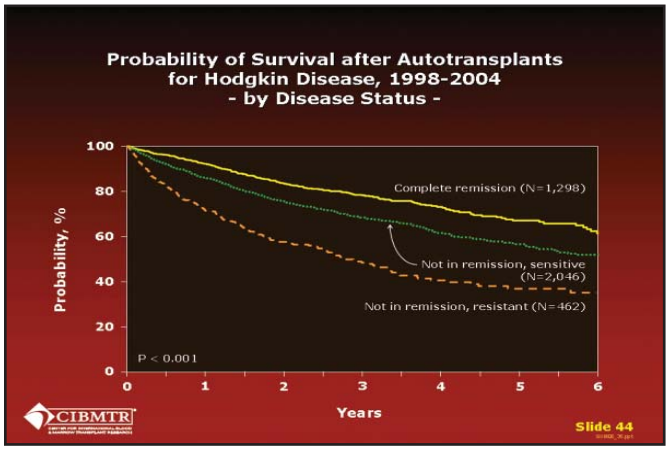
Slides 41 and 42: The median age of patients at diagnosis of MDS is 70 years, limiting the use of myeloablative conditioning regimens for most patients with this disease. Reduced intensity conditioning is used with the objective of establishing complete donor chimerism while minimizing regimen-related toxicity. Among 167 patients older than 50 years of age who received HLA-identical sibling HCT for early MDS, 3-year probabilities of survival were 44% ± 6% and 40% ± 7% with myeloablative and reduced intensity conditioning, respectively.



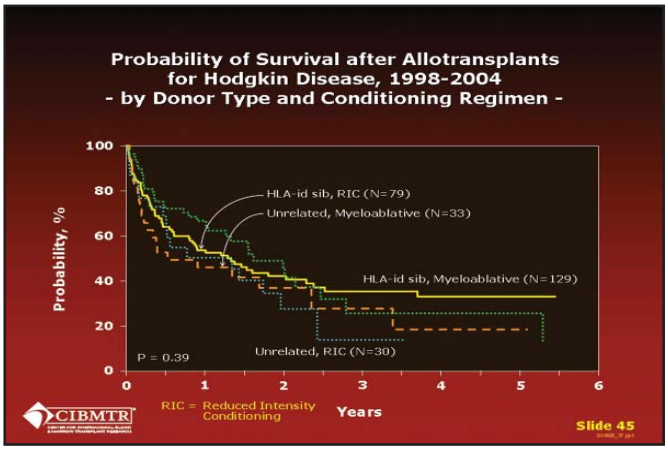
Corresponding probabilities in 83 patients receiving unrelated donor transplants for early MDS were 40% ± 8% and 38% ± 9%. Among 384 patients older than 50 years of age receiving HLA-identical sibling HCT for advanced MDS, 3-year probabilities of survival were 32% ± 3% and 39% ± 5% with myeloablative and reduced intensity conditioning, respectively. Corresponding probabilities for 256 recipients of unrelated donor transplants were 17% ± 4% and 31% ± 4%.



Slide 43: Allogeneic HCT is the treatment of choice for young patients with aplastic anemia with an HLA-identical sibling donor. Among 1,737 patients receiving HLA-identical sibling HCT for aplastic anemia, the 3-year probabilities of survival were 83% ± 1% and 70% ± 2% for those younger and older than 20 years of age, respectively. Among 600 recipients of unrelated donor transplants, the corresponding probabilities were 55% ± 3% and 50% ± 4%.

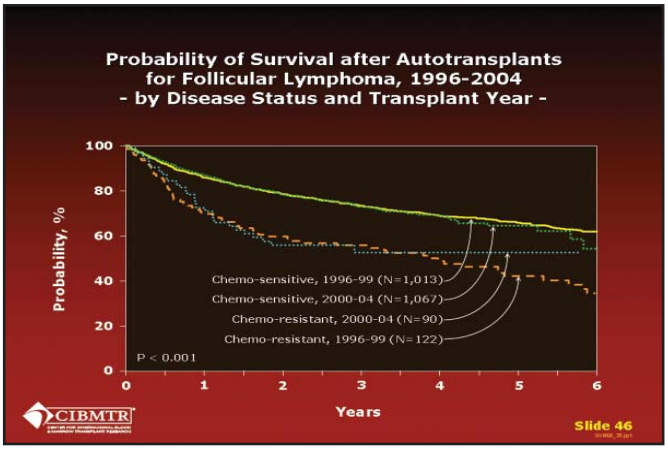


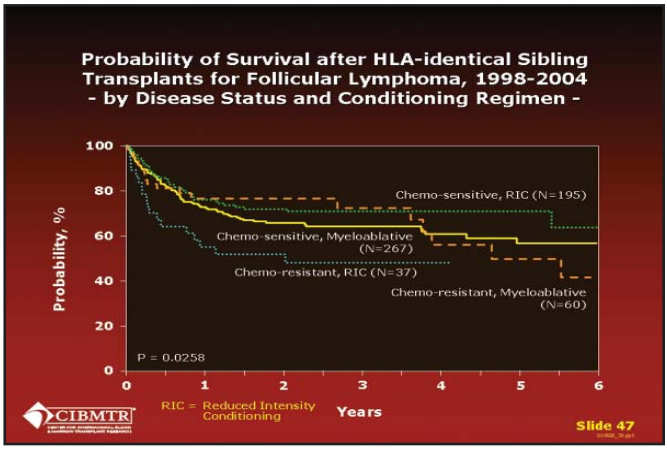
Slide 44: Most patients with Hodgkin Disease are cured with combination chemotherapy and/or radiation therapy. Transplantation is indicated in patients for whom initial therapy fails. Survival after HCT depends on disease response to previous salvage therapy. Among 3,806 patients receiving autotransplants for Hodgkin Disease, 3-year probabilities of survival were 78 ± 2%, 68% ± 1% and 57% ± 3% for patients in complete remission, with sensitive relapse or with resistant relapse, respectively.



Slide 45: Allogeneic HCT for Hodgkin Disease are generally performed in patients whose disease relapses after several lines of therapy or who have refractory disease and an available HLA-matched donor. Reduced intensity conditioning approaches offer graft-versus-lymphoma effects while minimizing regimen-related toxicity. This approach is often used in patients who relapse after autotransplantation. Among 208 patients receiving HLA-identical sibling HCT for Hodgkin Disease, 3-year probabilities of survival were 35% ± 5% and 26% ± 9% with myeloablative and reduced intensity conditioning, respectively. Few unrelated donor transplants have been done in this setting, making interpretation of these results difficult.

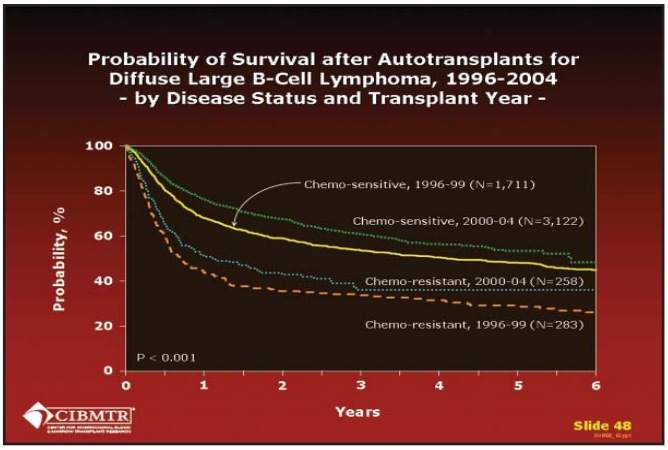
Slides 46 and 47: Similar to CLL and Hodgkin Disease, HCT in follicular lymphoma tends to be restricted to patients with aggressive or recurrent disease. Among 2,292 patients receiving autotransplants for follicular lymphoma between 1996 and 2004, 3-year probabilities of survival were 73% ± 1.5% and 52% ± 7% for chemo-sensitive and chemo-resistant disease, respectively. Allogeneic HCT is less

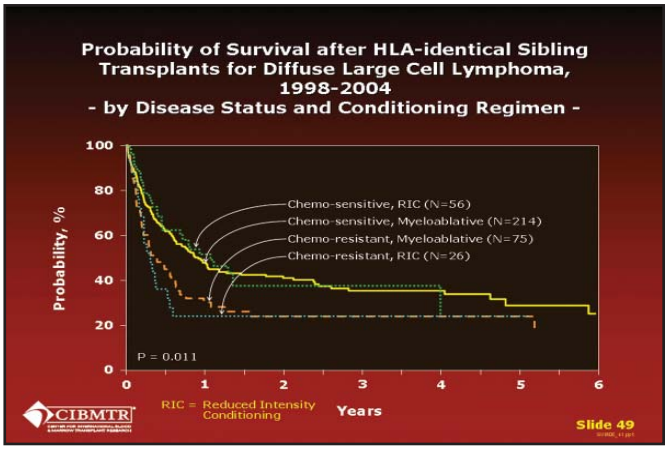




frequently done. Among 462 patients receiving HLA-identical sibling HCT for chemo-sensitive follicular lymphoma in 1998-2004, 3-year probabilities of survival were 64% ± 3% with myeloablative conditioning and 71% ± 4% with reduced intensity conditioning. Among 97 patients with chemo-resistant disease, the corresponding probabilities were 72% ± 7% and 52% ± 9%.

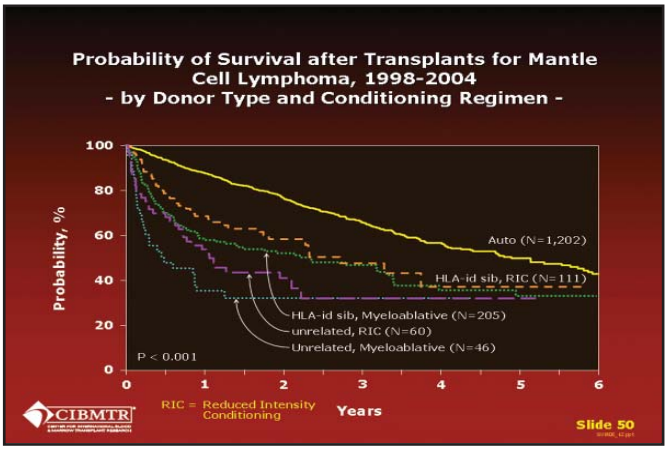
Slides 48 and 49: Autotransplants are an accepted therapy for high risk or relapsed diffuse large cell lymphoma. Outcomes have improved somewhat over time and are substantially better in patients with chemo-sensitive disease. Among 1,994 patients transplanted in 1996-1999, the 3-year probabilities of survival were 53% ± 1% and 34% ± 3% in patients with sensitive and resistant disease, respectively. Corresponding probabilities in 3,380 patients transplanted in 2000-2004 were 61% ± 1% and 36% ± 4%. Whether this is due to increasing use of rituximab or other changes in patient selection or treatment is unknown. Allogeneic HCT is much less frequently done for this disease. Among 371 patients receiving HLA-identical sibling HCT for diffuse large cell lymphoma in 1998-2004, the 3-year probabilities of survival were 35% ± 7% and 24% ± 8% for sensitive and resistant disease, respectively. Results were similar with myeloablative and reduced intensity conditioning.

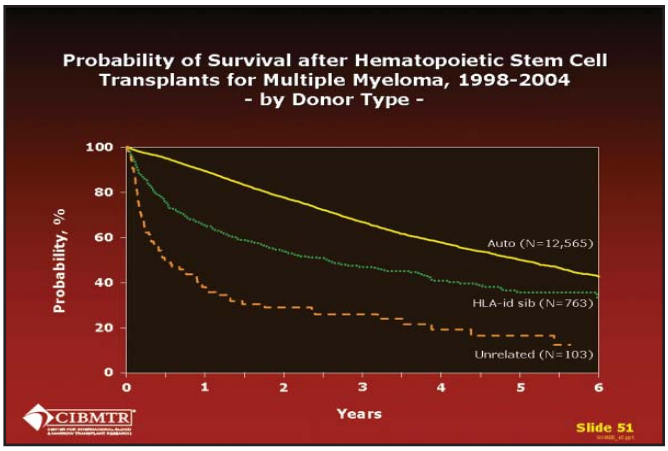




Slide 50: The optimal role of HCT in mantle cell lymphoma (MCL) and timing of transplant after initial chemotherapy are not well defined. Autologous HCT is the most common transplant approach. Among 1,202 patients who received autotransplants for MCL, the 3-year probability of survival was 65% ± 2%. Three-year probabilities of survival after 316 HLA-identical sibling and 106 unrelated donor transplants were 47% ± 4% and 32% ± 7%, respectively. Results were similar with myeloablative and reduced intensity conditioning.

Slide 51: Multiple myeloma is the most common indication for autologous HCT and there is increasing interest in using allogeneic HCT to offer a graft-versus-myeloma effect. Most allotransplants are done using reduced intensity conditioning. Among 13,431 patients receiving HCT for Myeloma, the 3-year probabilities of survival were 67% ±1% with autotransplantation, 47% ± 2% with HLA-identical sibling transplantation and 26%± 5% with unrelated donor transplantation.





CIBMTR — Milwaukee Data Solutions

By Mark Reitz

Although there are many impending data collection changes as we transition to the C.W. Bill Young Cell Transplantation Program, some basic processes still hold true. We will communicate any changes to the current processes, outlined below, as we strive to minimize the burden of data collection and assure that the most relevant data is collected. Please refer to the *"CIBMTR Awarded HRSA contract to administer the C.W. Bill Young Cell Transplantation Program Outcomes Database"* article in this newsletter and the *"AGNIS: Help for Data Management"* article in the May 2006 newsletter for more information on these new programs.

Importance of submitting the correct data for all Transplants (TX)

All patient transplants must be registered. This includes patients who start conditioning (even one dose) but die prior to infusion or choose not to receive the transplant. These registered patients must be assigned a unique, sequential ID (IUBMID), by your center. This system helps the CIBMTR make certain that there is no selective reporting of cases, and helps you make certain that you have not forgotten to register a patient. This is true for all BMT CTN, Research and Registering centers, although the processes for data submission are different and outlined below.

Research Centers
Must Pre-Register all TX's up to 2 weeks prior to start of high dose conditioning (including day 1 of conditioning) and no later than 28 days post TX using the CIBMTR Pre-Registration Form. This allows the rational selection of patients for comprehensive data reporting via the Report Form. Pre-Registration Form information is entered in a randomization algorithm that weighs cases based on the needs for current and future studies while ensuring adequate representation of all transplant types and indications. Rare disease cases or new therapies may ask for 100% of all registered cases to submit comprehensive data via the Report Form. Diseases that are more common are randomized for Report Form completion to insure a statistically significant representation.

All cases selected for the comprehensive Report Forms will be required to submit a Core, Graft and Disease insert at 100 days post TX and the yearly CoreFU and corresponding disease insert.

All cases NOT selected for the comprehensive Report Forms will be required to submit a MTED and yearly TEDFU.

CTN Research Centers
Even though CTN data is submitted to CIBMTR and EMMES, it is not a redundant data system. The CIBMTR collects slightly different data and at different time points than that collected in the EMMES electronic data entry system. These data are required by The National Heart, Lung, and Blood Institute (NHLBI) Data and Safety Monitoring Board (DSMB). The data is monitored regularly and compared for discrepancies.

Non-CTN patients: Must Pre-Register all TX's with a Pre-Registration Form under the same guidelines as the Research Center. Similarly, all non-CTN patients follow the same data submission guidelines as a Research center.

CTN enrolled patients: Must Pre-Register all TX's with a Pre-Registration Form which is crucial to analysis of CTN trials. However, the selection of patients for comprehensive data reporting via the Report Form is determined by CTN enrollment at EMMES, not by the CIBMTR randomization algorithm. A green CTN sticker placed on the Pre-Registration Form signifies a CTN patient.

All CTN enrolled patients will be required to submit the comprehensive Report Forms consisting of a completed Core, Graft and Disease insert at 100 days post TX and the yearly CoreFU and corresponding disease insert. Partially completed Report Forms (i..e. pre-TX info only) will not be accepted.

Registering Centers
Must register all TX's using the Transplant Essential Data Form (TED-01) at 100 days post transplant and yearly TEDFU to insure the CIBMTR database is representative of BMT population. Note that Registering Teams ***do not*** submit Pre-Registration Forms.

CTN Registering Centers
Non-CTN patients: Must register all TX's with a TED-01 form under the same guidelines as the Registering Center. Similarly, all non-CTN patients follow the same data submission guidelines as a Registering center.

CTN enrolled patients: Must Pre-Register all TX's with a Pre-Registration Form under the same guidelines as the CTN Research Center. Similarly, all CTN enrolled patients follow the same data submission guidelines as a CTN patient at a Research center.

Importance of using current versions of Forms and Electronic Data

Paper Forms
The most recent versions of all CIBMTR paper data collection forms can be found at http://cibmtr.org/DATA/data_idx.html. You are encouraged to look here frequently for updates to the forms, instructions on filling out the forms, answers to frequently asked questions and a link to a Web site devoted to issues faced by data managers in collecting and reporting data to the CIBMTR.

For example, there is one important data field that will require the most recent version of the pre-registration form to be used immediately. Usage of Kepivance (palifermin or KGF, keratinocyte growth factor) is increasing, and CIBMTR needs to capture its usage data to facilitate a new long term study of patient outcomes.

As of August 14, 2006, we no longer accept Pre-Registration Forms without KGF data. Incomplete Forms will be returned for clarification. All recipients who receive or plan to receive KGF will be selected for the comprehensive research data Report Form.

TED on the Web
Can be found at the link above and is useful for electronically submitting Pre-registration, MTED, TED and TEDFU forms. One benefit of using this tool is that you can be assured that the latest version of the "forms" are available.

StemSoft Data:
StemSoft has released a patch to incorporate the KGF question and other updates. The latest version is 3.2.4. Please consider updating to the most recent version of StemSoft (or any other future electronic reporting tool) especially with the upcoming release of harmonized NMDP and CIBMTR data collection forms.

Foundation and corporate support of the CIBMTR

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