PROGRESS REPORT
JANUARY – DECEMBER
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1.0 INTRODUCTION TO THE CIBMTR

The Center for International Blood and Marrow Transplant Research (CIBMTR) collaborates with the worldwide scientific community to advance hematopoietic cell transplantation (HCT) and cellular therapy research. As a combined research program of the Medical College of Wisconsin (MCW) and the National Marrow Donor Program (NMDP), the CIBMTR facilitates important clinical research to increase survival and enrich the quality of life for thousands of HCT patients. HCT is used primarily to treat disorders of hematologic malignancies including lymphoma, leukemia, myeloma, etc.

CIBMTR research arises from a base of collaborative scientific and statistical expertise, a large network of transplant centers, and a clinical database of more than 300,000 transplant recipients. Information from the database, and the support provided by the CIBMTR Statistical Center to analyze it, have led to successful completion of hundreds of studies that have had significant impact on clinical practice. This Progress Report focuses on CIBMTR’s research activities from January 1 through December 31, 2009.

1.1 BACKGROUND

The CIBMTR was formed in July 2004, when the International Bone Marrow Transplant Registry (IBMTR) of MCW and the research division of NMDP affiliated to create a combined research program.

IBMTR was a voluntary association of more than 400 transplant centers in almost 50 countries. These centers had shared patient outcomes data to facilitate HCT research since 1972. NMDP had been established in 1987 to create a registry of unrelated donors for patients in need of a transplant. Its research division performed analyses aimed at improving the outcomes of these transplants. NMDP had also established a research repository of unrelated donor-recipient (paired) biologic samples for a large subset of these transplants.

The CIBMTR affiliation capitalized on the resources and expertise amassed by these two organizations to create an enhanced research resource for the HCT community. CIBMTR is now in its sixth year, and continues to grow (see list of centers in Appendix A) and improve its systems and effectiveness. Personnel on its two campuses share a commitment to the highest level of transplant-related clinical research with a mission of increasing access to transplantation and improving outcomes of these complex and highly specialized procedures.

The Stem Cell Therapeutic and Research Act of 2005 (Public Law 109-129) established the C.W. Bill Young Cell Transplantation Program (the Program). The Program was designed to make information about HCT available to patients, families, health care professionals and the public; to provide better processes for identifying unrelated matched marrow and peripheral blood stem cell donors and cord blood units through one electronic system; to increase the numbers of unrelated adult volunteer marrow donors and cord blood units that are available; and to expand research to improve patient outcomes. Included in the Program is a Stem Cell Therapeutic Outcomes Database (SCTOD), which collects, analyzes and reports on outcomes for all allogeneic transplants and on other therapeutic uses of blood stem cells. The CIBMTR, through MCW, was awarded a contract with the Health Resources and Services Administration (HRSA) to administer the SCTOD for the Program.

A significant change brought about by the SCTOD program was mandatory reporting requirements of HCT outcomes for U.S. transplant centers, as well as centers elsewhere that use U.S. stem cell products for transplants. CIBMTR’s Information Technology group expanded and enhanced its mechanisms to meet the requirements of the Program.
These requirements include:

- **Collecting data**
  - ALL allogeneic hematopoietic cell transplants (HCTs) with a recipient or donor from the U.S.
  - Secure, efficient electronic data capture system
  - Related donor-recipient repository
  - Quality of life data
  - Other cellular therapies

- **Analyzing data**
  - Center-specific outcomes for U.S. transplant centers
  - Analyses of optimal size for the adult donor registry and cord blood unit inventory
  - Other research using the data collected under the contract

- **Disseminating data**
  - Within the Program
  - To the scientific and medical community
  - To patients, families and the public

As a footnote to this timeline, CIBMTR celebrated its five-year anniversary in July 2009. Several cross-campus celebration activities took place to commemorate the event.

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* In collaboration with NMDP Office of Patient Advocacy (OPA)

** The BMT CTN Data and Coordinating Center is a collaboration of CIBMTR, NMDP and the EMMES Corporation. The BMT CTN Progress Report is available at: https://web.emmes.com/study/bmt2/

--- Advisory Role
1.2 ORGANIZATIONAL STRUCTURE

CIBMTR is organized as shown in Figure 1. An Affiliation Board provides executive oversight on behalf of the two parent institutions. The Chief Scientific Director has primary responsibility for administrative and scientific operations. The CIBMTR Chief Statistical Director is responsible for the statistical quality of all studies. Scientific, Executive, Advisory and Oversight Committees provide policy and scientific oversight.

CIBMTR has four major areas of research activity:
- Observational Research
  - Clinical Outcomes
  - Health Services Research (HSR)
- Statistical Methodology
- Immunobiology
- Clinical Trials Support
  - Blood and Marrow Transplant Clinical Trials Network (BMT CTN)
  - Resource for Clinical Investigations in Blood and Marrow Transplant (RCI BMT)

One of CIBMTR’s major accomplishments in 2009 was establishing the HSR program as a branch of its Observational Research Program (Section 2.1). The objectives of the HSR Program are to improve access to HCT, improve HCT outcomes, and enhance the quality of life for patients undergoing a transplant.

1.3 COMMITTEE STRUCTURES

1.3.1 Scientific Working Committees

Observational research using CIBMTR’s large database is the organization’s core activity. Most scientific questions undertaken by CIBMTR’s 19 scientific Working Committees cannot be answered using data from single transplant centers or cannot be addressed adequately in randomized clinical trials.

The CIBMTR committee structure was designed to ensure that CIBMTR resources are meeting the needs and addressing the priorities of the scientific and medical community CIBMTR serves. This structure also ensures that CIBMTR receives broad input from members of the HCT community in designing and carrying out its research. The Working Committees are comprised primarily of HCT clinicians and scientists. Educational sessions are held during the BMT Tandem Meetings (Section 7.3) to orient newly-appointed Working Committee Co-chairs, and to educate investigators, particularly junior level ones, wishing to propose studies to CIBMTR.

A unique strength of the Working Committees is the statistical faculty who support them and provide expertise in HCT survival analysis. This ensures a rigorous methodological approach to all CIBMTR projects. Following is a list of the committees and their areas of focus:

- **Acute Leukemia**: HCT for acute leukemias, preleukemia and myelodysplastic disorders;
- **Autoimmune Diseases**: HCT for autoimmune disorders including autoimmune cytopenias;
- **Cellular Therapies**: non-transplant uses of hematopoietic stem cells;
- **Chronic Leukemia**: HCT for chronic leukemias and myeloproliferative disorders;
- **Donor Health and Safety**: safety issues and outcomes for hematopoietic stem cell donors;
- **Graft Sources and Manipulation**: comparative effectiveness of various graft types and graft manipulation techniques;
- **Graft-versus-Host Disease (GVHD)**: biology, prevention and treatment of GVHD (the most common complication following HCT) and its complications;
- **Health Policy and Psychosocial Issues**: access to HCT including social and economic barriers to care, and the influence of psychosocial factors on transplant outcomes;
- **Immune Deficiencies and Inborn Errors of Metabolism**: HCT for congenital and acquired immune deficiencies, and inborn errors of metabolism;
- **Immunobiology**: histocompatibility and other genetic and immunologic issues related to HCT;
- **Infection and Immune Reconstitution**: prevention and treatment of post-transplant infections and issues related to recovery of immune function;
- **International Studies**: studies of regional issues and differences, international cooperation; focus is on non-U.S. investigators;
• **Late Effects and Quality of Life:** issues related to long-term survivors of HCT, including the clinical and psychosocial effects of transplantation;
• **Lymphoma:** HCT for Hodgkin and non-Hodgkin lymphoma;
• **Non-Malignant Marrow Disorders:** HCT for aplastic anemia, congenital disorders of hematopoiesis and other non-malignant hematopoietic disorders;
• **Pediatric Cancer:** HCT for childhood leukemias and other issues related to use of HCT in children;
• **Plasma Cell Disorders:** HCT for multiple myeloma and other plasma cell disorders;
• **Regimen-Related Toxicity and Supportive Care:** preparative regimens, prevention and treatment of early non-GVHD toxicities, and supportive care in the early post-transplant period;
• **Solid Tumors:** the use of HCT for treatment of solid tumors.

1.3.2 **Assembly**
The CIBMTR Assembly is its voting membership. It is comprised of a single representative from each CIBMTR center that submits Comprehensive Report Form (CRF) data (Section 3).

1.3.3 **Advisory Committee**
Advisory Committee members (listed in Appendix D1) are elected by the CIBMTR Assembly. The CIBMTR Advisory Committee also includes appointed members representing donor centers (1), collection centers (1), patients (2), and individuals with expertise in business (1) and ethics (1), as well as representatives from NCI, NHLBI, NIAID and HRSA. Twelve at-large members also serve on the Advisory Committee, made up of six members from North American and six non North American members.

The CIBMTR Advisory Committee meets biannually, usually in November in conjunction with the NMDP Council Meetings and again in February during the BMT Tandem Meetings, to review scientific and other activities of the CIBMTR.

CIBMTR’s December 2009 elections filled vacancies on the Advisory, Nominating and Clinical Trials Advisory Committees for terms expiring February 28, 2010. Results of those elections can be found in the appendices. As of March 1, 2010, all of these terms will run for three years.

Educational sessions are held annually during the BMT Tandem Meetings (Section 7.3) to orient newly-elected Advisory Committee members.

1.3.4 **Executive Committee**
The CIBMTR Executive Committee (Appendix D1) is a subcommittee of the Advisory Committee that provides ongoing advice and counsel to the CIBMTR Statistical Center between meetings of the Advisory Committee. It includes the Advisory Committee Chair, the Chair-elect or Immediate Past Chair, four Vice-chairs (each representing a geographic region), appointed and ex officio members of the Advisory Committee. The Executive Committee is responsible for ensuring that the organization carries out its mission and adheres to the policies and procedures of CIBMTR. For instance in 2009, the Executive Committee clarified the rules of authorship for CIBMTR manuscripts to be submitted to journals, and asked that CIBMTR staff amend the Manual of Operations accordingly.

The Executive Committee meets four times annually by teleconference or in person. In this capacity it:

• Provides direction to the Chief Scientific Director and Statistical Center for scientific activities and policy decisions. For example in 2009, the Executive Committee recommended that the CIBMTR choose an individual who has made substantial contributions to HCT research to be honored at the 2010 BMT Tandem Meeting.
• Finalizes priorities for scientific studies after receiving input from the Working Committees;
• Reviews results of audits and recommends measures to correct deficiencies. In addition, in 2009, the Executive Committee helped plan the CIBMTR internal process review and external scientific review.
• Appoints a CIBMTR Program Chair and Organizing Committee for the Annual Meeting.

1.3.5 **Nominating Committee**
The Nominating Committee (Appendix D2) is comprised of five members elected by the CIBMTR Assembly. The Chair of the Nominating Committee
serves on the Advisory Committee. This committee meets annually in fall to prepare a slate of candidates for open positions on the Advisory, Nominating and Clinical Trials Advisory Committees. It also recommends nominees to the Advisory Committee for open Working Committee Chair appointments. The Nominating Committee seeks input from the CIBMTR Assembly, Advisory Committee and incumbent Working Committee Chairs to prepare a slate of candidates for election and of Working Committee Chair nominees for appointment.

The call for nominations was extended to the membership in September for positions with terms beginning on March 1, 2010. Once nominations were received, the Nominating Committee underwent deliberations and put forth a slate of candidates. Elections were held by confidential electronic ballot. The latest election results are listed in Appendix D1.

1.3.6 Oversight Committees
Two additional committees provide oversight for use of certain resources: the NMDP Histocompatibility Advisory Group, and the Clinical Trials Advisory Committee.

The NMDP Histocompatibility Advisory Group (Appendix E) reviews and approves the use of donor-recipient biologic specimens from the NMDP Repository for CIBMTR studies approved by the relevant Working Committee. These studies link outcomes data with biologic and genetic factors derived from analyses of these materials.

Members provide expertise in the following areas:
- Adult transplantation/HLA and matching
- Pediatric transplantation/HLA and matching
- Histocompatibility
- Immunogenetics
- International unrelated donor registries
- Biostatistics

Liaisons from CIBMTR, NMDP, the American Society for Histocompatibility and Immunogenetics (ASHI), NMDP Cord Blood Advisory Group, HRSA and the C.W. Bill Young Cell Transplantation Program provide additional input to the committee.

The Clinical Trials Advisory Committee (CTAC) (Appendix F) was created to serve as an independent advisory body for CIBMTR RCI BMT activities. The primary function of the CTAC is to review and provide recommendations regarding submitted proposals relative to scientific merit, feasibility, and alignment with CIBMTR’s scientific agenda, as well as to review the progress of ongoing studies.

1.3.7 Consumer Advocacy Committee (CAC)
The Consumer Advocacy Committee was created as a subcommittee of the Advisory Committee (Appendix G) to help provide patient and donor perspectives as the CIBMTR research agenda is developed, and to help communicate important information from CIBMTR studies to the non-medical community. The nine members meet in person annually at the BMT Tandem Meetings (Section 7.3) and by periodic conference calls. The CAC Co-chairs serve on the Advisory and Executive Committees. Members also serve on several of the Working Committees.

The Consumer Advocacy Committee’s primary task is to develop materials that describe the results of selected CIBMTR research projects in terms understandable to the lay public. In 2009, CAC members also helped with a pilot project to develop materials to share results of BMT CTN Study #0302 (Initial systemic treatment of acute GVHD: a phase II randomized trial evaluating etanercept, mycophenolate mofetil, denileukin diftitox, and pentostatin) with participants, by reviewing the documents from a lay perspective. Also in 2009, CAC members helped review several American Recovery and Reinvestment Act of 2009 (ARRA) grant applications that were submitted by CIBMTR.
1.4 CIBMTR PERSONNEL

1.4.1 CIBMTR Statistical Center
CIBMTR Statistical Center personnel work from both campuses (Milwaukee and Minneapolis) to provide statistical and administrative support for CIBMTR studies. The Statistical Center staff includes more than 135 people, with five new positions being added at the Milwaukee campus and a Clinical Research Coordinator position added in Minneapolis in 2009. (See Appendix B for current personnel listing.)

The statistical staff is led by John P. Klein, PhD, who is Chief of the Division of Biostatistics at MCW and Chief Statistical Director for CIBMTR. Dr. Klein is an internationally recognized expert in survival analysis. Also on the Milwaukee campus, Mei-Jie Zhang, PhD, has worked with the Statistical Center since 1991. He provides expertise in Cox regression analyses and other multivariate techniques and expertise in analysis of HCT transplant data that involve censored or truncated time-to-event data. Brent Logan, PhD, joined the Statistical Center in July 2001; he brought expertise in clinical trial design and analysis of multiple endpoints and serves as primary statistician for many BMT CTN protocols. He led the development of the statistical approach for NMDP’s current center-specific analysis (now the purview of the CIBMTR). Tao Wang, PhD, joined the Statistical Center in January 2002. He has special expertise in statistical genetics and helps analyze immunogenetic data.

Ruta Bajorunaite, PhD, joined the Biostatistics Division as Assistant Professor in June 2008, after holding a position as Assistant Adjunct Professor with this group since July 2004. Dr. Bajorunaite serves as biostatistician for the Late Effects and Quality of Life Working Committee. Kwang Woo Ahn, PhD, joined the Biostatistics staff in 2008, and serves CIBMTR on the Autoimmune Diseases, Chronic Leukemia, and Infection and Immune Reconstitution Working Committees. Jennifer Le-Rademacher, PhD, joined in January 2009, and serves the Immune Deficiencies/Inborn Errors and Non-malignant Marrow Disorders Working Committees and the BMT CTN.

Nine Master’s-level biostatisticians contribute to CIBMTR research activities on the Milwaukee campus: Kathleen Sobocinski, MS (Associate Statistical Director, has worked with the Statistical Center since 1973), Waleska Perez, MPH (Assistant Statistical Director, 1998), Jeanette Carreras, MPH (2003), Manza Agovin-Johnson, MPH (2006), Vincent He, PhD, MS (2006), Zhiwei Wang, MS (2007), Min Chen, MS (2008), Peigang Li, MS (2009) and Xiaochen Zhu, MS (2009). The following Biostatisticians serve the CIBMTR Statistical Center from the Minneapolis campus: Gene Nelson, BS (since 1997), Michael Haagenson, MS (since 2000), Tanya Pedersen (2004), Pintip Chitphakdithai, PhD (2004), Fiona Kan, MS, MA (2006), and Anna Hassebroek, MPH (2006).

1.4.2 Milwaukee campus Scientific Directors
The CIBMTR Milwaukee campus is an academic division of the Department of Medicine of MCW. The Department of Medicine and MCW provide administrative support for the Milwaukee campus for grants and account management, personnel issues and development activities.

Milwaukee campus physician staff members include CIBMTR Chief Scientific Director Mary M. Horowitz, MD, MS, two Associate Scientific Directors (J. Douglas Rizzo, MD, MS, and Mary Eapen, MD, MS) and three Assistant Scientific Directors (Parameswaran Hari, MD, MS, Marcello Pasquini, MD, MS, and Wael Saber, MD, MS), who provide scientific leadership for CIBMTR activities.

Mary M. Horowitz, MD, MS, is Chief Scientific Director of CIBMTR, as well as the Robert A. Uihlein Professor of Hematologic Research at MCW and an attending physician in the MCW adult HCT program. In addition to the MD degree she earned in 1980, Dr. Horowitz earned an MS in Biostatistics from MCW in 1991. In June 2006, she received MCW’s Distinguished Service Award, the college’s highest honor. Dr. Horowitz serves as Principal Investigator (PI) for the Data and Coordinating Center of the BMT CTN (Section 2.4), and is Research Director for the SCTOD program (Section 1.5). She has been with the organization since 1985.
J. Douglas Rizzo, MD, MS, is Professor of Medicine, Neoplastic Diseases and Related Disorders, as well as an attending physician in the MCW adult HCT program. Dr. Rizzo completed a Robert Wood Johnson fellowship in epidemiology and cost-effectiveness research at Johns Hopkins University in 1998. He received an MS degree in epidemiology from MCW in 2005. In addition to his responsibilities as Associate Scientific Director for CIBMTR, Dr. Rizzo became Project Director for the SCTOD in 2008, and has overall responsibility for successful execution of data operations related to that program. He oversees many operational aspects of the CIBMTR Statistical Center.

Mary Eapen, MD, MS, is a pediatric hematologist/oncologist who received her clinical training and an MS in Clinical Research at the University of Minnesota. In addition to serving as an attending physician in the MCW pediatric HCT program, she provides medical oversight and biostatistical support to the CIBMTR Pediatric Cancer, Non-malignant Marrow Disorders, Immune Deficiencies/Inborn Errors of Metabolism, and Graft Sources Working Committees. In 2009 she was the recipient of a Career Development Program – Scholar in Clinical Research award from the Leukemia & Lymphoma Society. She also serves as a Protocol Officer and Medical Monitor for the BMT CTN.

Parameswaran Hari, MD, MS, completed a hematology/oncology fellowship at MCW after serving as a Specialist Registrar in Haematology at Leicester University Teaching Hospitals in the UK. He is Board Certified in Medical Oncology, Clinical and Laboratory Haematology and Internal Medicine, and holds an MS degree in biostatistics from MCW. He was promoted to the rank of Associate Professor in 2009, and is now Clinical Director of the MCW HCT Program. He also serves as Scientific Director of the CIBMTR Lymphoma, and Plasma Cell Disorders Working Committees.

Marcelo Pasquini, MD, MS, completed a hematology/oncology fellowship at the University of Utah, and a one-year fellowship in HCT at MCW. He received an MS degree in epidemiology from MCW in 2006. Dr. Pasquini has been an Assistant Professor at MCW since July 2005, and is Scientific Director of the CIBMTR Autoimmune, International Studies, and Cellular Therapies Working Committees. In January 2009, he also assumed the role of Scientific Director for the Regimen-Related Toxicity/Supportive Care Working Committee. Dr. Pasquini serves as a Protocol Officer and Medical Monitor for the BMT CTN, and is an attending physician in the MCW adult HCT program.

Wael Saber, MD, MS, joined CIBMTR in 2009. He is Assistant Professor of Neoplastic Diseases/Hematology at MCW and an attending physician in the MCW adult HCT program. Dr. Saber completed a hematology fellowship at the University of Wisconsin from 2006-2009, with special training in epidemiology. He is board certified in Internal Medicine and Hematology, and his primary interests are acute leukemia and stem cell transplantation.

1.4.3 Minneapolis campus Scientific Directors
The CIBMTR Minneapolis campus is a department of the NMDP, which provides administrative and personnel support for CIBMTR activities. Several other NMDP departments, either under subcontract or through shared services, provide substantial support for CIBMTR activities, including the Finance, Bioinformatics, and Marketing and Communications departments.

Minneapolis campus physician staff members include Associate Scientific Director Dennis Confer, MD, Senior Research Advisor Daniel Weisdorf, MD, and three Assistant Scientific Directors: Mukta Arora, MD, MS; Navneet Majhail, MD, MS; and Willis Navarro, MD, MS; in addition to Senior Manager of Scientific Services, Stephen Spellman, MBS.

Dennis Confer, MD, has been Chief Medical Officer of NMDP since 1999, and an Associate Scientific Director of CIBMTR since 2004. Dr. Confer is Co-PI of the Data and Coordinating Center of the BMT CTN and serves as Scientific Director for the CIBMTR Donor Health and Safety Working Committee. He was PI for the development of CIBMTR’s A Growable Network Information System® (AGNIS®, 2006), which is improving and standardizing clinical data exchange to speed delivery of research results worldwide. He represents CIBMTR within the Worldwide Network for Blood and Marrow Transplantation (WBMT).
Daniel Weisdorf, MD, is Professor of Medicine and Director of the Adult Blood and Marrow Transplant Program at the University of Minnesota. He serves as Senior Research Advisor to CIBMTR and Scientific Director of the CIBMTR Acute Leukemia Working Committee. Dr. Weisdorf has been associated with NMDP since 2002, previously chaired the IBMTR Acute Leukemia Working Committee, and served as a member of the IBMTR Executive Committee. He is currently President-Elect of the ASBMT (American Society for Blood and Marrow Transplantation).

Mukta Arora, MD, MS, is an Assistant Professor in the Division of Hematology, Oncology and Transplantation at the University of Minnesota. She completed an MS degree in clinical research from the University of Minnesota in 2000, and fellowship training in Hematology, Oncology and Transplantation in 2002. Dr. Arora serves as Scientific Director of the CIBMTR Chronic Leukemia, GVHD and Solid Tumors Working Committees.

Navneet Majhail, MBBS, MD, MS, is Assistant Professor in the Division of Hematology, Oncology and Transplantation at the University of Minnesota. He received an MS degree in Clinical Research from the University of Minnesota in 2006. He leads the Adult BMT Late Effects Program at the University of Minnesota. In 2009, he took on leadership of the CIBMTR Health Services Research initiative. Dr. Majhail is an Assistant Scientific Director for the CIBMTR Health Policy and Psychosocial Issues, and Late Effects and Quality of Life Working Committees.

Willis Navarro, MD, serves as Medical Director of Search and Transplant Services at NMDP, and as of July 2009, moved into the role of Scientific Director of the RCI BMT (Section 2.4) upon the departure of Marcie Tomblyn. Dr. Navarro also serves as Associate Clinical Professor of Medicine, Adult Leukemia and Bone Marrow Transplant Program at the University of California, San Francisco. Prior to coming to NMDP, Dr. Navarro was Assistant Medical Director of Development, BioOncology, at Genentech, Inc., from 2005-2008.

Stephen Spellman, MBS, is Senior Manager of NMDP Scientific Services, which includes the biological sample repository. He also serves as Co-Scientific Director for the CIBMTR GVHD and Immunobiology Working Committees. He earned his MBS degree in 2000 from the University of Minnesota in Immunobiology and Molecular Biology.

1.4.4 CIBMTR Scientific Directors at other locations

Stephanie J. Lee, MD, MPH, is Associate Professor of Hematology at Fred Hutchinson Cancer Research Center in Seattle, Washington, and serves as Scientific Director of the CIBMTR Immunobiology Working Committee. Dr. Lee completed a fellowship at Brigham Women’s Hospital in Hematology/Oncology in 1996, and received her MPH from Harvard School of Public Health in 1996. She holds a grant from the National Institute of Allergy and Infectious Diseases studying Immune Mediated Disorders after Allogeneic HCT.

Marcie Tomblyn, MD, MS, is Director of BMT Clinical Research at Moffitt Cancer Center, Florida. Dr. Tomblyn continues to serve as Scientific Director of the CIBMTR Infection and Immune Reconstitution Working Committee. She completed a hematology/oncology fellowship at Northwestern University in 2003, followed by a fellowship in HCT at Northwestern. She received her MS degree in Clinical Investigation from Northwestern University in 2004.

1.4.5 Other Key Staff

CIBMTR Milwaukee

Janet Brunner joined the CIBMTR staff in September 2009, as Program Manager/Data Operations. She brought a breadth of experience to CIBMTR, having worked for more than 20 years as a Physician’s Assistant doing transplant patient care, donor evaluations and harvests, coordinating a university-based HCT program and serving as NMDP liaison to search and identify unrelated donors. She oversees a staff of Clinical Research Coordinators (CRCs) and other data management and analysis staff who review and analyze data; develops training programs; monitors transplant center performance; and works with the Database Administrator to develop electronic data submission systems that ensure compliance with submission schedules and data quality standards.
Huoy-Jii Khoo became Director of the Milwaukee-based Information Technology staff in 2008, after serving in several related positions at MCW over the previous ten years. His accomplishments include helping CIBMTR develop and migrate to an independent, segmented network to meet the security requirements of the HRSA SCTOD contract. He heads a Milwaukee IT staff of nine, as well as several on-site staff consultants. This staff has grown substantially in the past two years and now includes programmers, analysts, and information services technicians.

Sue Lorenz has been Business Manager of CIBMTR for three years and an MCW employee for 19. She is responsible for overseeing the program’s financial, personnel and office practices to ensure compliance with institutional and Federal policies and procedures.

Paula Watry, Associate Director-General Operations, joined CIBMTR in 2004 after 10 years of clinical experience as a Physician’s Assistant in the MCW HCT program. She provides high-level administrative oversight for several CIBMTR projects and initiatives. Reporting to her are two Program Coordinators (Carol Doleysh, SCTOD; Sarah Mull, BMT CTN), a Program Manager (Patricia Steinert, Kepivance Long-term Follow-Up Project) and a Medical/Scientific Writer (Beverly Ventura).

CIBMTR Minneapolis

Program oversight is provided by Roberta King, MPH, Vice President of CIBMTR-Minneapolis, who has worked with NMDP since 1990, and served in the research area since 1993. Her role includes oversight of the human subjects protection program, collaborating in developing policies governing data collection and quality, overseeing data collection, monitoring center performance for submission and accuracy of data, and overseeing the on-site data audit program. She also serves as Staff Liaison to the NMDP Donor and Patient Safety Monitoring Committee.

Marie Matlack, BS, who serves as Senior Manager of Data Management for the CIBMTR Minneapolis campus, has been with NMDP since 1990. She is responsible for ensuring that the CRCs, Senior Research Programmer, and the Data Entry and Imaging Staff who enter, retrieve, review and analyze data adhere to established standard operating procedures and perform effectively. Ms. Matlack oversees form revisions and new form development, the Continuous Process Improvement (CPI) program that ensures compliance with submission schedules and data quality standards, and works with bioinformatics staff on enhancements to the FormsNet™2 application.

Debra Christianson, BA, is Senior Manager of Auditing and Monitoring for CIBMTR Minneapolis. Her group is responsible for monitoring clinical trials and auditing the FormsNet2 clinical database. They also are responsible for writing the FormsNet2 instruction manual. In addition to her BA, Ms. Christianson also holds Associate and Applied Science degrees as well as certification as a Registered Health Information Technician through the American Health Information Management Association.

Rebecca Drexler, BS, AAS, serves as Senior Manager of Prospective Research on the Minneapolis campus. She has more than 20 years of experience in medical research and product development; seven of which were in clinical and regulatory affairs. Ms. Drexler joined the research department at NMDP in 2001 managing clinical trials, and joined the CIBMTR Minneapolis team in 2004. She contributed to the development of the RCI BMT and continues to manage this program.

Since receipt of the SCTOD contract, CIBMTR has subcontracted with NMDP for IT and bioinformatics services and support. Martin Maiers holds a key role in developing, launching and maintaining the FormsNet2 electronic data collection system for CIBMTR. He is Director of Bioinformatics at NMDP, where he has been employed for 14 years. He holds an MS degree in Computer Science from the University of Minnesota. He currently serves as vice-chair of the World Marrow Donor Association (WMDA) Information Technology Working Group that develops international informatics standards for cellular therapy.
1.5 FUNDING SOURCES

Federal grants and contracts provide 90 percent of the funding for CIBMTR. The remainder comes from MCW institutional support, NMDP support, corporate memberships, donations, corporate sponsored studies, endowment income and BMT Tandem Meeting revenue.

The major funding source for CIBMTR’s observational research program is a cooperative agreement funded by the National Cancer Institute (NCI), the National Heart, Lung and Blood Institute (NHLBI), and the National Institute of Allergy and Infectious Diseases (NIAID), for database development and to provide statistical support to database users.

Support for Data and Coordinating Center (DCC) administration of the BMT CTN (Section 2.4) comes from an NHLBI grant. Support for the SCTOD (Section 1.6) comes from a Health Resources and Services Administration (HRSA) grant.

Whether directly supported by a particular grant or not, each of the four major CIBMTR programs strengthens the work of the others. For example, because CIBMTR subcontracts for some SCTOD services with NMDP; the overlap resulted in a restructuring of the CIBMTR Statistical Center and significant increases in efficiency (Appendix B).

1.6 C.W. BILL YOUNG CELL TRANSPLANTATION PROGRAM

The Stem Cell Therapeutic and Research Act of 2005 required the Department of Health and Human Services (HHS) to establish and maintain the C.W. Bill Young Cell Transplantation Program (the Program).

As described in Section 1.1, the Program was designed to make information about HCT more readily available, provide better processes for identifying unrelated donors through one electronic system, increase the numbers of unrelated marrow donors and cord blood units available, and expand research to improve patient outcomes.

The Stem Cell Therapeutic Outcomes Database (SCTOD) is one feature of the Program. The function of the SCTOD is to collect data on all allogeneic (related and unrelated) HCTs performed in the U.S. and all HCTs done with products procured through the Program but performed outside the U.S. HRSA awarded a contract on September 27, 2006, to CIBMTR to administer the SCTOD for the Program.

Prior to the contract award, CIBMTR already had the expertise for collecting, managing and analyzing data from transplant centers. Following an expansion of this infrastructure, CIBMTR strives to manage its SCTOD responsibilities in an efficient and effective way, both for the government and for the transplant programs that are required to participate.

The emphasis of the SCTOD contract is on collecting a basic set of data that enables analyses of Program use, center-specific outcomes, donor registry and cord blood inventory size, and patient access to HCT. This is a much more restricted data set (in terms of data fields captured) than the CRF data set used by CIBMTR in its observational research programs, as shown in Figure 1.2. The SCTOD does not capture data on most allogeneic transplants done in non-U.S. CIBMTR centers or on autologous transplants. Though the research scope of the SCTOD is more narrowly specified compared to the full scope of data collected by CIBMTR, activities of the SCTOD enhance the value of the full database to researchers.

CIBMTR’s electronic data collection system, FormsNet2, was designed specifically for the SCTOD program. This is a very large project, but much was accomplished in 2009 utilizing the skills and resources of many individuals from the combined CIBMTR/ NMDP operations team. Several FormsNet2 releases (updates) in 2009 added features needed by centers to input their data more effectively, and added more of the required forms to the list of those that FormsNet2 can accommodate electronically. These updates increased donor and recipient form functionality, as well as adding clinical trials and CPI functions. (See Section 6.1 for more information about specific 2009 FormsNet2 feature additions and improvements.)
The March 2009 release of AGNIS® (A Growable Network Information System), an open source, peer-to-peer messaging system, also increased CIBMTR’s ability to respond to transplant center data reporting needs. Throughout the year, CIBMTR focused on educating teams (both U.S. and abroad), and on resolving early problems with FormsNet2 and electronic forms submission (Section 4.1).

### CIBMTR vs. SCTOD Outcomes Database

![CIBMTR vs. SCTOD Outcomes Database](image)

**Figure 1.2** Data set overlap between CIBMTR and the C.W. Bill Young Cell Transplantation Program Outcomes Database

### 1.7 2009 SCIENTIFIC AND PROCESS REVIEWS

An important initiative of 2009 was conducting a process to review internal procedures and scientific activities. A previous review of the IBMTR took place in 2002, and resulted in five major recommendations, all of which had been implemented in full or in part. The 2009 review took place over the course of several months during the summer of 2009.

#### 1.7.1 Internal review of CIBMTR processes

This process emphasized developing more efficient and effective operations. It included an examination of policies, procedures, staffing and communications, and provided an opportunity to further integrate operations on the two campuses.

With the aid of an external consultant, the review team from both campuses looked at CIBMTR processes for forms revision, data management and observational studies. That group, which generated more than 200 ideas, consolidated them into action items for immediate implementation:

- Six action plans to improve the forms revision processes.
- Five action plans for data management processes, focusing on moving data through the system more efficiently, improving internal communication and tracking study queries.
- Ten action plans were formed in the observational study area, focusing on efficient weekly statistics meetings, as well as uniform data retrievals and other measures to ensure more rapid assembly of high quality data files.

#### 1.7.2 External Review of Scientific Agenda

The 2009 Scientific External Review panel included individuals who represent a wide range of expertise that impacts CIBMTR, including outcomes research, immunobiology, clinical trials, statistics, health services research, cellular therapy, international issues, bioethics, and patient advocacy. Panel participants are listed in Appendix I.

Prior to the review, each participant received background documents. They then prepared written critiques that were consolidated and shared prior to meeting in person on Sept. 14, 2009. That all-day session started with an overview of CIBMTR by staff, followed by breakout sessions focusing on specific topics. Recommendations from the review were summarized and then distributed to the Review Panel for their review and feedback. The revised summary was presented to the CIBMTR Advisory Committee in November for development of action plans.

Strengths that the panel identified about CIBMTR:

- Strong leadership;
- Exceptional theoretical and practical biostatistical expertise;
- High quality longitudinal database;
- Large repository of cells and DNA;
- A focus on outreach to stakeholders in developing policies and processes;
- Facilitation of the mandatory reporting that has resulted from U.S. legislation;
- International collaboration;
- Scientific productivity for observational studies;
• Effective coordination of the BMT CTN and successful recruitment to clinical trials;
• New initiatives in Health Services Research and Cellular Therapy;
• Development of young investigators.

The Panel also made a series of recommendations for future development and implementation of the scientific agenda:
• Although in general endorsing CIBMTR’s “bottom up” approach to setting the scientific agenda, the panel suggested developing an oversight system to ensure that the agenda made the best use of CIBMTR resources to address the most important issues.
• Develop a formal process for setting the scientific agenda of the RCI BMT.
• Develop strategies to bring observational studies to completion more quickly, including
  o Principal Investigator education;
  o Project Manager support for committees;
  o More MS statistician support.
• Enhance data collection and sharing with transplant centers and cord blood banks.
• Facilitate access to data by use of technology.
• Enhance website to allow patients and investigators to get more relevant information, including “take home” messages from CIBMTR studies.
• Increase use of Repository for immunogenetic and immunobiologic studies to expand the portfolio of these studies.
  o Disseminate information about what is available in the Repository more widely, to reach persons with the necessary expertise to do appropriate studies.
  o Make the process for prioritizing/adjudicating use of samples more transparent.
• Expand the focus on other uses of hematopoietic stem cells in cellular therapy beyond hematopoietic reconstitution.
  o Initially focus on cellular therapy in a transplant setting, e.g. donor leukocyte infusion
  o Partner with investigators in cardiovascular area
  o Consider a joint meeting.
• Establish a long-term follow-up program that includes collecting information directly from appropriately-consented patients.
• Develop the Health Services Research Program. Convene a conference of experts to separately consider this issue and make recommendations for structure and prioritization. This will serve as a platform for discussing what CIBMTR is uniquely able to do.

Several criteria were used to prioritize the Panel’s recommendations, to determine what CIBMTR should focus on in the near term and into the future. These criteria included an evaluation of the plan’s potential cost, projected speed of implementation, probability of success, ownership of the plan, and who would review its progress.

A summary of the recommendations was presented to the CIBMTR Advisory Committee in November 2009, where action plans were developed for each. Teams were identified to work on the recommendations, and significant progress was made by several of them prior to the end of 2009. The RCI BMT and Immunobiology teams prepared reports on their progress, to be given during the February 2010 Advisory Committee meeting.
2.0 MAJOR PROGRAMS

2.1 OBSERVATIONAL RESEARCH PROGRAM

CIBMTR’s Observational Research is undertaken by its 19 Working Committees as described in Section 1.3. Each Working Committee is responsible for:

- Setting priorities for CIBMTR observational studies related to that Working Committee’s subject area using the CIBMTR’s large clinical database;
- Designing and conducting studies relevant to their subject area that use CIBMTR data, statistical resources, networks and/or centers;
- Evaluating proposals to use CIBMTR data for studies relevant to their subject area;
- Assessing and revising CIBMTR data collection forms as needed;
- Planning and conducting workshops at CIBMTR meetings.

Membership on Working Committees is open to any investigator willing to take an active role in studies that use CIBMTR data and/or resources. Proposals for CIBMTR observational studies are submitted to the appropriate Working Committee and evaluated by its committee members. The committees are also encouraged to develop studies in important areas when no relevant or appropriate proposals addressing those areas have been submitted, and to foster participation by junior investigators. A comprehensive report of all current CIBMTR studies, by Working Committee, can be found in Section 10. An abbreviated listing of these studies, noting their current status, is posted at www.cibmtr.org and updated biannually.

Each Working Committee is staffed, at a minimum, by an MS Statistician, a PhD Statistical Director, and an MD Scientific Director from the CIBMTR Statistical Center (see Appendix C1). Each has two to three Co-chairs who are appointed by the Advisory Committee to non-renewable five-year terms. Terms are staggered to facilitate succession while maintaining continuity. Individuals may serve as Chair more than once, but not consecutively on the same committee. Chairs are expected to participate in the nomination process for replacement positions, with special consideration given to mid-level investigators to promote ongoing leadership for the work of CIBMTR.

Nominations for open Working Committee Co-chair positions were received in fall 2009, and the recommendations of the Nominating Committee approved by the CIBMTR Advisory Committee at its meeting in November 2009. An effort is always made to encourage participation by experts from international centers as well as to find U.S. representatives from a broad range of transplant centers. Appendix C2 is a list of new Working Committee Chair appointments.

Chairs are selected for their proficiency in specific subject areas, to ensure adequate expertise with both autologous and allogeneic transplantation (where relevant), and adequate experience with CIBMTR activities. Chairs must be members of CIBMTR centers that submit Comprehensive Report Forms (CRFs) and are compliant with Continuous Process Improvement (CPI) standards (Section 4.3), unless an exception is granted by the Advisory Committee. Exceptions are made to allow individuals to serve who are not associated with a clinical center, but who have demonstrated scientific expertise and commitment, e.g. a basic scientist who is director of a histocompatibility laboratory, apheresis center or donor registry, or an expert in cell processing procedures.

Working Committee Chairs are expected to monitor and, where necessary, facilitate the progress of studies in their committee’s portfolio. They are responsible for communicating with the Principal Investigators (PIs) of studies when barriers or delays are encountered, and for participating in presentation of the studies for critique at CIBMTR Statistical Center meetings. In addition to chairing annual Working Committee meetings, Chairs are expected to meet by teleconference every 4-8 weeks with the Scientific Director and Biostatisticians of their committees to review study proposals and ongoing studies. Chairs are responsible for approving any meeting minutes.
Each Working Committee is allocated CIBMTR resources annually, including statistician time, by the Chief Scientific Director in consultation with the Chief Statistical Director and the Associate and Assistant Statistical Directors.

2.1.1 Health Services Research
As noted, a major highlight of activity in 2009 was establishment of the Health Services Research (HSR) Program, in collaboration with the NMDP Office of Patient Advocacy (OPA), as a branch of CIBMTR’s Observational Research Program. The objective of HSR is to improve access to HCT, and to improve outcomes and quality of life (QOL) of patients undergoing transplantation.

Since its inception, CIBMTR has been interested in the long-term effects (on both recipients and donors) of HCT, and conducted a key project in this area over the past several years under the auspices of the Late Effects Working Committee. CIBMTR plans to conduct additional research in health policy and QOL issues using the new partnerships between the HSR Program and the Late Effects Working Committee.

A QOL Pilot Project began under the auspices of the SCTOD and a Survey Research group was established on the Minneapolis campus to support these types of studies and data collection. The Pilot Project began in 2007, when the chairs of the Late Effects Working Committee commissioned a survey to obtain feedback from committee members on areas of focus for future studies. Late liver complications, post-transplant fertility, and QOL were identified as priority areas for committee research. Working groups were established to address late liver complications and post-transplant fertility in 2008. Each group reviewed existing literature, established research questions, suggested collection of additional data, and proposed additional studies for their specific areas.

Dr. J. Douglas Rizzo is leading the pilot QOL data collection project in five adult and three pediatric centers. The late liver complications working group includes Chair Linda Burns (University of Minnesota), and members Joerg Halter, Mutlu Arat, Rammurti Kamble, Sally Arai, Sarita Joshi, and John Wingard. The post-transplant fertility working group consists of chair Alison Loren (University of Pennsylvania), and members Eric Chow, Maria Gilleece, Joerg Halter, Sarita Joshi, and David Jacobsohn.

As of December 31, 2009, the QOL Pilot Project processes and consent forms were under review by the NMDP Institutional Review Board (IRB).

HSR Program Development
The HSR Program was established as follows:
- Development of a proposal for an HSR Program, including a preliminary scientific agenda and goals, took place from October 2008 through January 2009.
- Program details were presented, and establishment of the HSR program proposed and approved by the CIBMTR Advisory Committee at the 2009 BMT Tandem Meetings in February.
- Following its approval, members were invited to participate on the HSR Program Advisory Group. The Advisory Group includes the Executive Director and Chief Scientific Director of CIBMTR, Associate Scientific Director of CIBMTR-Minneapolis, Associate Scientific Director for Data Operations, Vice President of the NMDP OPA, and the Co-chairs of the Health Policy Working Committee (see Appendix H).
- The HSR scientific agenda and goals are now under review to identify priority research areas.

HSR studies that are underway, many of which use the combined resources of NMDP OPA, the SCTOD, and the new CIBMTR HSR program, include:

- Factors affecting participation in sickle cell disease clinical trials. This project was designed to identify and understand barriers to clinical trial participation among African-American/Black children with sickle cell disease, and their parents. Optimal methods to communicate information about sickle cell disease clinical trials to the African-American/Black community were identified. A tool used to recruit patients for BMT CTN trials was also evaluated. In addition to the OPA and CIBMTR, the University of Illinois at Chicago Medical Center, Children’s Medical Center of Dallas, and Emory University School of Medicine are participating in this study. Focus groups
completed their sessions in February 2009 and transcripts from the groups are being analyzed.

- **The financial impact of allogeneic HCT on the patient and family.** This is a pilot study that aims to determine the feasibility of conducting a study of out-of-pocket costs and long-term financial impact of allogeneic HCT. Patients and caregivers are evaluating the use of a patient-maintained diary to capture out-of-pocket costs over the first three months following allogeneic HCT. Based on this, the feasibility of conducting interviews to collect financial information at 6, 12, 18 and 24 months after allogeneic HCT will be studied and the results used to plan a broader multi-center investigation of the financial impact of allogeneic HCT. The pilot is open and accruing patients at three sites (University of Minnesota, MCW, and Roswell Park Cancer Center).

- **Caregiver initiative.** CIBMTR and the NMDP OPA have partnered with Michelle Bishop, PhD, of the University of Florida, to conduct a caregiver research pilot study. Dr. Bishop has published research about quality of life of patients and caregivers following HCT. This project is to evaluate a program specifically for caregivers, who are given a “toolkit” containing information and stress-management techniques. The long-term goal is to see if the toolkit decreases stress and improves quality of life for caregivers. Staff members from OPA serve as coaches for the pilot project, introducing the kit and techniques to participants and following them by telephone. The project is currently in recruitment phase.

- **Rural Health Initiative.** This project was designed to evaluate the effectiveness of a 12-week telephone support group for marrow or cord blood transplant survivors who live in rural areas, with a goal of decreasing their feelings of depression and anxiety. The support group is facilitated by a professionally trained CancerCare oncology social worker (a national nonprofit organization that provides professional support services for people affected by cancer) and an OPA case manager. It provides a chance to bring together survivors who live in rural areas, share transplant experiences and offer emotional support and information. Pre and post project surveys are being used to assess the impact of the support group on the emotional health of the participants. The post-project survey also asks participants to evaluate the support group format for future improvements.

- **OPA survey non-response research study.** CIBMTR is partnering with the NMDP OPA to study survey non-response. Currently, 34 surveys are distributed by the OPA to determine the usefulness of various programs, resources and case management services. Two of them, the OPA Survey and the Patient Satisfaction Survey, are approved by the U.S. Office of Management and Budget, and are being evaluated in this study. This research will determine differences between survey respondents and non-respondents, in order to improve patient satisfaction and compliance.

### 2.1.2 Other Observational Research Program accomplishments in 2009

- Sixty-five proposals for new studies were received in late 2008, prior to the annual BMT Tandem Meetings, and 48 were approved at the 2009 meeting for initiation.
- A record 248 studies were in progress at year end from the 19 Working Committees.
- Twelve studies (six oral, six posters) were presented at the BMT Tandem Meetings in February 2009, and nine were accepted for presentation (four oral and five posters) at the upcoming 2010 BMT Tandem Meetings.
- A total of 20 CIBMTR studies (14 oral and 6 poster presentations) were accepted for presentation at the ASH meetings in December 2009.
- Thirty-seven papers were published in peer-reviewed journals and another 13 were accepted for publication. Thirteen more papers were submitted for publication and are under review.
2.2 STATISTICAL METHODOLOGY RESEARCH PROGRAM

2.2.1 Research support
The main role of the CIBMTR Statistical Center is to make its resources on both campuses available to support observational and clinical research.

To help accomplish this, CIBMTR has a long-standing relationship with the faculty of the Division of Biostatistics in the MCW Department of Population Health. Dr. John Klein, the Chief Statistical Director of CIBMTR, is also the Chief of the Division of Biostatistics. His expertise in survival analysis has resulted in publishing important methodological research addressing issues in the analysis of post-HCT outcomes. Dr. Klein holds an R01 research grant from NCI to study statistical issues in analyzing HCT, and is co-author of the standard graduate reference text on survival analysis (survival analysis: techniques for censored and truncated data, 2nd edition, Klein, JP and Moeschberger, ML, Springer, New York, 2001). He and his staff actively participate in developing and adapting statistical methodologies for optimal analysis of CIBMTR and other transplant-related data.

HCT is a complex procedure with multiple competing risks. There can also be dramatic changes in the risks of specific events over time. The Biostatistical group has made valuable contributions to the development and rigorous evaluation of statistical models that facilitate research in this setting. CIBMTR also recognizes that it is important to guide the research community in appropriate application and interpretation of these sophisticated models. Thus, CIBMTR statistical research is two-fold: development of the models themselves and applying them to studies using CIBMTR clinical data.

The PhD Biostatisticians have substantial experience in assessing the unique problems associated with HCT, and collaborate with CIBMTR Scientific Directors and network investigators. The combined expertise of these partners represents a distinctive feature of CIBMTR, and is an important component of its success.

In 2009, Gisela Tunes de Silva, PhD, of the University of São Paulo, Institute of Mathematics and Statistics, worked as a visiting professor with the MCW Biostatistics group in analyzing CIBMTR data. These biostatisticians, in collaboration with CIBMTR scientific directors, BMT CTN investigators and MS-level statisticians, provide a combined expert foundation that contributes significantly to the overall success of the CIBMTR research mission.

The following HCT-related statistical methodology papers were published or accepted for publication in 2009 by this group, in peer-reviewed journals:


2.2.2 Statistical Center clinical trials support
As always, Statistical Center personnel provided statistical review of several HCT clinical trial protocols in 2009 and are increasingly seen as a resource of expertise in this area. CIBMTR statisticians also serve as statisticians for the BMT CTN to help determine study feasibility based on statistical power.

2.2.3 Center-specific analysis
CIBMTR statisticians have collaborated closely with NMDP since 2003 in generating center-specific outcomes reports for unrelated donor HCT for HRSA. These reports are well accepted by the HCT community. The 2005 Stem Cell Act substantially expanded the patient population to be considered in
these analyses. At most centers, the new requirement meant that the percentage of patients to be included would at least double. Centers which perform related donor HCTs will be included in these analyses for the first time beginning in 2010.

2.2.4 Survival data
The center-specific outcomes reporting project is similar to an analysis initially developed by the Chief Statistical Director and an MD/MS faculty member for displaying survival information. The goal of each of these reports is to provide information that can be useful in making decisions about transplant alternatives. Eventually, the Program website (http://bloodcell.transplant.hrsa.gov/index.htm) will display information using data reported on related and unrelated transplants through the SCTOD contract and data on autologous transplants reported on a voluntary basis to the CIBMTR.

Statistics are based on a moving five-year window of data. This window includes five years of “accrual” into the cohort and one year of follow-up. The cohort is updated every six months to allow for the most recent data. Only data from transplants conducted in the United States are presented in the accrual window.

The website for HCT data presents some unique challenges. First, there are many diseases and disease states. Second, samples sizes for some categories are quite small, so statistically valid estimates of outcome can be difficult. The website information is presented in three parts: demographic information, basic outcomes data, and an area that explains how to request data.
2.3 IMMUNOBIOLOGY RESEARCH PROGRAM

The overall goal of the Immunobiology Research Program is to facilitate collaborative research studies that are focused on:

- Improving outcomes after HCT, through a better understanding of the immune response pathways that participate in host-versus-graft and graft-versus-host mechanisms, and that modulate the risks of graft-versus-host disease, relapse and mortality;
- Increasing the availability of unrelated donor HCT through a better understanding of donor and recipient genetic determinants.
- Understanding the role of HLA-matched or mismatched related and unrelated donor HCT compared to other available graft sources.

The specific research supported by this program includes:

- Genes and gene products of the major histocompatibility complex;
- Natural killer cell repertoire;
- Cytokine/pro-inflammatory cytokine and immune response determinants;
- Minor histocompatibility loci;
- Other immune regulatory genes and products (such as anti-HLA antibodies);
- Comparative studies that involve HLA-mismatched related donors or any unrelated donors.

The CIBMTR Immunobiology Research Program is facilitated by the Immunobiology Working Committee, functioning in collaboration with the NMDP Histocompatibility Advisory Group (Appendix E). The NMDP Repository operates under the oversight of the latter group. Several CIBMTR staff members participate in the activities of both groups.

During the past year:
- 8,008 samples were distributed to PIs for eight studies.
- Working collaboratively with NMDP Scientific Services, another 3,700 samples were distributed for the ongoing NMDP retrospective high-resolution HLA typing program that generates data for CIBMTR studies.
- Related donor-recipient research sample collection was initiated in support of the SCTOD in seven pilot centers in December 2007. Since inception, 838 samples were submitted to the Repository, with 474 of them submitted in 2009. The monthly average in 2009 was 39.5 samples.

The NMDP Research Sample Repository provides a unique resource to investigators for retrospective analysis of immune response determinants and transplant outcome. Currently, there are more than 12,000 cases where samples from both the transplant donor and recipient are available and for whom complete clinical data has been collected and validated. The majority of the paired samples have complete high-resolution data available for HLA-A, B, C, DRB1/3/4/5, DQ, and DP loci. In addition, the NMDP began providing repository services support to the BMT CTN in 2009.

In return for access to the samples and data analysis support, investigators are required to submit the interpreted results of all assays performed on the samples to NMDP. This data submission requirement ensures that all sample testing yields information that is readily available to the HCT research community for subsequent analysis, and eliminates or reduces duplicative testing to preserve resources and sample inventory.
2.4 CLINICAL TRIALS SUPPORT PROGRAM

In addition to serving as the primary resource for the scientific Working Committees, the large CIBMTR database is an important research resource for clinical trials performed through the BMT CTN and RCI BMT mechanisms. These two groups conduct large and small clinical trials, respectively.

The CIBMTR Statistical Center makes its resources available to individuals and groups that are seeking to plan, implement and/or interpret other clinical trials as well. This is accomplished through:

**Trial Planning.** Investigators planning clinical HCT trials use the CIBMTR database to assess what patient populations may be available for trials under specific eligibility criteria. With the aid of CIBMTR Statistical Center staff, they can estimate the effects that changing eligibility criteria may have on patient accrual. The CIBMTR database provides a more precise and less biased estimate of the baseline outcomes of interest than literature reviews, expert opinions, or personal experience in limited numbers at a transplant center. The database can help PIs identify the most common supportive care and other practices in potentially eligible patients so that clinical protocols can be written to be acceptable to most transplant centers. CIBMTR routinely makes these types of information available to BMT CTN and RCI BMT protocol teams.

For example in 2009, the BMT CTN 0303 Protocol Team (T-cell depleted transplants for AML) discussed several proposals for a follow-on trial. The new protocol would be similar to the 0303 protocol, but include HCT using unrelated donors only. The Statistical Center assisted in evaluating various scenarios with the new patient population in order to assess feasibility and statistical power.

The Statistical Center helped with the planning of BMT CTN trial 0702 (A trial of single autologous transplant with or without consolidation therapy versus tandem autologous transplant with lenalidomide maintenance) and trial 0901 (Peri-transplant stress management), by using the database to identify appropriate study populations, transplant centers with a large volume of patients treated for these diseases, the most appropriate study primary endpoints and to help define clinical trial safety stopping rules.

**Data collection instruments.** In addition to the instruments and forms it uses in its Working Committee studies, CIBMTR has an open policy for sharing data collection forms and database structures with others for their research and trials. The latter reflect the knowledge and expertise not only of Statistical Center personnel but also of the many transplant experts on Working Committees who evaluate and recommend revisions to the data collection forms. These are a resource for investigators doing any HCT research that involves collection of clinical data. The forms are freely available on the CIBMTR website, and have been used as the basis for data collection instruments in many clinical trials as well, including those sponsored by the BMT CTN and RCI BMT.

CIBMTR is also working with NCI to build an entire library of common HCT-related data elements (CDEs) for forms. The project, which curates CDEs in NCI’s cancer data standards repository (caDSR), will define standard data elements for HCT and make these CDEs universally available.

Also in the last year, CIBMTR worked closely with the United States Immunodeficiency Network (USIDNET) to jointly revise disease-specific report forms for immune deficiency (Forms 2031/2131), Wiskott-Aldrich syndrome (Forms 2033/2133), and chronic granulomatous disease (Forms 2035/2135), to make use of data being collected by both organizations under the policy of “collect once, use often.” In the coming year, several more disease-specific forms will be developed or updated, including X-linked lymphoproliferative syndrome, hemophagocytic lymphohistiocytosis and DiGeorge syndrome.

**Trial interpretation.** The CIBMTR database is a valuable tool for evaluating results of clinical trials. The Statistical Center makes the database available to provide matched controls for patients enrolled in single arm clinical trials, assisting in trial interpretation and follow on trial planning.
2.4.1 Blood and Marrow Transplant Clinical Trials Network (BMT CTN)
CIBMTR participates in administration of the BMT CTN Data and Coordinating Center (DCC) along with NMDP and The EMMES Corporation. Detailed information about BMT CTN activities and protocols, including the latest Progress Report, can be found on the BMT CTN website: www.bmtctn.net.

Designing HCT trials that will produce meaningful results requires that special consideration be given to sample size, eligibility criteria, multiple, competing outcomes, center effects, early stopping guidelines, and other issues where the Statistical Center’s expertise and database are invaluable.

The BMT CTN, which opened its first trial in 2003, had its first manuscript regarding study results published in July 2009:


Results of another BMT CTN trial were presented at the 2009 American Society of Hematology (ASH)
Meeting in December 2009:

Devine SM, Soiffer RJ, Pasquini MC, Carter S, Hari PN, DeVore S, Stein A, Lazarus HM, Linker C, Stadtmauer EA, Keever-Taylor CA, O'Reilly RJ. **HLA-identical sibling-matched, CD34+ selected, T-cell depleted peripheral blood stem cells following myeloablative conditioning for first or second remission acute myeloid leukemia: Results of Blood and Marrow Transplant Clinical Trials Network Protocol 0303.**

In December 2009, NHLBI and NCI formally approved the issuance of an RFA to continue funding the BMT CTN for another five years.

2.4.2 Resource for Clinical Investigations in Blood and Marrow Transplant (RCI BMT)
CIBMTR created the RCI BMT clinical trial support program in 2006 as a way to make its resources more available to individuals and groups outside the BMT CTN that were seeking to plan, implement and/or interpret smaller, phase I and II clinical trials or survey studies. RCI BMT trials now underway include:

- Double cord blood HCT after myeloablative conditioning for hematologic malignancies (05-DCB): 10 centers were activated, 24 patients accrued in 2009. This trial is funded by a grant from the U.S. Office of Naval Research.
- Evaluating the safety and tolerability of lenalidomide after allogeneic HCT (07-REV): 11 centers were activated and 7 patients accrued. This study is funded by the Celgene Corporation.
- RDSafe: A multi-institutional study of hematopoietic stem cell donor safety and quality of life (DS05-02). This study will provide a comprehensive analysis of the related donor experience. It is funded by an R01 grant from NCI.
- Evaluating the importance of KIR for transplant outcome (University of Minnesota holds a PO1 grant; CIBMTR is responsible for donor specimen handling and IRB documentation).
- Plerixafor for the mobilization and transplantation of sibling donors in patients with hematological malignancies: protocol is in development. This study is funded by the Genzyme Corporation.

RCI BMT offers these smaller clinical trials:

- Statistical, medical, and logistical clinical trials expertise;
- Data management services for multi-center phase I/II trials including electronic data capture;
- Use of CIBMTR’s large observational database to help plan trials and identify transplant centers that will optimize accrual;
- Long-term follow-up beyond primary study endpoints;
- Collaboration with investigators to seek and secure necessary funding and support for trial completion.
The January 2010 update (release) of the FormsNet2 application included a module specifically designed to enhance clinical trial data collection. This release created the infrastructure needed to host clinical trials and specifically support the RDSafe study.

In 2009, the RCI BMT formed a collaborative relationship with the Pediatric Blood and Marrow Transplant Consortium (PBMTC), and is now in the process of selecting its first joint trial. This partnership will facilitate early phase pediatric transplant trials for both malignant and non-malignant conditions. The initial partnership activities are funded, in part, by a grant awarded to the PBMTC from St. Baldrick's Foundation. The PBMTC is comprised of more than 100 pediatric transplant centers in North America, Australia, and New Zealand. It is the largest clinical trials group focused exclusively on blood and marrow transplantation for children and adolescents. Working together, RCI BMT and PBMTC will be able to address unmet needs in the field of pediatric marrow transplantation research.
3.0 DATA ACCRUAL

The CIBMTR collects data from approximately 15,000 transplant recipients annually, including information on new patients and follow-up data on previously reported patients. Regardless of whether the data submission is mandatory (by virtue of the SCTOD) or voluntary, CIBMTR centers must report all consecutive transplants as a requirement of participation. Appendices A1 and A2 list the institutions currently reporting data to CIBMTR. The figure below shows cumulative accession of allogeneic transplants (related and unrelated) since CIBMTR data collection began in 1970, cumulative accession of autologous transplants since 1990 (when data collection for autotransplants was initiated) and cumulative accession of unrelated donor transplants through NMDP since 1987. Table 3.1 shows the distribution of diseases, through 2009, for which these transplants were performed.

The SCTOD requires U.S. transplant centers to submit outcomes data on allogeneic transplants to a single national registry: CIBMTR. CIBMTR also continues to receive voluntarily submitted data from its international centers and from U.S. centers performing autologous transplants, which are not covered by the new law.

3.1 DATA ACCRUAL FORMS DEVELOPMENT

CIBMTR collaborated with U.S. authorities, the ASBMT, European Group for Blood and Marrow Transplantation (EBMT), Asia-Pacific Blood and Marrow Transplant Group (APBMT), Foundation for Accreditation of Cellular Therapy (FACT), WMDA, cord blood banks and other organizations in the international HCT community to arrive at a consensus on a reasonable set of common data elements to be collected for all transplant recipients. Emphasis was placed on collecting the most relevant data while minimizing the burden on transplant center staff.

Both the Transplant Essential Data (TED) form (corresponding to the EBMT Med-A form) and the Comprehensive Report Form (CRF, corresponding loosely to the EBMT Med-B) were revised to contain these changes and serve as the CIBMTR’s tools for collecting HCT data.

Collection of this new level of data (pre-transplant TED and post-transplant TED forms) began on December 3, 2007. The system was not available to 100 percent of U.S. centers until early 2008, so data received via the new electronic system were not fully representative of all contributing centers until then.

Figure 3: Accession of patients registered with CIBMTR (data is incomplete for 2009)
## Table 3.1 Distribution of transplant indications in the CIBMTR database

<table>
<thead>
<tr>
<th>Disease</th>
<th>Allogeneic Transplants</th>
<th>Autologous Transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TED-level data</td>
<td>CRF data</td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>27,059</td>
<td>13,722</td>
</tr>
<tr>
<td>Acute myelogenous leukemia</td>
<td>42,594</td>
<td>20,313</td>
</tr>
<tr>
<td>Chronic myelogenous leukemia</td>
<td>26,996</td>
<td>14,507</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>3,067</td>
<td>1,415</td>
</tr>
<tr>
<td>Hodgkin disease</td>
<td>1,182</td>
<td>387</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>10,650</td>
<td>4,538</td>
</tr>
<tr>
<td>Plasma cell disorders</td>
<td>3,100</td>
<td>1,309</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>181</td>
<td>89</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>183</td>
<td>92</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>23</td>
<td>10</td>
</tr>
<tr>
<td>Melanoma</td>
<td>48</td>
<td>17</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Sarcoma (soft tissue, bone and other)</td>
<td>37</td>
<td>11</td>
</tr>
<tr>
<td>Ewing sarcoma</td>
<td>75</td>
<td>29</td>
</tr>
<tr>
<td>Wilm tumor</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Myelodysplastic syndromes</td>
<td>12,871</td>
<td>5722</td>
</tr>
<tr>
<td>Other leukemia</td>
<td>2,085</td>
<td>980</td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Germ cell tumor</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Brain tumors</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Testicular cancer</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Other malignancies</td>
<td>1,085</td>
<td>529</td>
</tr>
<tr>
<td>Autoimmune diseases</td>
<td>69</td>
<td>25</td>
</tr>
<tr>
<td>Severe aplastic anemia</td>
<td>10,143</td>
<td>6,068</td>
</tr>
<tr>
<td>Inherited erythrocyte abnormalities</td>
<td>4,865</td>
<td>3,044</td>
</tr>
<tr>
<td>SCID(^a) and other immunodeficiencies</td>
<td>3,768</td>
<td>1,943</td>
</tr>
<tr>
<td>Inherited disorders of metabolism</td>
<td>1,884</td>
<td>1,151</td>
</tr>
<tr>
<td>Histiocytic disorders</td>
<td>818</td>
<td>478</td>
</tr>
<tr>
<td>Other non-malignancies</td>
<td>380</td>
<td>136</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td><strong>153,210</strong></td>
<td><strong>76,531</strong></td>
</tr>
</tbody>
</table>

\(^a\) Since 1970
\(^b\) TED-level data collection began in 1991 and comprehensive data collection in 1992; data for 1989-90 were collected retrospectively.
\(^c\) Includes retinoblastoma, head and neck tumors, mediastinal neoplasms, GI tract tumors, pancreatic cancer, hepatobiliary, kidney and urinary tract tumors, prostate cancer, cervical, uterine cancer, vaginal cancer and thymoma.
\(^d\) Includes multiple sclerosis, systemic sclerosis, systemic lupus erythematos, rheumatoid arthritis, idiopathic thrombocytopenic purpura (ITP), Crohn’s disease and other in the TED-level data.
\(^e\) SCID=Severe Combined Immune Deficiency.
The FormsNet2 application was developed by CIBMTR and NMDP bioinformatics staff to collect data under the SCTOD contract. It has undergone significant improvements during 2009 (Section 6.1) and CIBMTR is receiving positive feedback from centers on this process.

All participating centers provide a standard, but limited, data set for all consecutive transplant recipients. These TED-level data, with some additional details of donor and graft characteristics, encompass the obligatory data to be submitted for the SCTOD for all U.S. allogeneic transplant recipients. It is also the data that is required for transplant center accreditation by FACT and the Joint Accreditation Committee of ISCT and EBMT (JACIE).

About two-thirds of CIBMTR centers voluntarily submit more detailed, comprehensive data on CRFs for a subset of their patients. The Statistical Center uses data from the pretransplant TED (pre-TED) forms and a weighted-randomization algorithm (Section 4) to select cases for CRF submission.

The CRF data are the critical tool for most of the observational studies conducted by CIBMTR’s Working Committees, and the work of the committees could not take place without them, along with good tools for accessing the data and the support of the CIBMTR Statistical Center for analyzing them.

CIBMTR reimburses transplant centers for completed CRFs. TED-level data is not reimbursed. Form submissions are reimbursed at the rates shown below on Table 3.2.

<table>
<thead>
<tr>
<th>Rate</th>
<th>CRF Number</th>
<th>Form Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>$135</td>
<td>2000</td>
<td>Recipient Baseline Form with required disease forms</td>
</tr>
<tr>
<td></td>
<td>2004</td>
<td>Infectious Disease Markers</td>
</tr>
<tr>
<td></td>
<td>2005</td>
<td>Confirmation of HLA Typing (related donor only)</td>
</tr>
<tr>
<td></td>
<td>2006</td>
<td>HCT Infusion (selected for full Comprehensive Report Forms)</td>
</tr>
<tr>
<td>$110</td>
<td>2100</td>
<td>100 Day Post-HCT with required disease forms</td>
</tr>
<tr>
<td>$85</td>
<td>2200</td>
<td>Six month to Two Year Post-HCT with required disease forms</td>
</tr>
<tr>
<td>$65</td>
<td>2300</td>
<td>Yearly follow-up for &gt; two years post-HCT with required disease forms</td>
</tr>
<tr>
<td>$25</td>
<td>2006</td>
<td>Unrelated HCT using U.S. donor (not selected for full CRF submission)</td>
</tr>
<tr>
<td>$15</td>
<td>2900</td>
<td>Recipient Death Data</td>
</tr>
</tbody>
</table>
4.0 DATA COLLECTION and MANAGEMENT

In late 2007, data management activities were integrated from the previously separate Milwaukee and Minneapolis operations, including data entry, auditing, and Continuous Process Improvement (CPI) standards for data quality assurance. All transplant centers were assigned a new five-digit CIBMTR center number (CCN). Centers now submit data either electronically via FormsNet2, or on paper forms to their assigned (Milwaukee or Minneapolis) campus. Each center is also assigned a CIBMTR CRC to serve as their liaison.

4.1 DATA ENTRY AND MANAGEMENT

Data entry and management activities take place under the supervision of Associate Scientific Director J. Douglas Rizzo, MD, and Roberta King, MPH, Vice President-CIBMTR Minneapolis, with expertise for several of these operations provided by Janet Brunner (Milwaukee) and Marie Matlack (Minneapolis). CIBMTR data collection and management activities, formerly two separate systems with similar, but not identical forms on the two campuses, are now fully integrated.

FormsNet2 is the web-based application transplant centers use for submitting their outcome data for both TED and CRF forms. CIBMTR processed more than 159,000 forms via FormsNet2 in 2009. (See Section 6.1 for more information about how FormsNet2 is used for data submission.)

4.2 REPORTING MECHANISMS

A transplant center’s level of participation determines the type of data collection forms that it submits to CIBMTR. A center may participate as either a TED-only center or a CRF center. All centers submit the pre-TED form for every patient. For CRF centers, a selection algorithm routes patient data to either the TED-only or CRF track. Table 4.1 on the next page shows these two mechanisms, their similarities and differences in forms submission requirements.

A transplant center designated as a TED-only center is required to submit the following forms: the CIBMTR Recipient ID Assignment (CRID, Form 2804), the Pre-TED (Form 2400) and Post-TED (Form 2450). This last form is required at 100 days, 6 months and 1 year post-transplant, and annually thereafter on the HCT anniversary date. In 2009, almost 79,000 pre-TED and post-TED forms were submitted to CIBMTR. The HCT Infusion Form (Form 2006) is required for recipients of all NMDP donor products, all cord blood recipients whether facilitated by NMDP or not, as well as all donor products when a research sample has been collected for the Related Sample Repository, whether facilitated by NMDP or not. Form 2804 is due only for a recipient’s first reported (to the CIBMTR) HCT.

A transplant center designated as a CRF Center is required to submit the following forms: the CIBMTR Recipient ID Assignment (Form 2804), the Pre-TED (Form 2400), followed by either a Post-TED or CRF. The type of follow-up forms that a CRF Center uses for a specific recipient is determined by the CIBMTR’s form selection algorithm, outlined below.

If the transplant recipient consents to participate in research and if the transplant takes place at a CRF center, the algorithm determines if that recipient is placed on the TED-only track or the CRF track. If the recipient does not consent to participate in research, then TED forms are due for that recipient and their data are only used for Federally-mandated analyses and not for research.

4.2.1 Forms selection algorithm

CIBMTR developed an algorithm to determine which set of forms is required for each HCT recipient at a CRF center. The goal of the algorithm is to randomly select an epidemiologic sample of recipients for whom a CRF will be requested. The algorithm includes, but is not limited to, type of HCT, age of the recipient, disease, etc., and is weighted to acquire sufficient information on rare diseases or types of transplantation. The algorithm is periodically reviewed to assess the burden of data submission for transplant centers.
### Table 4.1 CIBMTR Forms Submission Process

- Center submits CRID Assignment Form (Form 2804)
- CRID generated
  - If autologous transplant recipient declines consent for research participation, **stop here**
- Pre-TED (Form 2400) is added to Forms Due list
- Center completes and submits Pre-TED
- CRF Track: Pre-TED data is processed through the selection algorithm resulting in CRF or TED track. Follow appropriate track below
- TED Track: Follow TED track below

<table>
<thead>
<tr>
<th>CRF Track</th>
<th>TED Track</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
<td><strong>1</strong></td>
</tr>
</tbody>
</table>
| • Forms 2004 and 2005 due for each non-NMDP allogeneic donor  
• Form 2005 due for each non-NMDP allogeneic recipient  
• Form 2006 added for all products | • Forms 2004 and 2005 will be added if participating in related specimen repository  
• Form 2006 due for all NMDP products and all cord blood units |
| **2** Baseline and Follow-up Forms added to Forms Due list | Post-TED Follow-up Form 2450 added to Forms Due list |
| **3** Center completes Baseline form after infusion | Center completes Post-TED Forms at appropriate time points |
| **4** Center completes CRF Follow-up Forms at appropriate time points | Is recipient alive? If yes, go to Step 5. If no, go to Recipient Death Table |
| **5** Follow-up Form entered | Did recipient have a subsequent transplant? If yes, go to Step 6. If no, go to Step 3 |
| **6** Is recipient alive? If yes, go to Step 7. If no, go to Recipient Death Table | Contact Center Liaison with date of subsequent transplant |
| **7** Did recipient have subsequent transplant? If yes, go to Step 8. If no, continue reporting at next time point (Step 4). | Center completes and submits Pre-TED (Form 2400) for subsequent transplant. Go to Step 2. |
| **8** Future time points will be deleted for prior transplant from FormsNet2 when the form reporting the subsequent transplant is error free. Go to Step 2 for subsequent transplant. | Future time points will be deleted for prior transplant from FormsNet2 when the form reporting the subsequent transplant is error free. |

### Recipient Death Table

Death Form 2900 is completed to report the recipient’s death.* If a follow-up form is received and reports the recipient’s death, and a form 2900 has not been submitted, one will be made due on the Forms Due list. The recipient’s death is reported on the Post TED.

* Complete the Death Form 2900 even if autopsy is pending. Another Death Form will be requested to confirm cause of death if autopsy was pending.

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1. If center has chosen to submit autologous forms without consent, follow the TED track. These data are entered for the center’s own programmatic use, not for research.
2. Recipient has the option to withdraw consent at any time. If this happens, Center Liaison can move this transplant record to the TED Track.
3. 100 days, 6 months, annually
Data from the TED series forms are used to evaluate SCTOD operations, including Federally-required analyses such as center-specific outcomes, and to evaluate optimal registry and cord blood bank size. CRF-level data are typically required for research studies, although TED-level data may occasionally be used. When appropriate, CIBMTR shares data from these forms with other organizations, such as the New York Blood Center National Cord Blood Program.

Recipient data are considered in the purview of the SCTOD if they meet one of the following criteria:
- Allogeneic HCT occurs at a U.S. transplant center;
- Stem cell collection is performed within the United States;
- Cord blood unit is obtained from a cord blood bank within the United States.

4.2.2 Electronic forms submission summary
- All U.S. centers must submit TED-level data for all allogeneic HCTs to fulfill their obligation to provide outcomes data to the SCTOD.
- Many U.S. centers also voluntarily submit TED-level data for autologous transplants.
- Non-U.S. centers participate in the CIBMTR on a voluntary basis, submitting TED-level data for all consecutive allogeneic or autologous transplants.
- U.S. and non-U.S. CRF centers that choose to participate submit a detailed data set on the CRFs for a subset of patients, selected through the weighted selection algorithm, using information supplied on the pre-TED forms.

4.2.3 Paper Report Forms
Data collection and reporting forms can be found at: www.cibmtr.org/DataManagement/DataCollectionForms/index.html and may be printed, completed and faxed or mailed (U.S. Postal or FedEx) to the center’s assigned campus. Upon arrival, the forms undergo a review for completeness and are entered into FormsNet2 by CIBMTR staff. Any errors detected in the form can be corrected by the center via Error Correction forms, which are obtained and submitted in the same manner as the TED and CRF forms. A center may also correct errors detected on paper forms through FormsNet2. Paper forms and attached documents are imaged and electronically stored at CIBMTR for future reference; original documents are destroyed through a secure process.

Since the FormsNet2 system was introduced (Section 6.1), an increasing number of centers submit all their forms electronically. For example, in December 2009, of the 14,700 forms submitted, 87% were received through FormsNet2 and 13% on paper. About 230 centers per month submit their forms electronically.

4.2.4 Participation agreements
Data Transmission Agreements (DTAs) permit centers to transfer patient data to CIBMTR for use in its research. As of December 2009, 81% of DTAs were returned to the CIBMTR (93% for U.S. centers).

CIBMTR transplant centers are also required to provide evidence that their research activities are overseen and approved by an IRB. As of December 2009, 94% of active U.S. centers had submitted and received local IRB approval for the CIBMTR research protocol and associated consent forms. International transplant centers must follow their country’s laws and regulations governing human subjects and privacy protection. The transplant center is responsible for obtaining the necessary institutional review and approval.

A signed DTA and approved consent forms must be received by CIBMTR before centers can be reimbursed for CRFs they submit and the data used for research.

<table>
<thead>
<tr>
<th>Table 4.2</th>
<th>CPI Form Submission Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Form</td>
<td>Due Date</td>
</tr>
<tr>
<td>Pre-TED or Form 2000 and required disease forms and/or Infection Forms</td>
<td>HCT date</td>
</tr>
<tr>
<td>Post-TED or Form 2100 and required disease forms and/or Infection Forms</td>
<td>Day 100 post HCT</td>
</tr>
<tr>
<td>Post-TED or Form 2200 and required disease forms and/or Infection Forms</td>
<td>6 months, 1 year, and 2 years on HCT anniversary</td>
</tr>
<tr>
<td>Post-TED or Form 2300 and required disease forms and/or Infection Forms</td>
<td>Starting year 3, annually on HCT anniversary</td>
</tr>
</tbody>
</table>
4.3 DATA QUALITY: CONTINUOUS PROCESS IMPROVEMENT AND ON-SITE AUDITS

CIBMTR has established criteria for submitting pre- and post-TED and CRFs. The system to monitor how well these criteria are met is called Continuous Process Improvement (CPI). To be fully CPI compliant, a transplant center must submit at least 90% of its forms due within the time periods listed on Table 4.2 (above). This includes all legacy\(^1\) data forms that were due prior to CIBMTR’s implementation of revised data collection forms and FormsNet2, as well as all forms due since that time.

Transplant centers receive CPI reports three times per year (January, May and September), listing the number of follow-up forms that were due in the previous trimester, and the number and percentage of each that were submitted within the trimester. A form is not counted as complete until errors have been resolved, applicable inserts have been submitted, and it is designated as “error-free\(^2\)” in FormsNet2. Transplant centers not compliant with CPI standards must submit a forms-due remediation procedure. CPI was suspended with the launch of the SCTOD in December 2007, allowing centers to adapt to new systems and pending enhancements to FormsNet2. CIBMTR anticipates re-implementing CPI in early 2010.

4.3.1 CIBMTR on-site data audit program

Currently, three CRCs perform on-site transplant center audits, spending 1-3 days at each center reviewing the primary medical records to assess the accuracy of submitted data. The audit processes include:

**Audit cycle**

- Each eligible domestic and international center is audited once within a four-year audit cycle.
- To be eligible for an on-site audit, a transplant center must have submitted forms for a minimum of 20 HCTs.
- A new center’s first audit will occur in the year following submission of their 20th recipient data.

**Recipient selection and eligibility requirements**

- If a center performs more than 20 HCTs during the audit period, a maximum of 16 recipients will be randomly selected for audit.
- A recipient is eligible for audit if the pre-TED form and 100-Day Post-TED forms were submitted or, if the recipient is on the CRF track, the pre-TED and Forms 2000 and 2100 were submitted to CIBMTR. Each form must be considered complete and designated as “error-free” in FormsNet2.
- Recipients are selected for audit only once.

**Forms and data fields**

- All TED and CRF-level data are subject to audit.
- Critical data fields are audited for each recipient selected for audit. These are data fields that are included in most outcomes analyses. Additional data fields are randomly selected for audit to assess the accuracy of the center’s entire database.

**Methodology**

- Auditors compare the data submitted to CIBMTR with the data in the recipient’s medical record.
- Discrepancies are categorized into one of four categories:
  - Missing documentation
  - Omission
  - Interpretation
  - Non-audit errors
- Errors are reviewed with data coordinator.
- Auditors make corrections to the database and the transplant center is given a record of changes made to the forms.

**Audit analysis and reports**

- Transplant centers receive a detailed audit report summarizing the results of their audit.
- Centers may be required to submit a Corrective Action Plan in response to errors identified during the audit.

As of mid December, audits at 31 centers were completed for 2009. All of these centers passed the audit with fewer than 5% critical field errors. The average error rate was <2%. Audit results are reviewed and approved by the CIBMTR Executive Committee annually.

\(^1\) “Legacy data” are those submitted to CIBMTR or NMDP before FormsNet2 became available in December 2007.

\(^2\) Passed FormsNet2 application validation checks
4.3.2 Training and information resources
CIBMTR has developed comprehensive, secure applications and programs to allow data managers to submit data to CIBMTR as accurately and efficiently as possible. Following is a list of training and reference services that CIBMTR makes available to assist them in that process:

Programs and Presentations. Educational programs are presented at meetings sponsored by CIBMTR and related groups several times per year. They include access to audio and visual presentations on the form submission process.

In 2009, these included three days of Clinical Research Professionals/Data Management training in conjunction with the 2009 BMT Tandem Meetings in February and two days of training at the NMDP Council meeting in November.

Internet. A variety of training resources are available on the CIBMTR website:

- Training manual. This manual includes both general instructions and specific instructions for each form type and manuals for supplemental forms required for a specific study.

- FormsNet2 Training. The CIBMTR website has training and reference materials specific to data submission to CIBMTR through the Web-based FormsNet2 application.

- AGNIS Training. Specific training on the use of AGNIS to transmit data to CIBMTR directly from a center’s database is also available on this website.

- FAQs. CIBMTR has created a downloadable Frequently Asked Questions (PDF) reference document to answer common questions from transplant center administrators and data managers about: Data submission; FormsNet2; TED and CRF forms; Consent forms and CPI.

- Legacy Data and Backlog Resources. CIBMTR provides retired data manuals, forms and other archived documents for reference purposes and to help centers in making changes to legacy data.

- Cord Blood Resources. CIBMTR is working to create more materials to assist in Cord Blood reporting and retrieval of information. Information on which Donor/Cord Registry Codes are approved for use on the Pre-TED (Form 2400) and Infusion Form (Form 2006) can be found on the Cord Blood Resources page of the www.cibmtr.org website. This link includes a list of registries participating in Bone Marrow Donors Worldwide (BMDW).

- Data Manager Blog: datamanager.blogspot.com. This website was designed to help data managers who are collecting and reporting data for CIBMTR and for other HCT and cancer-related research. It includes contact information for mentors, FAQs, lists of acronyms and abbreviations, and tips from fellow data managers.
5.0 HUMAN SUBJECTS/HIPAA COMPLIANCE

All Statistical Center personnel, including administrative and data entry staff, are trained in ethical conduct of clinical research, in compliance with policies of the MCW and NMDP Institutional Review Boards (IRBs). All personnel on the CIBMTR Milwaukee and Minneapolis campuses are required to complete training through the Collaborative IRB Training Initiative Program (CITI). CITI completion certificates are on file for CIBMTR staff in administrative offices on the respective campuses, and are renewed every two years as required. New employees are required to complete this training when hired and existing employees are required to maintain certification.

All CIBMTR observational studies use existing data from records of patients treated in participating CIBMTR institutions. Studies performed using these data have been continuously reviewed by the MCW IRB since 1987. The MCW IRB reviews the CIBMTR research program and approves its activities annually (HRCC# 056-87). This approval review is active through March 2010. The NMDP IRB also approves activities of the CIBMTR research program annually. This includes approvals for use of the observational database (#2002-0062) and the research sample repository (#1991-0002). Seven other CIBMTR studies also received individual approvals in 2009.

5.1 COMMON RULE

In 1991, the HHS core regulations concerning IRBs and human subject protections became the basis of a common Federal policy on human subject protections. Known as the Common Rule, this policy is adhered to by HHS and 16 other Federal agencies. The main elements of the Common Rule include:

- Requirements for assuring compliance by research institutions;
- Requirements for researchers’ obtaining and documenting informed consent;
- Requirements for IRB membership, function, operations, review of research, and record keeping.

The Common Rule also includes additional protections for certain vulnerable research subjects, as follows:
- Subpart B provides additional protections for pregnant women, in vitro fertilization and fetuses;
- Subpart C contains additional protections for prisoners;
- Subpart D does the same for children.

In the past, CIBMTR collected data under a waiver of informed consent for the central observational database, with a signed agreement assuring that participating teams have active IRB oversight of the research function of submitting observational data. An observational database research protocol and accompanying consent documents were approved by the IRBs of both NMDP and MCW in July 2007 that cover submission of data for research for autologous and allogeneic transplant recipients. The protocol describes the anticipated research uses of the observational database and is accompanied by a consent form for patients and donors. Participating U.S. transplant centers must submit the protocol and consent documents to their local IRBs for review and approval (Section 4.2.4).

In 2008, CIBMTR established a related donor-recipient biologic sample repository for research purposes that is identical to the repository for unrelated donor-recipient pairs currently maintained by the NMDP. A research protocol that covers submission of related and unrelated recipient and donor samples, and its accompanying consent documents, was also approved by both the NMDP and MCW IRBs. Centers participating in the related and unrelated donor repositories must also have local IRB approval for submitting samples to the repository.

Patients enrolled on studies prior to December 2007 are covered by IRB oversight as established by the prior agreements described above. These agreements were considered to be in force until the new protocol was reviewed and approved by the local IRB. As of December 2008, U.S. centers are required to obtain
written IRB-approved consent from new patients to submit CRF data or to include TED data in research studies. Data from patients declining consent for research are not included in research studies, but due to CIBMTR’s status as a Public Health Authority (PHA, see next section), data from these transplants are collected on TED forms and only used in analyses required by the SCTOD contract.

NMDP IRB staff members experienced in actively maintaining compliance with IRB regulations track the IRB approval process and work with transplant centers to obtain approval of the database and repository protocols. Similarly, they ensure that all participating centers maintain active IRB approval on an annual basis. Non-U.S. centers are required to provide assurance to CIBMTR, via a Data Transmission Agreement, that data submission from their site is in compliance with all relevant human subject protections and privacy regulations for their locality. This approach was approved by the MCW and NMDP IRBs.

5.2 PRIVACY RULE: HIPAA

The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule enacted by the U.S. Congress in 1996 applies to health care providers that transmit any health information in electronic form in connection with certain standard transactions, such as health care claims. It ensures the privacy of health care information for all patients.

Historically, CIBMTR has maintained compliance with HIPAA by collecting a limited dataset under a Data Use Agreement with participating centers. Data Use Agreements were approved by MCW’s legal counsel and privacy officer early in 2003 and again in November 2004. However, with receipt of the SCTOD contract, the Office for Civil Rights and the Office of the General Counsel, U.S. Department of Health and Human Services determined that CIBMTR meets the Privacy Rule’s definition of a Public Health Authority (PHA). As such, CIBMTR is authorized by law to collect information necessary for the SCTOD to fulfill its statutory purpose and functions. HCT centers, regardless of their status as a “covered entity” are allowed to disclose protected health information to the CIBMTR without an individual’s written consent or authorization so the CIBMTR can fulfill its statutory obligations as a PHA. In this context, Data Use Agreements are no longer required. All data collected between April 2003 and July 2007 are maintained in compliance with the regulations under which they were collected.

5.3 OFFICE OF INFORMATION TECHNOLOGY SECURITY MEASURES

Physical and technical security measures at CIBMTR have been substantially enhanced since late 2006 to comply with the Federal security standards required by the SCTOD. These include: Appendix III of the OMB Circular A-130, the Computer Security Act of 1987, FIPS 199, HHS Risk Assessment, National Institute of Standards in Technology Special Publications 800-26 and 800-53, and the Federal Information Security Management Act. CIBMTR achieved Certification and Accreditation and Authority to Operate in December 2008 from the Chief Information Officer of HRSA’s Office of Information Technology. These security standards represent a significant elevation in information system security risk control and are more stringent than the standards established by HIPAA.

5.4 GENDER AND MINORITY INCLUSION

CIBMTR rules require that participating centers register all consecutive HCT recipients. The population available for study, therefore, includes women and minorities in the same proportion as they are found in the general HCT population. No patients are excluded on the basis of race or sex. In fact, the CIBMTR database is a valuable resource for determining whether HCT recipients differ from the general population in race or sex and whether patients enrolled in clinical trials differ from the general HCT population in race, sex or other characteristics. A study using these data and documenting decreased access to autologous, related donor and unrelated donor HCT among African-Americans was recently accepted for publication in the journal Cancer:

5.5 INCLUSION OF CHILDREN

CIBMTR rules require that participating centers register all consecutive HCT recipients, regardless of age. About 18% of patients in the CIBMTR database were younger than 18 years of age at time of transplantation. Children are included in most CIBMTR studies, unless the disease of interest (e.g. multiple myeloma) does not occur in the pediatric population or the technology to be studied has substantially different issues to be addressed in children and adults (e.g. comparisons of bone marrow and peripheral blood transplants, and comparisons of bone marrow and cord blood transplants were done separately for children and adults).

Additionally, the Pediatric Cancer and the Immune Deficiency/Inborn Errors of Metabolism Working Committees are committed to facilitating studies focused on issues specific to pediatric HCT recipients.

Table 5.1 shows the race and gender distribution for the CIBMTR database as a whole and for the last five years for which complete data are available, 2004 through 2008. The proportion of patients without race information is higher in the TED-only database because some non-U.S. TED-only centers are precluded from providing this information by their local regulations.

<table>
<thead>
<tr>
<th></th>
<th>Native American</th>
<th>Asian/ Pacific Isle</th>
<th>Black</th>
<th>Hispanic</th>
<th>White</th>
<th>Unknown</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>TED database</td>
<td>Male 248</td>
<td>7,554</td>
<td>7,491</td>
<td>4,516</td>
<td>105,238</td>
<td>31,582</td>
<td>156,629</td>
<td>54.0</td>
</tr>
<tr>
<td>All Years</td>
<td>Female 214</td>
<td>5,541</td>
<td>7,267</td>
<td>3,490</td>
<td>86,993</td>
<td>28,759</td>
<td>132,264</td>
<td>45.6</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>22</td>
<td>23</td>
<td>20</td>
<td>198</td>
<td>725</td>
<td>988</td>
<td>0.4</td>
</tr>
<tr>
<td>Total</td>
<td>462</td>
<td>13,117</td>
<td>14,781</td>
<td>8,026</td>
<td>192,429</td>
<td>61,066</td>
<td>289,881</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>0.1% 4.5% 5.1% 2.8% 66.4% 21.1%</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>TED database</td>
<td>Male 67</td>
<td>1,854</td>
<td>2,885</td>
<td>670</td>
<td>33,286</td>
<td>6,027</td>
<td>44,789</td>
<td>58.8</td>
</tr>
<tr>
<td>2004-2008</td>
<td>Female 69</td>
<td>1,415</td>
<td>2,448</td>
<td>434</td>
<td>22,591</td>
<td>4,227</td>
<td>31,184</td>
<td>41.0</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>8</td>
<td>5</td>
<td>5</td>
<td>48</td>
<td>93</td>
<td>159</td>
<td>0.2</td>
</tr>
<tr>
<td>Total</td>
<td>136</td>
<td>3,277</td>
<td>5,338</td>
<td>1,109</td>
<td>55,925</td>
<td>10,347</td>
<td>76,132</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>0.2% 4.3% 7.0% 1.5% 73.4% 13.6%</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRF database</td>
<td>Male 126</td>
<td>3,762</td>
<td>2,878</td>
<td>3,644</td>
<td>47,238</td>
<td>2,247</td>
<td>59,895</td>
<td>54.7</td>
</tr>
<tr>
<td>All Years</td>
<td>Female 113</td>
<td>2,717</td>
<td>2,827</td>
<td>2,567</td>
<td>39,507</td>
<td>1,862</td>
<td>49,593</td>
<td>45.2</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>4</td>
<td>6</td>
<td>10</td>
<td>56</td>
<td>31</td>
<td>107</td>
<td>0.1</td>
</tr>
<tr>
<td>Total</td>
<td>239</td>
<td>6,483</td>
<td>5,711</td>
<td>6,221</td>
<td>86,801</td>
<td>4,140</td>
<td>109,595</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>0.2% 5.9% 5.2% 5.7% 79.2% 3.8%</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRF database</td>
<td>Male 39</td>
<td>825</td>
<td>872</td>
<td>1,560</td>
<td>10,667</td>
<td>449</td>
<td>14,412</td>
<td>59.1</td>
</tr>
<tr>
<td>2004-2008</td>
<td>Female 42</td>
<td>635</td>
<td>804</td>
<td>1,036</td>
<td>7,139</td>
<td>277</td>
<td>9,933</td>
<td>40.7</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>28</td>
<td>21</td>
<td>57</td>
<td>0.2</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>1,461</td>
<td>1,678</td>
<td>2,601</td>
<td>17,834</td>
<td>747</td>
<td>24,402</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>0.3% 6.0% 6.9% 10.6% 73.1% 3.1%</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6.0 INFORMATION TECHNOLOGY SERVICES

6.1 INFORMATION TECHNOLOGY SUPPORT

IBMTR information systems resources and technologies are supplemented by the NMDP Bioinformatics Department, under the direction of Martin Maiers. These integrated information technology (IT) activities are expected to continue.

The role of the Milwaukee IT group under the direction of Huoy-Jii Khoo is to provide back-end operation and support for CIBMTR research objectives:

- To develop and maintain a data pipeline from the FormsNet2 data entry system to the observational research data repository in Milwaukee;
- To maintain the quality and integrity of data obtained through the pipeline by processing and validating the incoming data from FormsNet2;
- To process and disseminate data in the observational database by making it available to CIBMTR staff, statisticians, and external partners for research purposes and studies.

CIBMTR has spent considerable time and effort since the SCTOD contract was received (with NMDP support as noted) to develop two important initiatives for facilitating electronic data submission for all centers: FormsNet2 and AGNIS (A Growable Network Information Service). In addition, substantial improvements to all of CIBMTR’s IT functions and structures occurred in 2008 and 2009.

6.1.1 FormsNet™2

FormsNet2 is the Web-based application developed for submission of outcomes data. This system allows transplant centers to electronically submit data to the CIBMTR on TED forms and CRFs. Its features include real-time error validation and override capabilities and access to Forms Due Reports.

The major responsibility for FormsNet2 development lies with the Bioinformatics Department of NMDP and is supported by funds from NMDP and the Office of Naval Research.

Four major and three minor updates to FormsNet2 took place in 2009, adding functionalities requested by transplant centers and making the forms submission and retrieval processes easier and more secure. Forms Due Reports became available online in January 2009, and the capacity to submit several additional forms via FormsNet2 was gained during the year.

FormsNet2 eventually will offer pre-programmed queries for several outcomes reports, including the Uniform Request for Information report used by most U.S. insurers, as well as allowing customized reports to be generated. An interface with the NMDP adult donor and cord blood databases already allows data on unrelated donor grafts (e.g. HLA, infectious disease markers, donor sex and weight) and cord blood units (e.g. processing procedures, cell counts, etc.) to be provided directly from the NMDP databases to CIBMTR, decreasing both the burden on HCT centers and the possibility of data entry errors.

6.1.2 A Growable Network Information System (AGNIS)

Centers are increasingly asked to report the same data to multiple entities, as well as capture it for their own internal research and patient care requirements. CIBMTR (in collaboration with NMDP Bioinformatics) created AGNIS, which facilitates data sharing from diverse database systems without manual re-entry into a specific electronic interface. Using AGNIS, participating centers may collect their own data in the way that works best for them and share it with CIBMTR and others who link to AGNIS, facilitating an “enter once, use often” capability.

AGNIS is an open source Web service that communicates HCT data using a secure, standards-based system. It eliminates duplicate data entry because data enter the electronic network once, with AGNIS facilitating subsequent distribution and synchronization between databases. AGNIS software, distributed under a public license at www.agnis.net, can be installed by any interested center.
The first release of AGNIS took place in March 2009. AGNIS Version 1.0 allows centers to submit data to CIBMTR. AGNIS Version 2.0 allows CIBMTR to return data to centers. As of the end of 2009, one beta site was successfully submitting selected forms to CIBMTR through AGNIS and several other centers are at various stages of becoming beta sites. Support for the beta sites has been made available in several formats:

- Application download and documentation available on www.agnis.net;
- A Google group for exchange of highly technical support;
- Weekly calls between developers and beta sites.

AGNIS was developed using and building on open source tools available from the NCI and other well-supported projects. Work continues on AGNIS to better facilitate electronic data exchange between centers and the CIBMTR.

Data elements are being “curated” with the NCI’s caDSR so that all data exchanged will comply with a national data standard. Curation involves identifying data elements on different forms and standardizing them so that the elements are consistent among both CIBMTR forms and a national dictionary, in order to enhance communication and collaboration in clinical research.

The common data elements curated in caDSR represent most of the fields captured on CIBMTR forms. As noted in previous Progress Reports, the labor-intensive process for curation of CIBMTR forms continues to be a major challenge, and required many hours of additional work in 2009 from individuals with special skills, dedicated focus and knowledge about HCT. CIBMTR continues to collaborate with NCI, and recently contracted with two additional curators to support this task.

### Table 6.1 Forms received via FormsNet2 in 2009

<table>
<thead>
<tr>
<th>Form #</th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>Jun</th>
<th>Jul</th>
<th>Aug</th>
<th>Sep</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>574</td>
<td>530</td>
<td>617</td>
<td>667</td>
<td>646</td>
<td>615</td>
<td>629</td>
<td>578</td>
<td>450</td>
<td>430</td>
<td>312</td>
<td>382</td>
</tr>
<tr>
<td>2004</td>
<td>254</td>
<td>243</td>
<td>295</td>
<td>367</td>
<td>295</td>
<td>264</td>
<td>296</td>
<td>233</td>
<td>197</td>
<td>259</td>
<td>152</td>
<td>153</td>
</tr>
<tr>
<td>2005</td>
<td>458</td>
<td>560</td>
<td>691</td>
<td>755</td>
<td>554</td>
<td>443</td>
<td>461</td>
<td>452</td>
<td>311</td>
<td>538</td>
<td>253</td>
<td>327</td>
</tr>
<tr>
<td>2006</td>
<td>754</td>
<td>684</td>
<td>1116</td>
<td>813</td>
<td>823</td>
<td>719</td>
<td>636</td>
<td>613</td>
<td>572</td>
<td>666</td>
<td>537</td>
<td>607</td>
</tr>
<tr>
<td>2100</td>
<td>619</td>
<td>545</td>
<td>702</td>
<td>680</td>
<td>604</td>
<td>550</td>
<td>603</td>
<td>492</td>
<td>549</td>
<td>573</td>
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<td>488</td>
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<tr>
<td>2200</td>
<td>974</td>
<td>997</td>
<td>1,083</td>
<td>1,257</td>
<td>1,139</td>
<td>1,259</td>
<td>1,115</td>
<td>1,015</td>
<td>954</td>
<td>1,026</td>
<td>802</td>
<td>930</td>
</tr>
<tr>
<td>2300</td>
<td>920</td>
<td>1,067</td>
<td>1,094</td>
<td>926</td>
<td>1,168</td>
<td>1,195</td>
<td>930</td>
<td>863</td>
<td>865</td>
<td>971</td>
<td>832</td>
<td>1,172</td>
</tr>
<tr>
<td>2301</td>
<td>151</td>
<td>194</td>
<td>89</td>
<td>113</td>
<td>32</td>
<td>86</td>
<td>88</td>
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<td>29</td>
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<tr>
<td>2400</td>
<td>1,375</td>
<td>1,334</td>
<td>1,654</td>
<td>1,608</td>
<td>1,481</td>
<td>1,763</td>
<td>1,878</td>
<td>1,511</td>
<td>2,067</td>
<td>1,813</td>
<td>1,717</td>
<td>1,775</td>
</tr>
<tr>
<td>2450</td>
<td>4,499</td>
<td>4,765</td>
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<td>4,712</td>
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<td>6,287</td>
<td>5,631</td>
<td>4,171</td>
<td>3,909</td>
<td>5,240</td>
<td>5,177</td>
<td>4,978</td>
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<tr>
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<td>708</td>
<td>637</td>
<td>513</td>
<td>540</td>
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<td>1</td>
<td>14</td>
<td>3</td>
<td>3</td>
<td>12</td>
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<td>0</td>
</tr>
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<td>4</td>
<td>4</td>
<td>8</td>
<td>9</td>
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<td>265</td>
<td>185</td>
<td>192</td>
<td>291</td>
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<td>416</td>
</tr>
<tr>
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<td>1</td>
<td>42</td>
<td>21</td>
<td>18</td>
<td>8</td>
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<td>23</td>
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<td>15</td>
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<tr>
<td>2802</td>
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<td>1,076</td>
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<td>831</td>
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<td>346</td>
<td>771</td>
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<td>757</td>
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<tr>
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<td>680</td>
<td>902</td>
<td>449</td>
<td>518</td>
<td>426</td>
<td>432</td>
<td>456</td>
<td>317</td>
<td>343</td>
<td>404</td>
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<td>342</td>
</tr>
<tr>
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<td>12,203</td>
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<td>14,731</td>
<td>14,038</td>
<td>12,419</td>
<td>16,429</td>
<td>14,525</td>
<td>11,973</td>
<td>11,383</td>
<td>13,692</td>
<td>11,579</td>
<td>12,770</td>
</tr>
</tbody>
</table>

**Total forms received: 159,352**
6.2 SELECTED ADDITIONAL ACCOMPLISHMENTS

A number of important enhancements to both FormsNet2 and AGNIS were implemented in 2009:

- **DBtC (Data Back to Centers).** DBtC is a Web-based application launched by CIBMTR to help transplant centers retrieve data they submitted through FormsNet2 since December 3, 2007, which have been validated by CIBMTR. This application, greatly desired by the centers, was released to U.S. transplant centers in May 2009. DBtC is not designed to replace AGNIS – it gives centers an alternate way to retrieve data, and at least 100 centers were using the application at year end. Additional data and functionalities will be made available in future releases. The initial release:
  - Responds to the most immediate data needs of transplant centers;
  - Uses data available on select types of forms;
  - Provides centers with an alternate way to retrieve their data other than through AGNIS;
  - Provides centers with information about the total number of forms they have submitted.

  
  To ensure the publication of accurate information, CIBMTR generated data summary tables from FormsNet2, enumerating transplants performed. The data were sorted by center, by disease, by graft type, by donor, age, gender, and other relevant characteristics. This information was sent to centers for verification on August 24, 2009. Center staff were asked to review the data for accuracy, and then were given the choice to publish, to correct, or not to publish.

  The CIBMTR IT group built a Web application in 2009 called FN2 Center Volume Data to facilitate this process. It uses ASP.Net, SharePoint, SSRS (SQL Server Reporting Services), JQuery and relevant Web technology to facilitate data reporting. It has two components:
  - **Medical Director Dashboard,** for transplant center Medical Directors and Data Managers to use to view and confirm the statistical report on their Center Volume Data and choose an option that best describes the status of their data (e.g. Data is Complete/Correct; Publish All Data; Data Correction Pending; Publish only Auto, etc.).
  - **CRC Dashboard,** a management interface for CRCs on both campuses to manage these status responses from transplant centers, and to establish a line of communication between CIBMTR and Medical Directors about their FormsNet2 data status. CRCs can follow up, log their comments to the transplant centers, view statistics reports from each center, and enforce decisions if a center has to be contacted for updated data.
  
  These two components are providing a much-improved and efficient management and communication system between transplant centers and CRCs.

- **Database Extract, Transform and Load (ETL).** CIBMTR’s ETL program was developed to extract, transform and load data from FormsNet2 through AGNIS into the CIBMTR observational databases for research purposes. A custom application had to be developed in 2009 to accommodate the two programs’ different formats and values.

The IT team provides tools to support the fundamental research and communication missions of CIBMTR. Other projects the IT group began in 2009 that will continue in the upcoming year include:

- Development and promotion of the CIBMTR Web Presence (Section 7.2).
- Improvements to the self-service Portal for CIBMTR personnel and (eventually) centers to manipulate and interact with their own data entered into FormsNet2.
- Enhancing the secure Web custom application framework for all CIBMTR operations.
- Developing and maintaining a consolidated database. This several-year project began in July 2009, to reconcile and consolidate data from various entities (e.g. CIBMTR and NMDP legacy databases) with ongoing receipt of data provided via FormsNet2 since December 2007.
7.0 OUTREACH ACTIVITIES

7.1 INFORMATION REQUESTS & EDUCATIONAL MATERIALS

Information from CIBMTR studies was disseminated in formal presentations by CIBMTR faculty and others at national and international meetings in excess of 100 times in 2009. CIBMTR data were also used at local and regional meetings for teaching purposes.

CIBMTR aims to provide maximum access to the data it collects. In addition to providing data for proposals and approved studies, CIBMTR receives and responds to requests for information on its www.cibmtr.org and the http://bloodcell.transplant.gov websites, as well as by mail, fax and phone. Through its online data request process, CIBMTR responded to more than 850 requests for information in 2009, which is an increase of 160 requests over the previous year. (Table 7.1 summarizes the sources of these requests.)

Information requests most often come from physicians and patients who are seeking information about transplant outcomes in specific situations, to assist them in their medical decision-making. CIBMTR is generally able to provide this type of information, which is not readily available from the medical literature, within 24-48 hours.

Table 7.1. Requests for information received by CIBMTR, January 1 to December 31, 2009

<table>
<thead>
<tr>
<th>Type of Organization</th>
<th>2008 Total</th>
<th>2009 Total</th>
<th>Percent change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician</td>
<td>490</td>
<td>557</td>
<td>+14%</td>
</tr>
<tr>
<td>Pharmaceutical/Biotech Company</td>
<td>88</td>
<td>153</td>
<td>+74%</td>
</tr>
<tr>
<td>Patient or Relative</td>
<td>20</td>
<td>15</td>
<td>-25%</td>
</tr>
<tr>
<td>Patient Advocacy Group</td>
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<td>57</td>
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<tr>
<td>Market Research Firm</td>
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<td>19</td>
<td>+27%</td>
</tr>
<tr>
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<td>12</td>
<td>+20%</td>
</tr>
<tr>
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<td>2</td>
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</tr>
<tr>
<td>Insurance Company</td>
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<td>14</td>
<td>+40%</td>
</tr>
<tr>
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<td>4</td>
<td>-50%</td>
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<tr>
<td>Student</td>
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<td>13</td>
<td>+8%</td>
</tr>
<tr>
<td>News Media</td>
<td>10</td>
<td>5</td>
<td>-50%</td>
</tr>
<tr>
<td>Law Firm</td>
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<td>1</td>
<td>0%</td>
</tr>
<tr>
<td>Cord Blood Bank</td>
<td>2</td>
<td>3</td>
<td>+50%</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td><strong>685</strong></td>
<td><strong>855</strong></td>
<td><strong>+25%</strong></td>
</tr>
</tbody>
</table>

Registry data is also increasingly used by both individuals and organizations to plan and interpret clinical trials.

The Statistical Center also provides educational materials, which summarize current uses and outcomes of blood and marrow transplantation, upon request. These educational PowerPoint Summary Slides are distributed to all participating centers and others via the CIBMTR Newsletter. They are also posted on the www.cibmtr.org website.

CIBMTR data Summary Slides are updated and published in two parts and distributed twice annually. Part I focuses on trends in the use of HCT according to donor type, graft sources, patient age and transplant regimens. Early outcomes such as mortality rates at day 100 post HCT and causes of death are also included in this series. Part II focuses on survival outcomes by age, disease, transplant and donor type, and by conditioning regimen intensities.
7.1.2 Newsletters

Twice each year, CIBMTR publishes a newsletter for the HCT community. It is available in a printed copy, sent out via email, and posted on the www.cibmtr.org website. The primary audience is transplant center physicians and staff who participate in CIBMTR research by submitting data. Articles feature updates on CIBMTR Working Committees, research programs, data management and collection, newsworthy events in the blood and marrow transplant community, as well as the CIBMTR Summary Slides.

As an additional tool for enhancing communication between the Milwaukee and Minneapolis campuses, an internal monthly newsletter called Campus Connections is distributed via e-mail to staff in both locations. Content for this publication is provided by authors from both campuses, and ranges from upcoming major projects to internal, local events that feature individual and group accomplishments. A list of newly-published journal articles is a regular monthly feature.

7.2 WEBSITE AND INTERNET

During 2009, as in previous years, most visits to the www.cibmtr.org website were from transplant physicians and referring physicians. As can be seen from Table 7.2, the number of visitors and the average amount of information each viewed on the website increased over the previous year.

The www.cibmtr.org public website was undergoing a major redesign at year end, which involved significant resource use from within CIBMTR and NMDP in 2009. Currently housed at the Milwaukee campus, website management will be moved to Milwaukee in 2010. When the redesign is completed in January 2010, it will be a better, more user-friendly source of HCT information for the public and for physicians, scientists and others involved in HCT practice and research.

The www.cibmtr.org redesign is just one facet of a larger Web undertaking – the CIBMTR “Web Presence” project, which is comprised of three distinct websites, each with its own purpose and security model. CIBMTR was awarded an American Recovery and Reinvestment Act of 2009 grant to optimize and strengthen its Web Presence to provide better access to HCT information to the scientific community and the public.

The Web Presence project will mean that, depending on their credentials, a website user will have access to the Public (main) site, the Collaborative site or the Portal site. The goal is for each site to provide those who need information or to collaborate with CIBMTR – particularly transplant centers, Working Committee members and corporate partners – with the level of access they need, with a single sign-on to verify their credentials.

The Public website, among the many types of information it contains, posts answers to the questions that are most frequently asked of the CIBMTR. The redesign will make it a more efficient, intuitive and searchable tool for sharing knowledge and managing information. Access to this site is unrestricted and includes information designed for anyone seeking to learn about the research being done by CIBMTR (see Table 7.1).

The Portal and Collaborative sites are specialized, password-protected areas of the CIBMTR Web Presence, to be used for the organization to exchange confidential information with transplant centers and other data users.

The Portal site (https://portal.cibmtr.org) includes the Global Contact Management (GCM) system, the DBTC application (Section 6.2), and other custom applications that will serve the needs of CIBMTR partners, including investigators, transplant centers, data managers, clinical research coordinators, and others.

<table>
<thead>
<tr>
<th>Table 7.2 <a href="http://www.cibmtr.org">www.cibmtr.org</a> website usage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Number of visitors to website</td>
</tr>
<tr>
<td>Average number of pages viewed</td>
</tr>
<tr>
<td>Length of time spent on site</td>
</tr>
</tbody>
</table>
statisticians, corporate partners, and more. As of the end of 2009, 181 centers (308 individuals) were registered to use the Portal website for DBtC.

The Collaborative site is based on the SharePoint Server 2007, and is taking the CIBMTR Web-based infrastructure to a level substantially ahead of many in the industry. The collaborative site, located at https://collaborate.cibmtr.org, is being designed for use by all CIBMTR working partners, allowing them better, more secure access to managing their information housed on the CIBMTR site.

Working Committee members in particular will be able to share protocol documents, confidential Working Committee information, data, and manuscript drafts in real time with each other when the site is fully functional.

As part of its SCTOD responsibilities, CIBMTR also participates in the development, maintenance and data provision for a website under the HHS banner, http://bloodcell.transplant.hrsa.gov/index.htm.

<table>
<thead>
<tr>
<th>Country</th>
<th>Percent</th>
<th>Number of visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>69.4%</td>
<td>116,530</td>
</tr>
<tr>
<td>Unknown</td>
<td>6.7%</td>
<td>11,314</td>
</tr>
<tr>
<td>China</td>
<td>5.5%</td>
<td>9,254</td>
</tr>
<tr>
<td>Canada</td>
<td>2.9%</td>
<td>4,891</td>
</tr>
<tr>
<td>Japan</td>
<td>1.2%</td>
<td>2,032</td>
</tr>
<tr>
<td>Australia</td>
<td>1.1%</td>
<td>1,893</td>
</tr>
<tr>
<td>France</td>
<td>1.1%</td>
<td>1,838</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1.1%</td>
<td>1,825</td>
</tr>
<tr>
<td>Germany</td>
<td>1.0%</td>
<td>1,697</td>
</tr>
<tr>
<td>Brazil</td>
<td>1.0%</td>
<td>1,689</td>
</tr>
<tr>
<td>Other</td>
<td>8.9%</td>
<td>14,942</td>
</tr>
</tbody>
</table>

7.3 MEETINGS

Each year brings new opportunities for faculty and staff participation in a variety of internal and external meetings to enhance the research mission of CIBMTR. These serve many needs, including communication between various CIBMTR committee members that operate in diverse geographical areas, team building, educational sessions, process reviews and more.

7.3.1 BMT Tandem Meetings

CIBMTR collaborates with ASBMT to hold joint annual meetings of the two organizations. The BMT Tandem Meetings are a means to reach a common audience and share knowledge, while making efficient use of resources. This combined meeting attracts a large number of attendees each year; 2,457 participants from 45 countries attended the meetings in Tampa in February 2009. A major focus of the BMT Tandem Meetings is to create a venue where all aspects of CIBMTR’s work can be advanced.

The 2009 BMT Tandem Meetings included a full scientific agenda of HCT-related research presentations, summaries of CIBMTR activities, reviews of completed studies and discussions of planned studies, special educational workshops for data management personnel, BMT pharmacists, nurses, BMT center administrators, and a pediatric special interest group. Investigators submitted 470 abstracts for the 2009 meeting, and 498 were submitted for the 2010 meeting.

Since it attracts so many people with an active interest in HCT, the BMT Tandem Meetings provide an opportunity for other groups to meet, including FACT, the BMT CTN, PBMTC and others. Continuing Medical Education and Continuing Education credits are issued through MCW to physicians and allied health professionals from the United States attending these meetings. Dr. Mary Horowitz is the Continuing Medical Education director.

Medical Directors met during the 2009 BMT Tandem Meetings to review the recommendations made during the 2008 Center-Specific Outcomes Forum, and to approve them prior to their being sent to HRSA for enactment. Meetings of the CIBMTR
Working Committees, Advisory Committee, Clinical Trials Advisory Committee and Consumer Advocacy Committee were also held in conjunction with the 2009 BMT Tandem Meetings. Several of these groups also took advantage of the NMDP Council Meeting in November 2009 to meet face-to-face.

During the remainder of the year, these committees meet via teleconference and in conjunction with other scheduled meetings of national societies (e.g. ASH and American Society of Clinical Oncology).

### 7.3.2 Other Meetings

The wide variety of meetings CIBMTR staff participate in help in the research process by providing opportunities for better communication, networking, educational opportunities and providing an environment where new scientific ideas related to better HCT outcomes can arise. In 2009:

- A second Information Technology Summit was held in Minneapolis Sept. 2-3. The focus of this meeting was more technical than the previous year’s summit, and covered data standards and interoperability in depth. It was attended by about 135 participants, including IT staff, medical directors, data managers, and others.
- CIBMTR hosted a booth at the ASH meeting in December 2009. CIBMTR generally holds ancillary meetings, either formal or informal, at this meeting as well.
- A GVHD Workshop, co-sponsored by NHLBI, NCI, NIAID, FDA, CIBMTR, and ASBMT, was held May 19, 2009, to consider appropriate study endpoints and designs for evaluating agents and strategies aimed at reducing or treating GVHD. About 200 people participated.

Other meetings that involve significant participation by CIBMTR staff included:

- The NMDP annual Council Meeting in November;
- The CIBMTR Clinical Research Professionals/Data Management Fall Conference (Section 4.3.2);
- Worldwide Network for Blood and Marrow Transplantation (WBMT) meetings;
- Specialty meetings on “hot” topics, for example CIBMTR/EBMT/NIAID workshops on disease-specific applications of transplantation such as multiple sclerosis.

Planning began in 2009 for combined quarterly CIBMTR staff meetings on the two campuses, to begin in January. These teleconference-based meetings were designed to share information between the two campuses, provide updates on ongoing projects and new initiatives, discuss progress on strategic planning programs, departmental objectives and measures, and to highlight staff achievements.
8.0 SIGNIFICANCE/IMPACT OF CIBMTR RESEARCH

CIBMTR provides a unique resource of information and expertise to the medical and scientific communities. It serves a vital role in improving transplant outcomes, access to transplantation, and safer procedures, through its role as a facilitator of HCT research. The studies being conducted through the CIBMTR’s Working Committees are outlined in Section 10. Some of the most important are looking at the following issues in HCT:

- Determination of transplant outcomes in rare diseases, in common diseases for which transplants are rarely performed such as low-grade non-Hodgkin lymphoma and in new indications like autoimmune diseases.
- Description of trends in transplant activity such as increasing use and success in older patients, improved outcomes in specific diseases and availability and appropriateness of use.
- Identification of factors affecting transplant outcomes, including patient-related factors like age and performance score, disease-related factors like cancer stage and duration, and treatment-related factors like optimal pre-transplant therapy and conditioning regimens.
- The relative efficacy of HLA-identical sibling, alternative allogeneic donor and autologous transplants in specific diseases.
- The relative efficacy of transplant and non-transplant treatments.
- Long-term effects of HCT on quality of life and late complications like second cancers.
- Optimal statistical models to study post-transplant events.

CIBMTR enhanced its commitment in 2009 to:
- Health Services Research examining quality of life for transplant donors and recipients, and improving access to HCT;
- Collecting data on outcomes of other therapeutic applications of hematopoietic stem cells;
- Continued development of new biostatistical methodologies for analyzing HCT;
- Improving access to data and providing a better public outreach by redesigning and improving the www.cibmtr.org website;
- Collaborating with domestic and international organizations in the exchange of data to increase available data worldwide to study HCT for rare indications and new HCT technologies;
- Continued involvement as a founding member society of Worldwide Network for Blood and Marrow Transplantation, and activities planned in collaboration with the World Health Organization.

The inclusive nature of CIBMTR Working Committees and data access policies mean that CIBMTR data are available to a broad range of investigators in the field. Statistical Center staff members help make them more meaningful for physicians and patients dealing with difficult clinical decisions. Statistical Center funding is leveraged by thousands of hours of voluntary effort from physicians and scientists using CIBMTR data to address important issues in HCT and other cancer treatments. Integration with other NIH and HRSA-funded efforts (e.g. AGNIS, BMT CTN, and SCTOD) assures that these funds are used efficiently to provide maximum value to the scientific and medical communities.
9.0 CIBMTR STUDIES

9.1 STUDY PROPOSALS

CIBMTR supports investigators in conducting observational studies in HCT. Anyone willing to actively participate in the conduct of the study and follow the study development and management process may propose a study. In 2009, 84 proposals were submitted to CIBMTR for consideration by its Working Committees.

Prior to submitting a proposal, CIBMTR encourages investigators to review its website, including the CIBMTR Data Collection Forms, to familiarize themselves with the data fields available in the database, the list of already published works to review what has already been studied, and the list of studies in progress to determine what is ongoing.

Proposals are submitted to the CIBMTR Statistical Center, where they are assigned a number and distributed to the MS Biostatistician and Scientific Director of the relevant Working Committee. Statistical Center staff review all proposals for scientific merit, feasibility, overlap with other studies, etc. If duplication is identified, the proponent may be asked to join the Writing Committee of an ongoing study or combine their study proposal with another.

In advance of the February BMT Tandem Meetings, the Working Committee MS Biostatistician prepares a table of characteristics of patient data based on the population defined in the proposal. This is used during the presentation at the Working Committee meeting. Investigators are encouraged to personally present their proposals to the full Working Committee. After presentation and discussion, Working Committee members vote on the proposals, assigning a priority score to each.

Working Committee leadership makes its recommendations, based on the priority score assigned to each proposal, their requirements for biostatistician time, and allocation of resources within CIBMTR.

Most proposals will follow this path. However, occasionally a proposal deemed of high merit may be forwarded directly to the Working Committee for consideration during the year to be “fast tracked.”

If a study requires biological samples from the NMDP Research Sample Repository, in addition to the review process described here, investigators must include a biosketch or brief curriculum vitae documenting experience in the laboratory methods proposed. The NMDP Histocompatibility Advisory Group (Appendix E) also reviews these proposed studies before samples are distributed.

Based in part on a recommendation from the Scientific Review Panel (but already in motion before the panel convened), a monitoring system was established to determine the time from approval to completion of observational studies. The goal is to speed up the progress of studies through Working Committees from project proposal to published study. To effect this change, additional MS Statisticians are being hired, and CRCs and Administrative Assistants are working more closely with the Statisticians to move studies along more quickly. Once benchmarks are assessed, metrics for improvement will be established.

9.2 STUDY STAGES

Once a study proposal is accepted by a Working Committee, the PI of that study is asked to sign a Letter of Commitment, agreeing to put reasonable efforts into completing each stage of study development as efficiently and quickly as possible. Letters of Commitment delineate the responsibilities and expectations of both the PI and the Statistical Center. This requirement was implemented last year to clarify investigator responsibilities and to shorten study durations from proposal to publication. Fifty-two letters were sent to new PIs in 2009, in addition to the 221 that were sent out the previous year when this requirement was implemented.
Following are the stages of study development as they are conducted by CIBMTR Working Committees. This process pertains to studies for which CIBMTR provides data and statistical expertise. Data sets are also made available to investigators who have their own statistical resources. Manuscripts resulting from these analyses are reviewed and approved by the CIBMTR prior to journal submission.

9.2.1 Protocol development.
The first responsibility of a PI is to develop the initial study proposal into a comprehensive study protocol, with the help of invited Working Committee members. Study protocols are used by CIBMTR’s statisticians to prepare data files for analysis and define the detailed study design. This crucial document drives everything that happens as the study progresses. Once received by the Statistical Center, the draft is further refined in collaboration with the Working Committee Statisticians, Scientific Director and Chairs. A table with a preliminary description of the proposed study population is added and the comprehensive draft protocol is presented at a weekly Statistical Center meeting for refinement.

9.2.2 Supplemental forms/data collection.
Most studies will use data collected routinely on existing forms, but in special cases where an important study cannot be done without supplemental data, collection of a minimal amount of additional data may be undertaken. If the study requires supplemental collection (e.g. information not collected on CRFs), development of a supplemental form will be required prior to contacting centers for that additional data. These forms are prepared by Statistical Center staff in collaboration with the PI and Committee Co-chairs.

9.2.3 Data file preparation.
The objective of study file preparation is to create a data file of eligible subjects who are consecutively treated at participating centers with adequate follow-up, minimal missing data fields, and in large enough numbers to give the analysis sufficient statistical power to meet the stated study objectives. This process involves a series of steps by the MS Statistician, sometimes working with the CRC, to ensure data quality. They include finalizing:

- The adequacy of follow-up, and taking steps to obtain additional follow-up information if necessary;
- The extent and nature of missing values and their potential effect on the study;
- Data discrepancies/outliers, and reconciling these by examination of data collection forms, communication with centers and the PI;
- Included and excluded patients so that the investigators can determine whether the final study population is representative of the target population (unbiased sample).

9.2.4 Analysis.
Analysis proceeds in several phases. The first generally includes a detailed description of the patient population and univariate analyses of study endpoints. These data are distributed to Writing Committee members for their suggestions and comments. An iterative process then ensues. The PI works with Statistical Center staff to summarize and discuss comments from the Writing Committee. If substantive comments must be incorporated, the process is repeated until a final analysis is available. This final analysis serves as the basis for the manuscript.

9.2.5 Manuscript preparation.
The PI has primary responsibility for manuscript preparation, and is expected to prepare a draft manuscript within 30 days of receipt of final analysis results. This draft is then reviewed, revised as necessary, and approved by Working Committee Leadership. They ensure that description and interpretation of the statistical analyses are accurate, as well as contributing to the fundamental message of the manuscript. The Writing Committee includes persons who make a significant contribution to study development.

9.2.6 Submission.
The Statistical Center staff is responsible for submitting the manuscript and corresponding with the chosen journal. Usually the corresponding author is the Scientific Director. The MS Statistician forwards comments from editors and reviewers to the PI, Scientific Director and PhD statisticians. The PI is expected to prepare a response, if necessary. Communication with the journal, including any re-submissions, is done by Statistical Center personnel.
Table 9.1 CIBMTR Working Committee studies conducted in collaboration with other organizations in 2009

<table>
<thead>
<tr>
<th>Working Committee</th>
<th>CIBMTR only</th>
<th>Collabor</th>
<th>Total</th>
<th>Collaboration with:</th>
</tr>
</thead>
<tbody>
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<td>Acute Leukemia</td>
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<td>3</td>
<td>21</td>
<td>Gruppo Italiano Malattie Ematologiche Ddell'Adulto; Programa para el Estudio de la Terapéutica en Hemopatía Maligna; Australasian Bone Marrow Transplant Recipient Registry; European Acute Promyelocytic Leukemia Group; Cancer and Lymphoma Group B; International MDS risk analysis workshop; Groupe Francophone des Myelodysplasies; MD Anderson Cancer Center (MDACC); Dana Farber Cancer Institute (DFCI); Fred Hutchinson Cancer Research Center (FHCRC); EBMT; Pavia group; International Vidaza High-Risk MDS Survival Study Group; Nordic Group</td>
</tr>
<tr>
<td>Autoimmune Disease</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td>FHCRC; EBMT</td>
</tr>
<tr>
<td>Cellular Therapies</td>
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<td>1</td>
<td>3</td>
<td>International Society for Cellular Therapy; AABB; ASBMT; Production Assistance for Cellular Therapies</td>
</tr>
<tr>
<td>Chronic Leukemia</td>
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</tr>
<tr>
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<td>1</td>
<td>15</td>
<td>RCI BMT; NMDP OPA</td>
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<tr>
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<td>8</td>
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<td>International Studies</td>
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</tr>
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<td>1</td>
<td>15</td>
<td>United States Renal Disease System (USRDS)</td>
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<tr>
<td>Solid Tumors</td>
<td>5</td>
<td>1</td>
<td>6</td>
<td>EBMT</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>206</strong></td>
<td><strong>42</strong></td>
<td><strong>248</strong></td>
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</tbody>
</table>
9.3 ADDITIONAL PUBLICATIONS

Following are papers published by CIBMTR personnel in 2009 that do not fall within the confines of one of the 19 Working Committees, yet demonstrate use of HCT research or research methodologies, and which showcase the high level of expertise within the CIBMTR in performing HCT research.

- Gale RP, Eapen M, Logan B, Zhang MJ, Lazarus HM. Are there roles for observational database studies and structured quantification of expert opinion to answer therapy controversies in transplants? Bone Marrow Transplant 2009 43:435-446.

The next section is a complete listing of Working Committee studies, categorized by studies that have published results, those that have preliminary results, studies in progress, and planned studies. Visit www.cibmtr.org for a status update of CIBMTR Working Committee studies.
10.1 ACUTE LEUKEMIA WORKING COMMITTEE

Committee Leadership

Co-Chair: Martin Tallman, MD, Northwestern University
E-mail: m-tallman@northwestern.edu

Co-Chair: John DiPersio, MD, PhD, Washington University, St. Louis, MO
E-mail: jdipersi@im.wustl.edu

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E-mail: weisd001@umn.edu

Acute Leukemia Working Committee Publications

Study # LK02-02


Purpose: To identify factors associated with outcomes for patients undergoing allogeneic hematopoietic stem cell transplantation (HCT) for therapy-related myelodysplastic syndromes (t-MDS) and acute myeloid leukemia (t-AML).

Patients/Methods: We analyzed outcomes in 868 persons with t-AML (n=545) or t-AML (n=323) receiving allogeneic HCT from 1990-2004.

Results: Treatment-related mortality and relapse were 48% and 31% at 5 years. Disease-free (DFS) and overall survival (OS) were 21% and 22% at 5 years. In multivariate analysis for survival, four risk factors: (1) age >35 years; (2) poor risk cytogenetics; (3) AML not in remission or MDS untreated; and (4) donor other than an HLA-identical sibling had adverse impacts on DFS and OS. Five-year survival for subjects with none, 1, 2, 3 or 4 of these risk factors were 50%, 26%, 21%, 10% and 4%, respectively.

Conclusion: These data suggest that younger patients with treatment-induced AML/MDS in remission at the time of transplantation are most likely to benefit from allogeneic transplants, particularly with available matched sibling donors. However, those with more than two of the identified high risk factors have poorer outcomes and need alternate transplant or non-transplant approaches considered.
Study # LK07-03a

Purpose: To assess outcomes in older patients with AML and MDS who undergo allogeneic HCT.

Patients/Methods: We analyzed patients receiving reduced-intensity conditioning HCT for MDS/AML in first complete remission (CR1) from 1995-2005 to examine the effects of age on outcome. Age cohorts were compared.

Results: Univariate analyses demonstrated no age group differences in non-relapse mortality (NRM), grade II-IV acute graft-versus-host disease (GVHD), chronic GVHD or relapse. Patients age 40-54, 55-59, 60-64 and ≥ 65 years had two-year survival rates as follows: AML, 44 (37-52)% 50 (41-59)% 34 (25-43)% and 36 (24-49)% (p=0.06); MDS, 42 (35-49)% 35 (27-43)% 45 (36-54)% and 38 (25-51)% (p=0.37). Multivariate analysis revealed no significant impact of age on NRM, relapse, DFS, or overall survival (OS) (all p >0.3). Greater HLA disparity adversely affected two-year NRM, disease-free survival (DFS), and OS. Unfavorable cytogenetics adversely impacted relapse, DFS and OS. Better pre-HCT performance status predicted improved two-year OS.

Conclusion: Outcomes of HCT in older adults undergoing allogeneic HCT are no different than those for younger adults. Age should not be the limiting factor for allogeneic HCT in older patients.

Acute Leukemia Working Committee Preliminary Results

Study # R02-05
Title: Unrelated donor HCT in acute myelogenous leukemia (AML) and acute lymphoblastic leukemia (ALL) patients who failed an autologous transplant

Study Chair: James M. Foran (University of Alabama at Birmingham)

Steven Z. Pavletic (National Institutes of Health)

MS Statistician: Manza Agovi (magovi@mcw.edu)

PhD Statistician: Brent Logan (blogan@mcw.edu)

Study Status: Manuscript preparation

Purpose: To determine the outcome of patients who received an unrelated donor (URD) HCT after failing a previous autologous HCT.

Patients/Methods: Patients who received a second URD bone marrow or peripheral blood HCT for AML or ALL after a failed prior autologous transplant for relapse or persistent disease between 1995 and 2005. Multivariate analysis performed for AML patients; univariate analysis for ALL due to small sample size.

Results: ALL patients had an OS of 11% at 3 years (95%CI, 4-20). Donor-recipient cytomegalovirus status -/- (relative risk [RR] 0.64, 0.44-0.94, p<0.001), Karnofsky score ≥90 (relative risk [RR] 0.62, 0.47-0.82, p<0.001), and RIC/nonmyeloablative HCT (RR 0.62, 0.47-0.82, p<0.001) were associated with better leukemia-free and OS for the AML patients. While there was a significant negative effect of acute GVHD on OS (RR 1.92, 95%CI: 1.36-2.71, p<0.001) and TRM (RR 2.23, 95% confidence interval [CI]: 1.43-3.48 p<0.001), there was no effect of chronic GVHD on OS or relapse.

Conclusion: Second URD allogeneic HCT is feasible after failed autologous HCT for AML patients. Excessive TRM and low OS in ALL patients suggest that alternative strategies should be considered in this setting.
Study # LK03-03
Title: HCT in acute leukemia in relapse or primary induction failure: pre-transplant variables define subgroups with different outcomes
Study Chair: Michel Duval (Centre Hospitalier Universitaire Sainte-Justine, Montreal)
MS Statistician: Vincent He (vhe@mcw.edu)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To determine whether some pre-transplant variables may define subgroups of patients with a better prognosis for the use of HCT in acute leukemia without complete remission.
Patients/Methods: 2,255 patients transplanted after myeloablative conditioning regimen between 1995 and 2004 for acute leukemia in relapse or primary induction failure.
Results: Three-year OS was 19% for AML and 16% for ALL patients. For AML patients, five adverse pre-transplant variables significantly impacted survival. For ALL patients, four pre-transplant variables impacted survival. A scoring system was established. AML patients with a score of 0 had a 42% OS at 3 years, whereas OS was 6% for a score ≥3. ALL patients with a score of 0 or 1 had a 46% OS, whereas OS was 9% for a score ≥3.
Conclusion: HCT can induce long-term survival in acute leukemia in relapse or refractory to chemotherapy.

Study # LK04-02
Title: Comparison of myeloablative (MA) vs. reduced-intensity (RIC) vs. non-myeloablative (NMA) autologeneic transplantation in patients with acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS)
Study Chair: Selina M. Luger (University of Pennsylvania)
Michael A. Pulsipher (University of Utah School of Medicine)
Olle Ringdén (Huddinge Hospital)
MS Statistician: Waleska S. Pérez (wperez@mcw.edu)
PhD Statistician: Mei-jie Zhang (meijie@mcw.edu)
Study Status: Submitted
Purpose: To compare MA vs. RIC vs. NMA autologeneic transplantation in patients with AML or MDS.
Patients/Methods: We compared disease status, donor, graft and recipient characteristics with outcomes of 3,731 MA with 1,500 RIC/NMA procedures between 1997 and 2004. Five-year univariate probabilities and multivariate relative risk outcomes of relapse, transplant related mortality (TRM), disease free survival (DFS) and overall survival (OS) are reported.
Results: Adjusted OS at 5 years was 34%, 33%, and 26% for MA, RIC and NMA transplants, respectively. By three years, there was no longer any difference among the groups with respect to TRM. NMA conditioning resulted in slightly inferior DFS and OS, but there was no difference in DFS and OS between RIC and MA regimens.
Conclusion: We found similar outcomes with RIC/NMA versus MA regimens. The data indicate that late TRM negates any early advantage offered by RIC and NMA regimens. Prospective trials are warranted, comparing MA and RIC regimens in patients eligible for either approach.

Study # LK04-03
Title: Comparison of autologous blood cell and HLA-identical sibling transplantation for acute myeloid leukemia (AML) in first complete remission (CR1)
Study Chair: Armand Keating (Princess Margaret Hospital)
MS Statistician: Waleska S. Pérez (wperez@mcw.edu)
PhD Statistician: Gisela Tunes da Silva (tunes@ime.usp.br)
Study Status: Manuscript preparation

Purpose: To study the effect of lower treatment-related mortality after peripheral blood autologous transplantation for AML in CR1.

Patients/Methods: 1,133 patients 19-60 years of age in CR1 reported to the CIBMTR from 1995-2004. Patients receiving autologous peripheral blood (PB) transplants were compared with those receiving HLA-identical myeloablative bone marrow (BM) or PB allogeneic transplants, for TRM, relapse, leukemia-free survival, and overall survival. Outcomes were evaluated in univariate and multivariate analyses using the pseudo-value technique.

Results: Five-year transplant outcomes by univariate analysis for allogeneic BM, allogeneic PB and autologous PB, respectively, were 20% (95% CI17-24%), 26%(21-30%), 45% (38-52%) for relapse (p<0.001); 19%(16-23%), 20% (17-24%), 8%(5-12%) for TRM (p<0.001); 61% (56-65%), 54%(49-59%), 47% (40-54%) for LFS (p=0.13) and 64%(59-68%), 59%(54-64%), 54% (47-60%) for survival (p=0.19).

Conclusion: Autologous transplantation using PB may provide acceptable alternative post-remission therapy for AML CR1 in the absence of a matched sibling donor; hence its role should be re-investigated prospectively.

Study # LK05-01

Title: Outcome of allogeneic hematopoietic cell transplantation (HCT) in acute myelogenous leukemia (AML) with adverse-risk karyotype in first complete remission (CR1) using matched sibling or alternative donors

Study Chair: Vikas Gupta (Princess Margaret Hospital)
Martin S. Tallman (Northwestern Memorial Hospital)

MS Statistician: Vincent He (vhe@mcw.edu)
PhD Statistician: Brent Logan (blogan@mcw.edu)

Study Status: Manuscript preparation

Presentation: Presented orally at the 2009 American Society of Hematology Meeting.

Purpose: To evaluate the prognostic impact of donor type on the outcomes of AML with unfavorable risk cytogenetics in CR1, a patient population considered as an indication for MSD and URD HCT. In patients with AML in CR1, the applications for matched sibling donor (MSD) and unrelated donor (URD) transplantation are different.

Patients/Methods: We evaluated the outcomes of 584 patients (MSD, 226; URD 358). URDs were: well-matched (71%) with no known disparity at HLA A, B, C, DRB1; and, partially matched (29%). Cytogenetics abnormalities were: complex (≥3 abnormalities), 32%; and non-complex further divided as chromosome 7 abnormalities, 25%; chromosome 5 abnormalities, 9%; MLL rearrangements, 18%; t (6;9), 5%; and others, 10%.

Results: In multivariate analysis, well-matched URD and MSD yielded similar leukemia-free survival (LFS) and OS, while outcomes were significantly inferior for partially matched URD. Cytogenetically defined subsets had similar outcomes.

Conclusion: Well-matched URD and MSD lead to similar LFS and OS in AML CR1 patients with unfavorable risk cytogenetics.

Study # LK06-01

Title: Outcome of allogeneic HCT compared to chemotherapy only in AML patients 60 years and older: A CIBMTR/ Cancer and Leukemia Group B (CALGB) Study

Study Chair: Sherif S. Farag (Indiana University School of Medicine)

MS Statistician: Waleska S. Pérez (wperez@mcw.edu)
Kati Maharry (kati.maharry@osumc.edu)
Conclusion: RIC HCT in CR1 is associated with longer leukemia-free survival due to a reduction in relapses in older AML patients. Reducing NRM of HCT will likely lead to significant improvement in overall survival.

Study # LK08-03
Title: The outcome of full-intensity versus reduced-intensity conditioning (RIC) matched sibling or URD transplantation in adults with Philadelphia chromosome negative acute lymphoblastic leukaemia (Ph-ALL) in first and second complete remission (CR1 and CR2)
Study Chair: David I. Marks (Bristol Children’s Hospital)
MS Statistician: Waleska S. Pérez (wperez@mcw.edu)
PhD Statistician: Tao Wang (taowang@mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To assess the efficacy of RIC for allogeneic transplantation using sibling and URD for ALL in CR1 or CR2 by comparing outcomes of 93 patients >16 years who had RIC with 1,428 patients who underwent conventional full-intensity conditioning.
Patients/Methods: The RIC group included busulfan ≤ 9 mg/kg (27), melphalan ≤ 150 mg/m2 (23) or low-dose total body irradiation (36) and others (7). The RIC group was older, and more received peripheral blood grafts, but other prognostic factors were similar.
Results: The RIC vs. full-intensity groups had lower acute grade 2-4 GVHD (39% vs. 46%), less chronic GVHD (34% vs. 42%) but similar TRM. RIC led to slightly more relapse (35% vs. 26%, p=0.08) yet similar age-adjusted survival (38% vs. 43%, p=0.39). Multivariate analysis showed that conditioning intensity did not affect TRM (p=0.89) or relapse risk (RR=1.34, p=0.15), but demonstrated significantly improved OS with KPS>80, CR1, lower white blood counts, well-matched URD or sibling donors, transplant since 2001, age <30y, conditioning with total body irradiation and no T-cell-depletion.
Conclusion: RIC merits further investigation in prospective adult ALL trials.

Acute Leukemia Working Committee Studies in Progress

Study # R02-09
Title: Evaluation of donor leukocyte infusions to treat relapsed hematologic malignancies after related and unrelated donor myeloablative allogeneic stem cell transplantation
Study Chair: Allison W. Loren (Hospital of the University of Pennsylvania)
MS Statistician: Zhiwei Wang (zwang@mcw.edu)
PhD Statistician: TBD
Study Status: Supplemental data collection
Study # LK04-01
Title: Comparison of autologous and allogeneic hematopoietic stem cell transplants for patients with acute promyelocytic leukemia in second complete remission
Study Chairs: Morel Rubinger (CancerCare Manitoba)
Andrew Grigg (Royal Melbourne Hospital)
Jeffrey Szer (Royal Melbourne Hospital)
Jacob M. Rowe (Rambam Medical Center)
Martin S. Tallman (Northwestern Memorial Hospital)
MS Statistician: Waleska S. Pérez (wperez@mcw.edu)
PhD Statistician: TBD
Study Status: Supplemental data collection complete; data file preparation

Study # LK07-01
Title: Cytogenetic risk groups for patients with acute myelogenous leukemia or myelodysplastic syndromes undergoing allogeneic transplantation
Study Chairs: Phillipe Armand (Dana Farber Cancer institute)
Robert J. Soiffer (Dana Farber Cancer institute)
MS Statistician: Waleska S. Pérez (wperez@mcw.edu)
PhD Statistician: TBD
Study Status: Supplemental data collection complete; data file preparation

Study # LK07-02
Title: CIBMTR scoring system to predict the outcome after allogeneic hematopoietic cell transplantation for acute myelogenous leukemia
Study Chair: Jorge Sierra (Hospital Santa Creui Sant Pau)
MS Statistician: Waleska S. Pérez (wperez@mcw.edu)
PhD Statistician: TBD
Study Status: Data file preparation

Study # LK07-03b
Title: Assessment of allogeneic HCT in older patients with non-Hodgkin lymphoma and chronic myelogenous leukemia
Study Chair: Brian McClune (University of Minnesota)
Erica Warlick (University of Minnesota)
MS Statistician: Tanya Pedersen (tpederse@nmdp.org)
PhD Statistician: TBD
Study Status: Data file preparation

Study # LK08-01
Title: Using Landmark analysis to provide updated relapse and leukemia-free or overall survival estimates to patients
Study Chair: Stephanie J. Lee (Fred Hutchinson Cancer Center)
Paul Martin (Fred Hutchinson Cancer Center)
MS Statistician: Waleska S. Pérez (wperez@mcw.edu)
PhD Statistician: TBD
Study Status: Data file preparation
### Study # LK08-02
**Title:** A decision analysis of reduced-intensity conditioning allogeneic HCT for older patients with de novo myelodysplastic syndromes  
**Study Chairs:** John Koreth (Dana Farber Cancer institute)  
Corey Cutler (Dana Farber Cancer institute)  
**MS Statistician:** Waleska S. Pérez (wperez@mcw.edu)  
**PhD Statistician:** TBD  
**Study Status:** Analysis

### Study # LK09-01  
**Title:** Role of CNS therapy for outcome of patients undergoing allogeneic HCT  
**Study Chairs:** Natia Esiashvili (Emory University Hospital)  
John Horan (Emory University Hospital)  
Kuang-Yueh Chiang (Emory University Hospital)  
Ann Haight (Emory University Hospital)  
**MS Statistician:** TBD  
**PhD Statistician:** TBD  
**Study Status:** Protocol received/in development

### Study # LK09-02  
**Title:** Monosomal karyotype and chromosome 7 abnormalities in allogeneic HCT for AML and myelodysplastic syndromes  
**Study Chairs:** Minoo Battiwala (Roswell Park Center Institute)  
Marcelo Pasquini (Medical College of Wisconsin)  
**MS Statistician:** Waleska S. Pérez (wperez@mcw.edu)  
**PhD Statistician:** TBD  
**Study Status:** Protocol received/in development

### Study # LK09-03  
**Title:** Relapsed good risk acute myelogenous leukemia: outcome of patients with core binding factor t(8;21) or inv(16) cytogenetic abnormalities treated with allogeneic or autologous HCT after relapse  
**Study Chair:** Luke Akard (Indiana Blood and Marrow Transplantation)  
**MS Statistician:** Wael Saber (wsaber@mcw.edu)  
**PhD Statistician:** TBD  
**Study Status:** Protocol received/in development

### Acute Leukemia Working Committee Planned Studies

#### Study # LK08-04/IB08-05  
**Title:** Lymphotoxin alpha alleles in acute myelogenous leukemia relapse  
**Study Chair:** Phillip Posch (Georgetown University Medical Center)  
**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)  
**PhD Statistician:** TBD  
**Study Status:** Protocol Development

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10.2 AUTOIMMUNE DISEASES WORKING COMMITTEE

Committee Leadership

Co-Chair: Harold Atkins, MD, FRCPC, Ottawa Hospital  
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Co-Chair: Paulo Muraro, MD, PhD, Imperial College London  
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Statistician: Manza-A. Agovi-Johnson, MPH, CIBMTR Statistical Center Milwaukee  
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Statistician: Kwang Woo Ahn, PhD, CIBMTR Statistical Center, Milwaukee  
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Scientific Director: Marcelo Pasquini, MD, MS, Medical College of Wisconsin  
E-mail: mpasquin@mcw.edu

Autoimmune Diseases Working Committee Preliminary Results

Study # AI06-03

Title: Overview of hematopoietic stem cell transplantation (HCT) for autoimmune diseases (AID)  
performed in North and South America

Study Chair: Peter McSweeney (Rocky Mountain Bone Marrow Transplant Group)  
Marcelo Pasquini (CIBMTR Milwaukee)

MS Statistician: Marcelo Pasquini (mpasquin@mcw.edu)

PhD Statistician: TBD

Study Status: Manuscript preparation

Purpose: To assess HCT as a treatment option for autoimmune diseases.

Patients/Methods: 340 patients with AID who underwent HCT were reported to the CIBMTR from 1996 to 2008  
from 74 North and South American transplant centers.

Results: The most common disease indications for HCT in AID are multiple sclerosis (MS), systemic  
sclerosis and systemic lupus erythematosus. The median age at transplantation is 28 and 40  
years for allogeneic and autologous HCT, respectively. Cyclophosphamide-containing regimens  
either with radiation or antilymphocyte globulin (ATG) are the most common conditioning  
regimens. Among patients with MS, the mean Expanded Disability Status Scale score was 6.0  
and the majority of patients presented with secondary progressive course. Overall survival  
rates after autologous HCT were 90% and 86%, and after allogeneic HCT were 75% and 52% at  
1 and 3 years after transplantation. Fifty patients died and the most common causes of death  
were related to AID, infection and organ failure.

Conclusion: According to data reported to the registry, the activity of transplantation for AID is increasing in  
these regions. Autologous HCT is a treatment option for AID, however selecting patients in the  
peak inflammatory phase of the disease prior to end organ failure would maximize the effect of  
transplantation for these diseases.
Autoimmune Diseases Working Committee Studies in Progress

Study # AI05-02
Title: Cross-sectional analysis of patients with MS who received allogeneic HCT for other indications.
Study Chair: Richard Nash (Fred Hutchinson Cancer Research Center)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: Brent Logan (blogan@mcw.edu)
Study Status: Manuscript preparation

Study # AI06-01
Title: Hematopoietic stem cell transplantation for autoimmune cytopenias.
Study Chair: Harold Atkins (Ottawa General Hospital)
          Marcelo Pasquini (Medical College of Wisconsin)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: TBD
Study Status: Manuscript preparation

Study # AI07-01
Title: Work-up guidelines of patients with MS who present for allogeneic HCT for other indications: Results from a consensus panel
Study Chair: Harold Atkins (Ottawa General Hospital)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: TBD
Study Status: Manuscript preparation

Study # AI09-01
Title: Long-term follow up analyses of outcomes from autologous HCT for multiple sclerosis
Study Chair: Paolo Muraro (Imperial College of Medicine)
          Riccardo Saccardi (European Bone Marrow Transplant-Autoimmune Working Party)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

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10.3 CELLULAR THERAPIES WORKING COMMITTEE

Committee Leadership

Co-Chair: Joshua Hare, MD, University of Miami  
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Co-Chair: Helen Heslop, MD, Baylor College of Medicine  
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Co-Chair: Armand Keating, MD, Princess Margaret Hospital  
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Statistician: Kathleen A. Sobocinski, MS, CIBMTR Statistical Center Milwaukee  
E-mail: ksobo@mcw.edu

Statistician: John Klein, PhD, CIBMTR Statistical Center Milwaukee  
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Scientific Director: Marcelo Pasquini, MD, MS, Medical College of Wisconsin  
E-mail mpasquin@mcw.edu

Cellular Therapies Working Committee Studies in Progress

Study # CT09-01
Title: Follow-up of subjects receiving genetically modified cell products post transplant
Study Chairs: Helen Heslop (Baylor College of Medicine)  
Armand Keating (Princess Margaret Hospital)  
Edwin Horwitz (Children’s Hospital of Philadelphia)
MS Statistician: Kathleen Sobocinski (ksobo@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # CT09-02
Title: Cellular therapy for regenerative medicine 2008 Activity Survey in the U.S. and Canada
Study Chairs: Marcelo Pasquini (CIBMTR, Milwaukee)  
Helen Baldomero (Basel Kantonsspital)
MS Statistician: Kathleen Sobocinski (ksobo@mcw.edu)
PhD Statistician: TBD
Study Status: Data Collection
Cellular Therapies Working Committee Planned Studies

Study # CT09-03
Title: Follow-up of subjects receiving ex vivo expanded cord blood and mesenchymal stem cell products
Study Chairs: Cath Bollard (Baylor College of Medicine)
               EJ Shpall (MD Anderson Cancer Center)
MS Statistician: Kathleen Sobocinski (ksobo@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol Development

Go to www.cibmtr.org for a biannual study status update.
10.4 CHRONIC LEUKEMIA WORKING COMMITTEE

Committee Leadership

Co-Chair: Jeffrey Szer, MD, Royal Melbourne Hospital
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Co-Chair: Jorge Cortes, MD, M.D. Anderson Cancer Center
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Co-Chair: Richard Maziarz, MD, Oregon Health and Science Institute
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Statistician: Xiaochun Zhu, MS, CIBMTR, Milwaukee
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Statistician: Kwang Woo Ahn, PhD, CIBMTR Statistical Center, Milwaukee
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Scientific Director: Mukta Arora, MD, MS, University of Minnesota
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Chronic Leukemia Working Committee Publications

Study # CK00-02

Purpose: To evaluate the outcomes of patients receiving allogeneic transplantation for primary myelofibrosis, from the database of the CIBMTR.

Patients/Methods: 289 subjects received allogeneic transplant for primary myelofibrosis between 1989 and 2002. Separate analyses were conducted for patients receiving a transplant from HLA-identical sibling donor (n=162), unrelated donor (n=101) and other related donors (n=26). Major endpoints included transplant related mortality, survival and disease-free survival.

Results: The 100-day transplant-related mortality was 18% for HLA identical sibling transplants, 35% for unrelated transplants, and 19% for transplants from alternative related donors. Corresponding 5-year overall survival rates were 37%, 30%, and 40% respectively. Disease-free survival rates were 33%, 27% and 22% respectively. Disease-free survival for patients receiving reduced-intensity transplants was comparable, 39% for HLA identical sibling donors and 17% for unrelated donors at three years.

Conclusions: In this large retrospective series, allogeneic transplantation for myelofibrosis resulted in long-term relapse-free survival in about one-third of patients.
Study # CK07-02

Purpose: To determine clinical outcomes after allotransplant for patients with PLL.

Patients/Methods: Clinical outcomes were evaluated in all patients who underwent an allogeneic transplant for prolymphocytic leukemia (PLL) between 1995 and 2005 and reported to CIBMTR (n=47).

Results: We identified 47 patients with a median age of 54 years (range, 30-75). With a median follow-up of 13 months, progression-free survival was 33% (95% Confidence Interval 20-47%) at two years. The most common cause of death was relapse or progression (49%). Treatment-related mortality occurred in 28% of patients. The small patient population prohibited prognostic factor analysis but these data support consideration of allotransplant for PLL.

Conclusion: Further study of a larger population of patients is needed to determine which patients are more likely to benefit.

Study # R02-25

Purpose: To determine comparative outcomes of bone marrow transplantation (BMT) from allele-matched and mismatched unrelated donors and matched sibling donors in patients with CML in first chronic phase (CP).

Patients/Methods: Clinical outcomes after bone marrow transplantation from matched sibling donor transplants (MSDs) (n=3514), HLA-A, B, C, DRB1 allele matched unrelated donor transplants (URDs) (“8/8”), and mismatched URDs (n=1052) in patients with CML in CP1 were compared.

Results: Five-year overall and leukemia-free survival after 8/8 matched URD BMT was worse than after MSD BMT (five-year survival 55% versus 63%, RR 1.35 (95% CI 1.17-1.56) p<0.001; LFS 50% versus 55%, RR 1.21 (95% CI 1.06-1.40), p=0.006). Survival was progressively worse with greater degrees of mismatch. Similar and low risk of relapse was observed after either MSDs or URD transplantation.

Conclusions: In this homogenous cohort of good risk patients with CML, 5-year overall and leukemia-free survival (LFS) after transplant from 8/8 allele-matched donors, was modestly, though significantly worse than that of MSD transplantation. Additive adverse effects of multi-locus mismatching are not well tolerated and should be avoided if possible.

Chronic Leukemia Working Committee Preliminary Results

Study # CK03-02
Title: Myeloablative allogeneic hematopoietic-cell transplantation for chronic myeloid leukemia in first chronic phase: incidence of relapse and late mortality in 5-year survivors.

Presentation: Presented orally at the 2009 American Society of Hematology Meeting.

Study Chair: John M. Goldman (Imperial College-Hammersmith Hospital)

MS Statistician: Zhiwei Wang (zwang@mcw.org)

PhD Statisticians: John P. Klein (klein@mcw.edu)
Kathy Sobocinski (ksobo@mcw.edu)

Study Status: Submitted
Purpose: To evaluate the long-term outcomes of CML patients in first chronic phase who receive an allogeneic HCT.

Patients/Methods: 2,444 patients who received myeloablative HCT for CML in first chronic phase between 1978 and 1998 and survived in continuous complete remission for at least five years (median follow-up 11 [range, 5-25] years) were included. Donor sources were HLA-matched siblings in 1,692, unrelated donors in 639 and other related donors in 113 patients.

Results: Overall survival rates at 15 years were 88% (86-90%) for sibling and 87% (83-90%) for unrelated donor HCT. Corresponding cumulative incidences of relapse were 8% (7-10%) and 2% (1-4%), respectively. The latest relapse was reported 18 years post-HCT. In multivariable analyses, history of chronic graft-versus-host disease increased risks of late overall mortality and non-relapse mortality but reduced risks of relapse. In comparison with age-, race- and gender-adjusted normal populations, the mortality of HCT recipients was significantly higher until 14 years post-HCT; thereafter mortality rates were similar to that of the general population (relative mortality ratio at 15 years, 2.3 [0-4.9]).

Conclusion: Recipients of allogeneic HCT for CML in first chronic phase who remain in remission for at least five years have very favorable subsequent long-term survival and their mortality rates eventually approach that of the general population.

Study # CK03-01b
Title: Impact of pre-transplant imatinib mesylate (IM) on outcomes of allogeneic transplantation in advanced phase chronic myeloid leukemia: analysis from the CIBMTR
Study Chair: Hanna J. Khoury (Emory University Hospital)
MS Statistician: TBD
PhD Statistician: Tao Wang
Study Status: Submitted
Purpose: To assess the impact of pre-transplant IM on outcomes of allogeneic HCT in patients in second chronic phase (CP2, n=184), advanced phase (AP, n=185), and blast phase (BP, n=80) CML who received HLA-identical sibling (27%), related (3%), and matched or mismatched unrelated donor (70%), peripheral blood (47%) or bone marrow (53%) HSCT after myeloablative (78%) or non-myeloablative (22%) conditioning. Fifty-two percent of patients in CP2, 49% in AP, and 46% in BP received IM for a median of 7 (1-60), 11 (1-54), and 8 (1-36) months, respectively, prior to a planned transplant (43% or transplantation for IM intolerance (6%), or failure (51%). Endpoints included overall survival, leukemia-free survival, transplant-related mortality, relapse, and acute and chronic GVHD.

Results: Pre-transplant IM was not associated with transplant outcomes. Traditional prognostic factors such as time from diagnosis to HCT, degree of HLA matching, and others were associated with outcomes. CP2 and AP patients had similar outcomes while BP patients did very poorly.

Conclusions: Conventional prognostic indicators remain the major determinants of transplant outcomes in advanced phase CML. The administration of IM prior to HCT was not associated with improved outcomes in patients transplanted for advanced phase CML.

Study # CK02-03
Title: Matched pair intravenous (IV) vs. oral Busulfan (Bu)
Study Chair: Mary Horowitz (CIBMTR)
MS Statistician: Kathy Sobocinski (ksobo@mcw.edu)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Manuscript preparation
Purpose: To determine if patients receiving IV Bu as part of a Busulfan/Cytoxan (BuCy) conditioning regimen have less toxicity than similar patients receiving oral BuCy

Patients/Methods: We conducted a matched pair analysis comparing 101 patients with hematologic malignancies who received IV Bu and Cy prior to auto- (31%) or allo- (69%) HCT to 216 similar patients receiving oral Bu and Cy, whose data were reported to the CIBMTR. The primary outcome was veno-occlusive disease (VOD) or death at day 28 (VOD28). Engraftment and 100-day mortality were also compared.

Results: Among allogeneic transplant recipients, overall incidences of VOD28 were 4.6% with IV Bu and 20.3% with oral Bu (p<0.001). Overall 100-day mortality was 6.2% and 19.2% for patients receiving IV and oral BU, respectively (p=0.005). Multivariate logistic regression analysis indicated that only the mode of Bu administration was a significant factor for the risk of VOD28, with IV Bu associated with a greatly reduced risk (p=0.004) compared to oral Bu.

Conclusions: There appears to be a beneficial effect of IV Bu compared to oral Bu on early outcomes of HCT.

Chronic Leukemia Working Committee Studies in Progress

Study # CK02-01
Title: Busulfan versus total body irradiation for conditioning prior to allogeneic HCT
Study Chair: Edward Copelan (The Cleveland Clinic)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Data file preparation

Study # CK04-01
Title: Comparison of outcome of allogeneic HCT and imatinib mesylate therapy in patients with chronic phase chronic myeloid leukemia
Study Chair: Farhad Ravandi (MD Anderson Cancer Center)
Richard Champlin (MD Anderson Cancer Center)
MS Statistician: Tanya Pederson (tpederse@nmdp.org)
PhD Statistician: TBD
Study Status: Data file preparation

Study # CK06-01
Title: Outcomes after allogeneic HCT for polycythemia vera and essential thrombocytosis
Study Chair: Karen Ballen (Massachusetts General Hospital)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Data file preparation

Study # CK06-03
Title: Reduced-intensity conditioning prior to allogeneic HCT for chronic lymphocytic leukemia/small lymphocytic lymphoma
Study Chairs: Jose Leis (Mayo Clinic Arizona)
Ronald Sobeck (The Cleveland Clinic)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # CK06-04
Title: Decision analysis: allogeneic vs non-bone marrow transplantation treatment for myelofibrosis
Study Chair: Karen Ballen (Massachusetts General Hospital)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # CK07-01
Title: A comparison of total body irradiation-based conditioning vs. chemotherapy-based conditioning in chronic lymphocytic leukemia
Study Chair: Mitchell Sabloff (Ottawa Hospital)
MS Statistician: Wael Saber
PhD Statistician: TBD
Study Status: Data file preparation

Study # CK08-01
Title: Outcome of allogeneic HCT for imatinib-resistant chronic myelogenous leukemia
Study Chair: Jeffrey Szer (Royal Melbourne Hospital)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Data collection

Study # CK08-02
Title: Allogeneic hematopoietic cell transplantation for hairy cell leukemia
Study Chairs: Robert Kreitman (National Institute of Health)
Steven Pavletic (National Cancer Institute)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

Chronic Leukemia Working Committee Planned Studies

Study # CK09-01
Title: A comparison of outcomes of reduced-intensity and non-myeloablative conditioning regimen for patients with myelofibrosis
Study Chair: Vikas Gupta (Princess Margaret Hospital, Toronto)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol development

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10.5 DONOR HEALTH AND SAFETY WORKING COMMITTEE

Committee Leadership

Co-Chair: Susan Leitman, MD, National institutes of Health  
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Statistician: Brent Logan, PhD, CIBMTR Statistical Center Milwaukee  
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Donor Health and Safety Working Committee Publications

Study # D01-84a


Purpose: To assess the limited data available describing donor adverse events (AE) associated with filgrastim mobilized peripheral blood stem cell (PBSC) collections in unrelated volunteers.

Patients/Methods: Results in 2408 unrelated PBSC donors reported to the National Marrow Donor Program between 1999 and 2004 were prospectively evaluated.

Results: Female donors had higher rates of AE, requiring central line placement more often (17 vs. 4%, p<0.001), experiencing more apheresis related AE (20 vs. 7%, p<0.001), more bone pain (OR=1.49), and higher rates of grades II-IV and III-IV CALGB adverse events (OR=2.22 and 2.32). Obese donors experienced more bone pain (obese vs. normal, OR=1.73) and heavy donors had higher rates of CALGB toxicities (>95 kg vs. <70 kg, OR=1.49). Six percent of donors experienced grade III-IV CALGB toxicities and 0.6% experienced toxicities that were considered serious and unexpected. Complete recovery is universal, however, and no late AE attributable to donation were identified.
Conclusions: PBSC collection in unrelated donors is generally safe, but most donors will experience bone pain, one in four will have significant headache, nausea or citrate toxicity and a small percentage will experience serious short-term adverse events. In addition, women and larger donors are at higher risk for donation-related AE.

Study # D01-84b

Purpose: To analyze the outcomes of patients receiving unrelated donor (URD) peripheral blood stem cell (PBSC) HCT.

Patients/Methods: We reported outcomes of 932 recipients of unrelated donor PBSC HCT facilitated by NMDP from 1999 through 2003 (median follow-up 3.3 years).

Results: Preparative regimens included myeloablative (MA, N=611), reduced-intensity conditioning (RIC, N=160), and non-myeloablative (NMA, N=161). For MA recipients, CD34+ counts >3.8 x 106/kg improved neutrophil and platelet engraftment, whereas improved OS and reduced TRM were seen for all preparative regimens when CD34+ cell doses exceeded 4.5 x 106/kg. Higher infused doses of CD34+ cell dose did not result in increased rates of either acute or chronic GVHD. Three-year OS and disease-free survival (DFS) of recipients of MA, RIC, and NMA approaches were similar (33%, 35%, and 32% OS; 33%, 30%, and 29% DFS, respectively). In summary, recipients of unrelated donor PBSC HCT receiving preparative regimens differing in intensity experienced similar survival. Higher CD34+ cell doses resulted in more rapid engraftment, less TRM, and better 3-year OS (39% versus 25%, MA, P = .004; 38% versus 21% RI/ NMA, P =.004) but did not increase the risk of GVHD.

Donor Health and Safety Working Committee Preliminary Results

Study # DS06-01
Title: Related donor and recipient management practice pattern survey.
Study Chair: Paul O’Donnell (Fred Hutchinson Cancer Research Center)
MS Statistician: Tanya Pedersen (tpedeser@nmdp.org)
PhD Statistician: Brent Logan (blogan@mcw.edu)
Study Status: Submitted

Purpose: To evaluate practice patterns of HCT centers in the United States related to overlap of care.

Background: An argument can be made that a real or perceived conflict of interest may arise when the same physician is responsible for the care of two individuals whose care is interdependent. In HCT from unrelated donors facilitated by NMDP, and for solid organ transplantations from living donors, the standard of care is for donors and recipients to be under the care of separate physicians, in order to provide unbiased care and eliminate the potential for a conflict of interest. However, the practice patterns of evaluation and care of related donors and recipients at centers performing HCT are unknown.

Methods: A practice pattern survey of HCT centers in the United States reporting to the CIBMTR was conducted by the Donor Health and Safety Working Committee, from December 2007 to July 2008. The survey was administered online with center medical directors. It focused primarily on determining the type of provider involved in medical clearance, informed consent and medical management of the donor, and the relationship of that provider to the recipient.
Results: Of 222 centers surveyed, 98 evaluable responses were received (40%). The median number of related donor transplants per year at responding institutions was 15 (range: 1-400); the median total number of transplants per year was 70 (5-600). Transplant physicians in more than 70% of centers were involved in overlapping care of the donor and the recipient during the donor evaluation, clearance and collection phases. These patterns were similar between transplant teams caring for adult and pediatric donors and recipients.

Conclusions: Among responding centers, it appears that medical management of recipients and their related donors by the same provider is common. Whether this practice pattern presents a potential conflict of interest that may affect donor care is unclear, and deserves further investigation.

Donor Health and Safety Working Committee Studies in Progress

Study # DS05-02
Title: RDSafe: A multi-institutional study of HCT donor safety and quality of life
Study Chair: Michael A. Pulsipher (Primary Children’s Medical Center)
MS Statistician: Tanya Pedersen (tpederse@nmdp.org)
PhD Statistician: Brent Logan (blogan@mcw.edu)
Study Status: Data Collection

Study # DS08-01
Title: Abnormal cytogenetics in donor derived stem cells after allogeneic HCT
Study Chair: Noelle Frey (University of Pennsylvania)
MS Statistician: Tanya Pedersen (tpederse@nmdp.org)
PhD Statistician: TBD
Study Status: Data Collection

Study # DS09-03
Title: Effects of multiple donations on marrow/PBSC donors
Study Chair: David Stroncek (NHLBI)
MS Statistician: Tanya Pedersen (tpederse@nmdp.org)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # DS09-05
Title: PBSC vs. bone marrow donor toxicities
Study Chair: Michael Pulsipher
MS Statistician: Tanya Pedersen (tpederse@nmdp.org)
PhD Statistician: TBD
Study Status: Protocol received/in development

Donor Health and Safety Working Committee Planned Studies

Study # DS09-01/GS09-01
Title: Impact of growth factor mobilization on donor bone marrow harvest
Study Chair: Steve Pincus (St. Louis University Medical Center)
MS Statistician: Tanya Pedersen (tpederse@nmdp.org) and Fiona Kan
PhD Statistician: TBD
Study Status: Protocol Development
### Study # DS09-02
- **Title:** Monoclonal B-cell lymphocytosis in matched unrelated donor HCT
- **Study Chair:** Matthew Seftel (CancerCare Manitoba, Manitoba University Hospital)
- **MS Statistician:** Tanya Pedersen ([tpederse@nmdp.org](mailto:tpederse@nmdp.org))
- **PhD Statistician:** TBD
- **Study Status:** Protocol Development

### Study # DS09-04
- **Title:** Race/socioeconomic status and donor center size on bone marrow and PBSC donor experience
- **Study Chair:** Michael Pulsipher
- **MS Statistician:** Tanya Pedersen ([tpederse@nmdp.org](mailto:tpederse@nmdp.org))
- **PhD Statistician:** TBD
- **Study Status:** Protocol Development

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10.6 GRAFT SOURCES AND MANIPULATION WORKING COMMITTEE

Committee Leadership

Co-Chair: Adrian Gee, PhD, Baylor College of Medicine
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E-mail: champli@mdanderson.org

Co-Chair: Mary Laughlin, MD, Ireland Cancer Center
E-mail: mary.laughlin@case.edu

Statistician: Fiona Kan, MS, CIBMTR Statistical Center Minneapolis
E-mail: fkan@nmdp.org

Statistician: Mei-Jie Zhang, PhD, CIBMTR Statistical Center Milwaukee
E-mail: meijie@mcw.edu

Scientific Director: Mary Eapen, MD, MS, Medical College of Wisconsin
E-mail: meapen@mcw.edu

Graft Sources and Manipulation Working Committee Publications

Study # R02-12

Purpose: To assess if the transport of hematopoietic stem cell grafts for transplant affects recipient outcome.

Patients/Methods: Effects of graft transport time were reported on outcomes after transplantation of 938 unrelated donor bone marrow or 507 peripheral blood progenitor cells in patients with acute and chronic leukemia and myelodysplasia. Bone marrow (BM) grafts were collected at 107 centers and peripheral blood progenitor cells (PBPC) were collected at 89 centers.

Results: Median time from end of collection to infusion was 14 hours for BM and 15 hours for PBPC. Platelet recovery was less likely in BM recipients when the interval from end of collection to receipt at transplant center was ≥20 hours (odds ratio 0.47, p=0.01) and when the interval from receipt to infusion was ≥6 hours (odds ratio 0.57, p=0.001). Transport times had no demonstrable association with neutrophil recovery. Mortality rates were higher in recipients of HLA-matched BM when the interval from end of collection to receipt at transplant center was ≥20 hours (relative risk 2.67, p<0.001) after adjustment for other significant prognostic factors. Transport times had no demonstrable effect on outcomes after PBPC transplants.

Conclusions: Longer transport times primarily occurred when grafts were transported to or from locations outside of the U.S. These data support a general review of current transport procedures, especially for BM grafts requiring longer transport times.
**Study # R02-42**


**Purpose:** To analyze unrelated donor grafts prospectively in a multicenter study to determine the relationship between clinical outcomes and graft composition.

**Patients/Methods:** Samples from 94 bone marrow and 181 peripheral blood progenitor cell grafts from patients with hematologic malignancies treated at 40 transplant centers were analyzed at a single immunophenotyping reference laboratory for total white blood count cell dose, myeloid cell dose (CD34+ and CD34+/CD38+) and lymphoid cell dose (CD3+, CD4+, CD8+, and activation antigens CD25, CD69, and HLA-DR). Multivariate analysis adjusted for patient demographics and assessment of transplant characteristics was performed to identify correlations between graft composition and the transplantation outcomes of neutrophil and platelet engraftment, acute and chronic GVHD, and survival.

**Results:** Substantial variability was seen in the cellular graft composition between patients in both groups. In BM grafts, the cellular composition was not associated with engraftment, GVHD, or survival. In PBPC grafts, superior survival was seen when grafts contained > 5x10^6 CD34+/kg, and superior platelet recovery was seen when grafts contained > 8 x 10^7 CD8+/kg.

**Conclusions:** Neither overall survival nor acute or chronic GVHD could be predicted by any cellular subsets in PBPC grafts. Overall, no specific subsets predicted clinical outcome in the grafts analyzed. An optimal graft mix of myeloid, lymphoid and activated lymphoid subsets was not identified.

**Graft Sources and Manipulation Working Committee Preliminary Results**

**Study # HC03-01**

**Title:** Prevalence of microbially contaminated hematopoietic stem cell products

**Study Chair:** Richard Champlin (Anderson Cancer Center)

**MS Statistician:** Mary Eapen (meapen@mcw.edu)

**PhD Statistician:** Mei-Jie Zhang (meijie@mcw.edu)

**Study Status:** Manuscript preparation

**Purpose:** To examine the potential of microbially-contaminated hematopoietic stem cell products to produce morbidity and mortality in transplant recipients.

**Patients/Methods:** 121 U.S. transplant centers were surveyed revealing a total of 2,972 transplants reported to the CIBMTR in the years 2000-2001. Information regarding microbial contamination of infused grafts was obtained from 94 transplant centers for 2,312 patients. Two percent (52) of 2,286 infused grafts tested were culture positive for bacterial or fungal organisms. The microbial isolates included: coagulate negative staphylococcus (56%), gram negative organisms (15%), coagulate positive staphylococcus (10%), gram positive rods (10%), streptococcus (8%), and fungus (1%). Prophylactic antibiotics targeted at the contaminant were given to 17 of the 52 recipients of contaminated grafts. Antibiotic regimens included vancomycin alone (76%), aminoglycosides and vancomycin (12%), or cephalosporin and vancomycin (12%). Fifty percent (47) of the centers that participated have existing policies regarding contaminated products.

**Results:** Patients with non-malignant disorders or who received bone marrow were more likely to have a contaminated graft. No differences in age distribution, sex, race, type of transplant (allogeneic versus autologous) and year of transplant were noted between recipients of contaminated and non-contaminated grafts. The unadjusted 100-day survival of persons
receiving contaminated grafts was 86% (72-93) versus 81% (80-83) among those receiving non-contaminated grafts, p=0.35.

Conclusion: Approximately 2% of hematopoietic stem cell products infused for allogeneic or autologous transplantations in U.S. centers will test positive for microbial contamination, but such contamination does not increase post-transplant mortality. The absence of significant 100-day mortality among patients infused with contaminated grafts suggests that stringent regulatory policies regarding the use of contaminated hematopoietic cell products may not be indicated.

Study # GS05-02
Title: Comparison of outcomes after transplantation of granulocyte colony-stimulating factor (G-CSF) mobilized bone marrow versus non-mobilized bone marrow (BM) grafts or peripheral blood (PBSC) grafts from human leukocyte antigen (HLA)-matched sibling for severe aplastic anemia (SAA)
Study Chairs: Roland Chu (Children’s Hospital of Michigan)
Kuang-Yueh Chiang (Emory University)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: Ruta Bajorunaite (ruta@mcw.edu)
Study Status: Manuscript preparation
Purpose: To compare outcomes of SAA patients receiving G-CSF stimulated bone marrow graft vs. unstimulated bone marrow vs. G-CSF stimulated peripheral blood stem cell graft.
Patients/Methods: 78 G-CSF simulated bone marrow (G-BM), 547 unstimulated BM (BM), and 134 PBSC transplants from HLA-identical sibling donors for SAA occurred from 1997-2003.
Results: Hematologic recoveries were similar. Rates of grades 2 to 4 acute GVHD were higher for PBSC (p = 0.011 and <0.0001 for G-BM and BM). G-BM had similar rates of grades 3 to 4 acute GVHD (p = 0.54 and 0.32, to BM and PBSC). Chronic GVHD was higher in PBSC compared to G-BM (p <0.0001). BM had a marginally significant lower rate of overall mortality compared to G-BM (p = 0.0502).
Conclusions: G-BM and BM have similar risks of GVHD. PBSC should be avoided in patients with aplastic anemia. A larger prospective study is needed to evaluate if cell dose offered by G-BM compared to BM may be of benefit to patients with high-risk SAA.

Study # GS06-01B
Title: Donor characteristics as risk factors in recipients after transplantation (HCT) of bone marrow or peripheral blood from unrelated donors
Study Chairs: Jakob Passweg (University of Geneva Hospital)
Alois Gratwohl (Kantonsspital Basel)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Submitted
Purpose: To analyze donor characteristics associated with outcome. Of particular interest were H-Y effects, e.g. more GVHD if female donor for male recipient and more graft failure if male donor for female recipients. Donor selection for unrelated donor reduced-intensity conditioning (RIC) transplants is crucial for transplant success. Donors are selected by HLA matching but non-HLA criteria such as age, sex, parity, etc. may be of importance.
Patients/Methods: 715 patients receiving matched unrelated donor, RIC HCT for malignancy were evaluated.
Results: Graft failure rates were higher with BM grafts vs. PB grafts. The only donor characteristic associated with survival was HLA disparity. Donor age, parity, donor-recipient sex match and
cytomegalovirus serostatus were not associated with engraftment, risks of acute or chronic GVHD or survival.

Conclusions: We failed to demonstrate any impact of donor characteristics other than HLA-matching on outcome of unrelated RIC transplantation for malignancy.

Graft Sources and Manipulation Working Committee Studies in Progress

Study # GS05-01
Title: An audited matched pair analysis of transplants using red cell depleted vs. plasma depleted umbilical cord blood stem cells.
Study Chair: Robert Chow (StemCyte, Inc.)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: TBD
Study Status: Data Collection

Study # GS06-01A
Title: Donor characteristics as risk factors in recipients after transplantation of bone marrow or peripheral blood from HLA-identical sibling donors.
Study Chairs: Jakob Passweg (Geneva University Hospital)
            Alois Gratwohl (Basel Kantonsspital)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: TBD
Study Status: Data Collection

Study # GS06-02
Title: Elucidating the role of human leukocyte antigen-C (HLA-C) matching on engraftment in umbilical cord blood transplantation.
Study Chairs: Mary Eapen (CIBMTR, Medical College of Wisconsin)
            Vanderson Rocha ((Hôpital Saint Louis)
MS Statisticians: Mary Eapen (meapen@mcw.edu)
                Vanderson Rocha (vanderson.rocha@sls.aphp.fr)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Analysis

Study # GS07-01
Title: Peripheral blood vs. bone marrow for nonmyeloablative HCT
Study Chairs: Richard Champlin (MD Anderson Cancer Center)
            Mary Eapen (CIBMTR, Medical College of Wisconsin)
MS Statistician: Mary Eapen (meapen@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Analysis

Study # GS07-03
Title: Bone marrow or peripheral blood stem cells as graft source using unrelated donors to children and adolescents with leukemia
Study Chairs: Olle Ringdén (Karolinska University Hospital Huddinge)
            Franco Locatelli (IRCCS Policlinico San Matteo)
MS Statistician: Mary Eapen (meapen@mcw.edu)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Analysis

Study # GS08-01
Title: Reassessment of impact of donor age on outcome after unrelated/related donor HCT
Study Chair: Craig Kollman (Jaeb Center for Health Research)
MS Statistician: Anna Hassebroek (ahassebr@nmdp.org)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # GS08-02
Title: Compare elderly donor vs. younger matched unrelated donor for an elderly recipient
Study Chair: Amin Alousi (MD Anderson Cancer Center)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: Jennifer Le-Rademacher (jlerade@mcw.edu)
Study Status: Analysis

Study # GS08-03
Title: In vivo T-cell depletion in reduced-intensity conditioning
Study Chairs: Robert Soiffer (Dana-Farber Cancer Institute)
              Vincent Ho (Dana-Farber Cancer Institute)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # GS08-04
Title: Compare leukemia-free survival post unrelated donor, peripheral blood or cord blood HCT for acute myelogenous leukemia in adults
Study Chair: John Wagner (University of Minnesota)
MS Statistician: Mary Eapen (meapen@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Analysis

Study # GS08-05/R04-88
Title: Cord blood outcomes
Study Chair: Elizabeth Shpall (MD Anderson Cancer Center)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: Jennifer Le-Rademacher (jlerade@mcw.edu)
Study Status: Analysis

Study # GS09-02
Title: Parameters of banked cord blood units that may be associated with graft failure
Study Chairs: Mary Eapen (Medical College of Wisconsin)
              Vanderson Rocha (Hôpital Saint Louis)
              Steve Spellman (NMDP)
MS Statistician: Mary Eapen (meapen@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development
Study # GS09-03
Title: Comparison of outcomes of unrelated donor peripheral blood stem cells and umbilical cord blood after reduced-intensity conditioning.
Study Chair: Claudio G. Brunstein (University of Minnesota)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: TBD
Study Status: Protocol received/in development

Graft Sources and Manipulation Working Committee Planned Studies

Study # GS09-01/DS09-01
Title: Impact of growth factor mobilization on donor bone marrow harvest
Study Chair: Steven Pincus (Saint Louis University)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: TBD
Study Status: Protocol Development

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### 10.7 GRAFT-VERSUS-HOST DISEASE WORKING COMMITTEE

#### Committee Leadership

<table>
<thead>
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#### Graft-Versus-Host Disease Working Committee Publications

**Study # D96-01**


**Purpose:** To determine whether improved HLA typing and prophylaxis have changed incidence and risk factors for acute GVHD (aGVHD), and the impact of GVHD on treatment-related mortality and relapse.

**Patients/Methods:** Outcomes of 638 myeloablative unrelated transplants were analyzed, which had been reported to CIBMTR between 1990 and 2003 for AML, ALL, CML or MDS. All recipients were <18 years of age and had available high-resolution HLA typing for HLA A, B, C and DRB1.

**Results:** Overall, 45% of children developed aGVHD grades II-IV, and 27% aGVHD grades III-IV. The risk of aGVHD was significantly higher in recipients of T-replete grafts. Survival was reduced in children with grades II-IV aGVHD compared to those without. The risk of aGVHD was higher in children transplanted in earlier years (1990-1998, n=365) compared to 1999-2003 (n = 220),
suggested that current prophylactic regimens may be more effective. In contrast, the risk of relapse was lower in children transplanted 1990-1998 compared with 1999-2003.

Conclusions: As more intense risk-adapted chemotherapy has improved outcomes of upfront treatment of leukemia, children who are referred for transplant may have more resistant disease, increasing the difficulty of controlling disease with standard irradiation and chemotherapy preparative regimens. Overall survival of children with unrelated HCT has not changed over time, although it is possible that current results reflect treatment of children with more resistant disease compared with 10 years ago.

Study # D01-91

Purpose: To assess the hypothesis that B-cell depletion by prior rituximab (RTX) therapy in lymphoma might result in reduced incidence of acute GVHD. Animal models of acute GVHD suggested the critical role of host antigen-presenting cells in the pathogenesis of acute GVHD.

Patients/Methods: The outcomes of allogeneic transplantation using peripheral blood stem cell therapy in 435 B-cell lymphoma patients reported to CIBMTR from 1999 to 2004 were analyzed. There were 256 patients who did not receive RTX within 6 months of transplantation (No-RTX group) and 179 patients who received RTX (RTX group).

Results: One-year progression-free survival for No-RTX and RTX groups were 54% and 66% (P=0.01), respectively. One-year overall survival for No-RTX and RTX groups were 58% and 71% (P=0.009), respectively.

Conclusions: In this study, prior RTX therapy correlates with less acute GVHD and similar rate of chronic GVHD. Prior RTX is also correlated with less transplant-related mortality and better survival. There is no impact on disease progression or relapse. This study suggests the role of B-cells in the pathogenesis of acute GVHD.

Study # GV05-04

Purpose: To determine if some patients benefit from an unrelated donor transplant because of a stronger graft-versus-leukemia (GVL) effect. Because of minor transplantation antigens, the hypothesis was that the GVL effect should be stronger using an unrelated (URD) compared to an HLA-identical sibling donor.

Patients/Methods: 4,099 patients reported to the CIBMTR between 1995 and 2004 with acute myeloid leukemia AML, acute lymphoblastic leukemia and chronic myeloid leukemia, undergoing myeloablative allogeneic HCT from a URD (n=941), or HLA-identical sibling donor (n=3158) were analyzed.

Results: Acute and chronic GVHD were added as time-dependent variables in a Cox regression model. Unrelated donor transplant recipients had a higher risk of relapse (RR 1.5; p<0.0018) in patients with AML, but not ALL or CML. Leukemia-free survival was decreased in patients with AML.
without acute GVHD receiving URD transplants (RR 2.02; p<0.0001), but was comparable to those receiving HLA-identical sibling transplants in patients with ALL and CML.

Conclusions: The risk of relapse was the same (ALL, CML) or worse (AML) in unrelated donor transplant recipients compared to HLA-identical sibling transplants, suggesting a similar GVL effect.

Graft-Versus-Host Disease Working Committee Preliminary Results

Study # D01-91
Title: Prior rituximab correlates with less acute graft-versus-host disease and better survival in B-cell lymphoma patients who received allogeneic peripheral blood stem cell transplantation (PBSCT).
Study Chair: Voravit Ratanatharathorn (Karmanos Cancer Center)
MS Statistician: Erik Iverson (eiverson@nmdp.org)
PhD Statistician: Brent Logan (blogan@mcw.edu)
Study Status: Submitted
Purpose: To assess the hypothesis that B-cell depletion by prior rituximab (RTX) therapy in lymphoma might result in reduced incidence of acute GVHD. Animal models of acute GVHD suggested the critical role of host antigen-presenting cells (APC) in the pathogenesis of acute GVHD.
Patients/Methods: The outcomes of allogeneic transplantation using PBSCT in 435 B-cell lymphoma patients reported to CIBMTR from 1999 to 2004 were analyzed. There were 256 patients who did not receive RTX within six months of transplantation (No-RTX group) and 179 patients who received RTX (RTX group).
Results: One-year progression-free survival (PFS) for No-RTX and RTX groups were 54% and 66% (P=0.01), respectively. One-year overall survival for No-RTX and RTX groups were 58% and 71% (P=0.009), respectively.
Conclusions: In this study, prior RTX therapy correlates with less acute GVHD and similar rate of chronic GVHD. Prior RTX is also correlated with less transplant-related mortality (TRM) and better survival. There is no impact on disease progression or relapse. This study suggests the role of B cells in the pathogenesis of acute GVHD.

Study # D96-01
Title: Recent decrease in acute GVHD and increased relapse in children with leukemia receiving unrelated donor bone marrow transplantation.
Study Chair: Stella M. Davies (Cincinnati Children’s Hospital)
MS Statistician: Erik Iverson (eiverson@nmdp.org)
PhD Statistician: Tao Wang (taowang@mcw.edu)
Study Status: Submitted
Purpose: To determine whether improved HLA typing and prophylaxis have changed incidence and risk factors for acute GVHD, and the impact of GVHD on treatment-related mortality and relapse.
Patients/Methods: Outcome of 638 myeloablative unrelated transplants were analyzed that were reported to the CIBMTR between 1990 and 2003 for AML, ALL, CML or MDS. All recipients were <18 years of age and had available high-resolution HLA typing for HLA A, B, C and DRB1.
Results: Overall, 45% of children developed aGVHD grades II-IV, and 27% aGVHD grades III-IV. The risk of aGVHD was significantly higher in recipients of T-replete grafts. Survival was reduced in children with grades II-IV aGVHD compared to those without. The risk of aGVHD was higher in children transplanted in earlier years (1990-1998, n=365) compared to 1999-2003 (n= 220), suggesting that current prophylactic regimens may be more effective. In contrast, the risk of relapse was lower in children transplanted 1990-1998 compared with 1999-2003.
Conclusions: As more intense risk-adapted chemotherapy has improved outcomes of upfront treatment of leukemia, children who are referred for transplant may have more resistant disease, increasing the difficulty of controlling disease with standard irradiation and chemotherapy preparative regimens. Overall survival of children with unrelated HCT has not changed over time, although it is possible that current results reflect treatment of children with more resistant disease compared with 10 years ago.

Graft-Versus-Host Disease Working Committee Studies in Progress

Study # D01-92/GV05-02
Title: Study of risk factors on incidence and outcome of acute GVHD after allogeneic stem cell transplantation for hematologic malignancies
Study Chairs: Nelson Chao (Duke University Medical Center)
Madan Jagasia (Vanderbilt University Medical Center)
Theresa Hahn (Roswell Park Cancer Institute)
Philip McCarthy (Roswell Park Cancer Institute)
MS Statistician: Mukta Arora (arora005@umn.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
John P. Klein (klein@mcw.edu)
Study Status: Analysis

Study # GV04-02/R04-82/GV05-03
Title: Chronic GVHD relapse and risk factor analyses
Study Chairs: Steven Pavletic (National Cancer Institute)
Michael Boyiadzis (University of Pittsburg Cancer Institute)
David Jacobson (Children’s Memorial Hospital)
MS Statistician: Anna Hassebroek (ahassebr@ndmp.org)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Analysis

Study # GV06-01
Title: Comparison of GVHD prophylaxis regimens with and without methotrexate in matched, related and unrelated donor transplantation
Study Chairs: Corey Cutler (Dana-Farber Cancer Institute)
Joseph Antin (Dana-Farber Cancer Institute)
Marcelo Pasquini (CIBMTR, Medical College of Wisconsin)
MS Statistician: Marcelo Pasquini (mpasquin@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # GV06-04
Title: Current trends in chronic GVHD: updated report from the CIBMTR/NMDP
Study Chair: Sally Arai (Stanford University Medical Center)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development
Study # GV08-01
Title: The role of the HLA DRB1 antigen, DR15 in determining immunobiologic outcomes (graft-versus-host disease and graft-versus-leukemia effect) in HLA-matched BMT
Study Chair: Minoo Battiwala (Roswell Park Cancer Institute)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Data File Preparation

Study # GV08-02
Title: Balancing acute graft versus host disease (AGVHD) and survival after allogeneic hematopoietic progenitor cell transplantation (HCT) in hematological malignancies: a potential for graft engineering by T-cell dose control
Study Chair: Ayman Saad (Medical College of Wisconsin)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # GV08-03
Title: Risk factors for acute GVHD after haploidentical sibling donor or 8/8 allele level matched unrelated donor transplants for leukemia in patients receiving reduced-intensity conditioning
Study Chairs: Olle Ringdén (Karolinska University Hospital)
Steven Pavletic (National Cancer Institute)
Mary Flowers (Fred Hutchinson Cancer Research Center)
MS Statistician: Min Chen (minchen@mcw.edu)
PhD Statistician: TBD
Study Status: Data File Preparation

Study # GV08-04
Title: Outcomes of relapsed patients with and without chronic GVHD
Study Chairs: Michael Boyiadzis (University of Pittsburg Cancer Institute)
Steven Pavletic (National Cancer Institute)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # GV08-05
Title: Clinical presentation of chronic GVHD inpatients receiving reduced-intensity conditioning
Study Chairs: Olle Ringdén (Karolinska University Hospital)
Steven Pavletic (National Cancer Institute)
Mary Flowers (Fred Hutchinson Cancer Research Center)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Data File Preparation
Study # GV08-06

Title: Graft-vs.-leukemia effect after 8/8 unrelated donor vs. HLA matched sibling reduced-intensity conditioning or non-myeloablative transplantation

Study Chairs: Olle Ringdén (Karolinska University Hospital)
Steven Pavletic (National Cancer Institute)
Mary Flowers (Fred Hutchinson Cancer Research Center)

MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

Go to www.cibmtr.org for a biannual study status update.
10.8 HEALTH POLICY AND PSYCHOSOCIAL ISSUES WORKING COMMITTEE

Committee Leadership

Co-Chair: Susan Parsons, MD, MRP, Tufts Medical Center
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Co-Chair: Steve Joffe, MD, MPH, Data Farber Cancer Institute
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Statistician: Anna Hassebroek, MPH, CIBMTR Statistical Center Minneapolis
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Statistician: John Klein PhD, CIBMTR Statistical Center Milwaukee
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Scientific Director: Navneet S. Majhail, MD, MS, University of Minnesota
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Consumer Advocacy Committee Representatives:
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Health Policy and Psychosocial Issues Working Committee Publications

Study # HS05-01

Purpose: To assess the impact of socioeconomic status (SES) and race on the success of HCT.

Patients/Methods: To evaluate the role of race and SES, we studied 6,207 unrelated-donor myeloablative HCT recipients transplanted between 1995-2004 for acute or chronic leukemia or myelodysplastic syndrome. Patients were reported by transplant center to be White (n=5253), African-American (n=368), Asian/Pacific-Islander (n=141), or Hispanic (n=445). Patient income was estimated from residential ZIP Code at time of HCT.

Results: Cox regression analysis adjusting for other significant factors showed that African-American (but not Asian or Hispanic) recipients had worse overall survival (OS) compared to Whites. Treatment-related mortality (TRM) was higher in African-Americans and in Hispanics. Across all racial groups, patients with median incomes in the lowest quartile (<$34,700) had worse OS and higher risks of TRM.

Conclusions: Inferior outcomes among African-Americans are not fully explained by transplant-related factors or SES. Potential other mechanisms such as genetic polymorphisms that impact drug metabolism or unmeasured co-morbidities, socioeconomic factors and health behaviors may be
important. Low SES, regardless of race, has a negative impact on unrelated donor HCT outcomes.

**Study # HS05-07**


**Purpose:** To conduct a feasibility study to help guide the planning of a larger scale, prospective cohort study on outcome and disparity in HCT. Outcome disparity associated with race or ethnicity in the United States has been observed in HCT. In the United States, an optimal study of health care disparity by race or ethnicity involves consideration of both biologic and psychosocial determinants.

**Patients/Methods:** This was a multi-center prospective study. Centers enrolled any patient receiving allogeneic HCT for cancer within a six-month period. Data were obtained from the patients at baseline, 100 days, 6 months and at 1 year. Outcomes evaluated included: accrual rate, proportion of missing data, and loss to follow-up.

**Results:** Three of five centers enlisted successfully enrolled a total of 24 patients; 19 minorities and 5 Caucasian. There was 100% participation rate among invited patients; however retention rate at 100 days, 6 months and 1 year went from 95%, to 75% then to 65%. Important missing information includes details about insurance (47%) and income (26%). Information about religiosity, spirituality, cultural beliefs, medical decision making, quality of life, and social support were well collected. Data on general adherence were also well collected over time.

**Conclusions:** Despite the difficulty in conducting disparity studies in racial and ethnic minorities, such studies are essential to ensure that people of all ethnic and racial backgrounds have the best chance possible of benefiting from HCT.

**Study # HS06-01/MM06-03**


**Purpose:** To describe the influence of race on outcomes of autologous HCT for MM. Blacks are twice as likely to develop and to die from multiple myeloma (MM), and are less likely to receive an autologous HCT for MM compared to whites.

**Patients/Methods:** We compared transplant outcomes among black (N=303) and white (N=1892) recipients of autologous HCT for MM, who were transplanted from 1995 to 2005.

**Results:** The black cohort was more likely to be female, had better Karnofsky performance scores but lower hemoglobin and albumin levels at diagnosis. Black recipients were younger and more likely to be transplanted later in their disease course. Black and white recipients had similar probabilities of five-year overall and progression-free survival as well as cumulative incidences of disease progression and non-relapse mortality. In multivariate analyses, race was not associated with any of these endpoints.
Conclusions: Black recipients of autologous HCT for MM have similar outcomes compared to whites, suggesting that the reasons underlying lower rates of autologous HCT in blacks need to be studied further to ensure equal access to effective therapy.

Study # HS06-06
Citation (pending): Joshua TV, Rizzo JD, Zhang M-J, Hari PN, Kurian S, Pasquini M, Majhail NS, Lee SL, Horowitz MM. Access to hematopoietic stem cell transplantation: effects of race and gender. [Accepted by Blood, PMCID not yet available]

Purpose: To determine whether utilization of HCT to treat leukemia, lymphoma or multiple myeloma differs by race and gender.

Patients/Methods: We estimated the annual incidence of leukemia, lymphoma and multiple myeloma in the US in people 70 years or younger by race and gender using the SEER Cancer Registry between 1997 and 2002, and US Census Reports for year 2000. The annual incidence of autologous, HLA-identical sibling and unrelated HCT performed in these groups in the U.S. was estimated using CIBMTR data from 1997 to 2002. Logistic regression was used to calculate the age-adjusted odds ratio of receiving HCT for Caucasians versus African-Americans and men versus women.

Results: The likelihood of undergoing HCT was higher for Caucasians than for African-Americans for each type of HCT. Men were somewhat more likely overall to receive HCT than women; however, this difference was statistically significant only for autologous transplantation.

Conclusions: HCT is more frequently used to treat leukemia, lymphoma and multiple myeloma in Caucasians than in African-Americans. African-Americans have lower rates of both autologous and allogeneic HCT, indicating that donor availability cannot fully explain the differences. Women are also less likely than men to receive autologous HCT for reasons unexplained by age or disease status.

Study # HS08-02

Purpose: To determine if patients who live in rural areas have worse clinical outcomes compared with patients living in urban areas.

Patients/Methods: We studied whether place of residence (rural vs. urban) is associated with clinical outcomes of patients with leukemia or myelodysplastic syndrome who received an unrelated donor HCT. Patients’ residential ZIP code at the time of transplant was used to determine rural or urban designation based on the Rural Urban Commuting Codes. The study included 1,179 patients from rural areas and 4,961 from urban areas.

Results: Rural and urban patients were similar in patient-, disease- and transplant-related characteristics aside from household income and distance travelled to HCT center. After adjusting for income and other significant variables, the risk of overall mortality between patients residing in rural and urban areas were not statistically significant. Similar outcomes were noted for transplant-related mortality, disease-free survival and relapse. Patient’s income, derived from U.S. Census and based on residential ZIP code, was independently associated with outcomes.

Conclusions: In summary, our study showed no differences in the clinical outcomes of patients from rural or urban areas after unrelated donor HCT.
Health Policy and Psychosocial Issues Working Committee Preliminary Results

Study # HS05-02

Title: Consolidation, volume and outcomes in leukemia treatment
Study Chairs: Albert Bravo-Biosca (National Endowment for Science, Technology and the Arts, UK)
Friederike Schneider (University Hospital-Munich)
MS Statistician: Anna Hassebroek (ahassebr@nmdp.org)
Status: Submitted
Purpose: To study the effect of consolidation on survival by empirically analyzing the causal nature of the volume-outcome relationship.

Patients/Methods: Focus was on the market of matched unrelated donor bone marrow transplants for leukemia treatment. Controlling for average hospital quality during the study period, we find that a one standard deviation increase in hospital volume during the six months preceding an unrelated transplant is associated with a 12% increase in the patient's survival probability three years after the transplant. We address the potential endogeneity due to time variant hospital quality with instrumental variables, using changes in the number of competitors adjusted by their distance to a hospital as exogenous predictor of changes in volume. Predicted volume was then used to establish a causal relationship between volume and outcome.

Results: Evidence showed a strong and causal relationship between volume and survival. A one standard deviation increase in volume is associated with a 36% increase in survival. Finally, we find evidence for perfect forgetting. This implies that high volume is not sufficient, but rather that regular performance of the procedure and hence high and constant average volume is essential.

Conclusions: This evidence suggests that some consolidation would be beneficial for patient survival, even at the cost of lower competition.

Study # HS07-01

Title: Description of transplantation utilization, procedure patterns and patient characteristics
Study Chairs: Philip McCarthy (Roswell Park Cancer institute)
Theresa Hahn (Roswell Park Cancer institute)

MS Statistician: Anna Hassebroek (ahassebr@nmdp.org)
PhD Statistician: TBD
Study Status: Analysis
Presentation: Accepted for presentation as a poster at the 2010 BMT Tandem Meetings.
Purpose: To determine whether recent advances in HCT techniques and supportive care, new HCT indications, and improvements in survival outcomes may have increased access to and utilization of HCT, since autologous (Auto) and allogeneic (Allo) HCT have been used to cure malignant and non-malignant conditions for >40 years.

Patients/Methods: We describe the HCT population, utilization and procedure patterns in U.S. and Canadian HCT centers from 1994-2005. All data exclude donor lymphocyte infusions.

Results: Because of a decrease in Auto HCT for breast cancer, the number of Auto HCTs increased by >30% from the mid to late 1990s, then declined by >30% in the early 2000s, but rose again in 2004-05. In this same period, Auto HCT increased for MM and NHL/HL, whereas acute or chronic leukemia decreased and solid tumors remained stable. The number of Allo HCTs increased over this 12-year period, mostly due to an increase in unrelated donor Allo HCTs. From 1994-95 to 2004-05, Allo HCT increased for AML/ALL, MDS/MPS, and NHL/HL, but decreased for CML and MM. Allo HCT conditioning regimen intensity was 100% myeloablative in 1994-95, whereas reduced-intensity/nonmyeloablative regimens were used in 28% of Allo...
HCTs in 2004-05. The use of peripheral blood and cord blood has dramatically increased. The median age and upper age limit have increased for both Auto HCT and Allo HCT. The percent of non-White race recipients increased from 1994-95 to 2004-05 for both auto HCT and Allo HCT.

Conclusions: The HCT population has changed dramatically over time. Further analyses are ongoing to determine the impact of these changes on the success of HCT.

Study # HS08-04
Title: Autologous HCT for breast cancer
Study Chair: David Howard (Emory University)
MS Statistician: Anna Hassebroek (ahassebr@nmdp.org)
PhD Statistician: TBD
Study Status: Manuscript preparation
Purpose: To study the mechanisms for incorporating the findings of comparative effectiveness research into clinical practice. There are a number of factors that promote adoption of new treatments, but these same factors may work against disadoption of established treatments found to be ineffective.

Patients/Methods: In this study, we use patient-level data from CIBMTR to examine disadoption of high dose chemotherapy followed by autologous blood and marrow transplantation (HDC/BMT) as a treatment for breast cancer following the release of negative clinical trials results in early 1999.

Results: There was rapid disadoption; one year after the results became public, procedure volume was 20% of the early 1998 peak. Hospitals that participated in the trials, teaching hospitals, and comprehensive cancer centers were no slower to disadopt HDC/BMT compared to other hospitals. Further examination suggests that hospitals passively abandoned HDC/BMT as demand declined rather than actively deciding to discontinue offering HDC/BMT to patients.

Conclusions: The case of HDC/BMT suggests that randomized controlled trials of questionable treatments, though costly, can yield long-run savings.

Health Policy and Psychosocial Issues Working Committee Studies in Progress

Study # HS06-02
Title: Comparison of cord blood utilization and transplant outcomes among different racial/ethnic groups undergoing HCT.
Study Chair: Karen Ballen (Massachusetts General Hospital)
MS Statistician: Tanya Pedersen (tpeders@nmdp.org)
PhD Statistician: John Klein
Study Status: Analysis
Purpose: To determine if the clinical outcomes of Umbilical cord blood transplantation (UCBT) for White patients is comparable to the outcomes of other racial groups. UCBT is a useful alternate stem cell source for patients with leukemia in need of an allogeneic transplant who have no matched related or unrelated donor. Extensive resources have been mobilized to increase the number of non-White UCB donors, in an effort to provide an adequate stem cell source for non-White patients who may have a difficult time finding a compatible unrelated marrow or peripheral blood stem cell donor.

Patients/Methods: The study population includes AML, ALL, CML, and MDS patients who received an unrelated single UCBT from 1995-2006. Patients receiving multiple cord blood units will be excluded. Outcomes of interest are hematopoietic recovery, acute GVHD, chronic GVHD, TRM, relapse, disease-free survival and overall survival.

Results: Analysis in progress
**Study # HS06-03**

**Title:** Survival trends among adolescent and young adult recipients of sibling allogeneic HCT for the treatment of acute myelogenous leukemia

**Study Chair:** Brandon Hayes-Lattin (Oregon Health and Science University)

**MS Statistician:** Anna Hassebroek (ahassebr@nmdp.org)

**PhD Statistician:** Ruta Bajorunaite

**Study Status:** Analysis

**Purpose:** To determine whether less favorable trends have occurred in transplant outcomes among the adolescents and young adults (AYA) population than among other age cohorts, due to biologic, social and/or behavioral factors. There has been a lack of incremental improvement in survival rates within the AYA population with cancer since the 1970’s. Because a large proportion of AYA patients are diagnosed with hematologic malignancies and many are treated with HCT, we seek to compare trends in transplant outcomes in the AYA population with those of younger and older cohorts.

**Patients/Methods:** The study population will include patients of all ages who received an allogeneic transplant for AML from 1980-2005. Patients with APL will be excluded, as will patients who have received a prior autologous transplant. Outcomes of interest are Overall survival, TRM, relapse and progression-free survival.

**Results:** Analysis in progress

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**Study # HS07-02**

**Title:** The financial impact of allogeneic HCT on patient and family

**Study Chairs:** Kate Pedersen (Office of Patient Advocacy, NMDP)

Navneet Majhail (University of Minnesota)

**MS Statistician:** Tanya Pedersen (tpederse@nmdp.org)

**PhD Statistician:** TBD

**Study Status:** Data collection

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**Study # HS08-03**

**Title:** Estimating current burden/future trends in the number of HCT survivors in the United States

**Study Chair:** Navneet Majhail (University of Minnesota)

**MS Statistician:** Navneet Majhail (majha001@umn.edu)

**PhD Statistician:** TBD

**Study Status:** Analysis

**Purpose:** To estimate the present overall number of HCT survivors in the US, to estimate the present number of allogeneic and autologous HCT survivors, and to estimate the future number, through 2020, of survivors of HCT for leukemia, lymphoma and myeloma in the US.

**Patients/Methods:** To estimate the number of present HCT survivors, all patients reported to the CIBMTR through 2007 will be included. To estimate future HCT survivors, patients with acute or chronic leukemia, myelodysplastic syndrome, lymphoma and multiple myeloma will be included.

**Results:** Analysis in progress

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**Study # HS09-02**

**Title:** Outcome comparison after HCT between patients treated by the Department of Veterans Affairs and the U.S. sample population

**Study Chairs:** Cesar Freytes (University of Texas Health Science Center)

Juan Toro (University of Texas Health Science Center)

**MS Statistician:** Anna Hassebroek (ahassebr@nmdp.org)
PhD Statistician: TBD
Study Status: Data collection

Health Policy and Psychosocial Issues Working Committee Planned Studies

**Study # HS08-01**
Title: Accreditation deficiencies and survival outcomes post HCT
Study Chair: Fausto Loberiza (University of Nebraska Medical Center)
MS Statistician: Tanya Pedersen (tpederse@nmdp.org)
PhD Statistician: TBD
Study Status: Protocol development

**Study # HS09-01**
Title: Practice patterns in HCT for AML
Study Chair: Navneet Majhail (University of Minnesota)
MS Statistician: Anna Hassebroek (ahassebr@nmdp.org)
PhD Statistician: TBD
Study Status: Protocol development

Go to www.cibmtr.org for a biannual study status update.
10.9 IMMUNE DEFICIENCIES/INBORN ERRORS OF METABOLISM WORKING COMMITTEE

**Committee Leadership**

**Co-Chair:** Mitchell Horwit, MD, Duke University  
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**Co-Chair:** Ed Horwit, MD, PhD, Children’s Hospital of Philadelphia  
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**Statistician:** Anna Hassebroek, MPH, CIBMTR Statistical Center Minneapolis  
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**Statistician:** Jennifer Le-Rademacher, PhD, CIBMTR Statistical Center Milwaukee  
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**Scientific Director:** Mary Eapen, MD, MS, Medical College of Wisconsin  
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**Immune Deficiencies/Inborn Errors Working Committee Publications**

**Study # ID02-02**  

**Purpose:** To evaluate the possibility that allogeneic hematopoietic stem cell transplantation (HCT) offers the possibility of curative therapy for Leukocyte Adhesion Deficiency (LAD), a rare primary immune disorder caused by defects of the CD18 b-integrin molecule on immune cells. The condition usually presents in early infancy and is characterised by deep tissue infections, leukocytosis with impaired formation of pus and delayed wound healing.

**Patients/Methods:** The course of 36 children with a confirmed diagnosis of LAD who underwent HCT between 1993 and 2007 was retrospectively analysed. Data was collected by the registries of the European Society for Immunodeficiencies /European Group for Blood and Marrow Transplantation and CIBMTR. Patient numbers at any individual center being limited, we surveyed the transplant experience at 14 centers worldwide.

**Results:** At median follow-up of 62 months (extending to 14 years), overall survival was 75%. Myeloablative conditioning regimens were used in 28 patients, and reduced intensity conditioning in 8 patients, with no deaths in this subgroup. Survival after matched family donor and unrelated donor transplants was similar, with 11/14 matched family donor and 12/14 unrelated donor recipients alive. Mortality was greatest following haplo-identical transplants, where 4/8 children did not survive. Twenty-seven transplant recipients are alive, with full donor
Patients/Methods: Engraftment in 17 cases, mixed multi-lineage chimerism in 7 patients, and mononuclear cell restricted chimerism in a further 3 cases.

Conclusions: HCT offers long-term benefit in LAD and should be considered as an early therapeutic option if a suitable HLA-matched stem cell donation is available. Reduced intensity conditioning was particularly safe and mixed donor chimerism appears sufficient to prevent significant symptoms, although careful long-term monitoring will be required for these patients.

Immune Deficiencies/Inborn Errors Working Committee Preliminary Results

Study # ID98-05
Title: Hematopoietic cell transplantation for infantile osteopetrosis
Study Chair: A Fasth (Queen Silvia Children’s Hospital)
              PJ Orchard (University of Minnesota)
MS Statistician: Mary Eapen (meapen@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Manuscript preparation
Purpose: To assess the effectiveness of reconstituting osteoclast function offering the possibility of cure for infantile osteopetrosis, a rare lethal disorder. Children are severely affected within months after birth and, if left untreated, only about 30% survive to 6 years of age. Some small studies show HCT to be effective, thus offering the possibility of cure.

Patients/Methods: 94 children receiving HCT for osteopetrosis from 1978-1999 were studied. Median age at HCT was 6 months (range 1-132 months). Median interval from diagnosis to HCT was 4 months (range 1-119). 48% of allogeneic transplants were from HLA-identical siblings, 22% from alternative related donors and 30% from unrelated donors. Twelve children received umbilical cord blood grafts, one, a peripheral blood graft and the remainder, bone marrow. Busulfan/Cyclophosphamide (BuCy) (77%) was the most frequently used preparative regimen; 18% received total body irradiation. 14% of grafts were T-cell depleted.

Results: 44 children were alive post HCT with a median follow-up of 49 months (range 4-266). Three-year probabilities of overall survival among recipients of HLA-identical sibling, alternative related and unrelated donors were 50% (35-64), 57% (34-75) and 38% (20-55), respectively.

Conclusions: This analysis is the largest yet conducted on the outcome of HCT for osteopetrosis and confirms the effectiveness of HCT as therapy for this disorder.

Study # ID99-02
Title: The role of HCT in Langerhans cell histiocytosis
Study Chair: RM Egeler (Leiden University Medical Center)
              Alexandra Filipovich (Children’s Hospital Medical Center)
MS Statistician: Anna Hassebroek (ahasbr@nmdp.org)
PhD Statistician: Not applicable/descriptive study
Study Status: Manuscript preparation
Purpose: To assess the feasibility of HCT in patients with Langerhans cell histiocytosis (LCH), a poorly understood and occasionally aggressive disorder that features lesional cells akin to Langerhans cells.

Patients/Methods: The results of HCT for LCH were studied through the collaborative use of three large observational databases. The study included 22 allogeneic transplantations (HLA-identical and non-identical related as unrelated donors) for LCH reported to the CIBMTR, the EBMT and the general Japanese Registry. Twenty of the 22 patients (91%) in this cohort were younger than two years of age at transplantation. All patients received front-line therapy for LCH, but failed
to achieve remission. All patients had multi-organ involvement and 20 of 22 (91%) had bone marrow involvement prior to or at transplantation. All but one patient had at least one poor prognosis organ involvement (bone marrow, liver or lung). Six had stable disease at transplantation and 16 had progressive disease. With a median follow-up of more than four years, 8 of 22 patients were alive.

Results: The 1- and 2-year probabilities of overall survival were 45% (range 25-66) and 35% (range 16-56), respectively. Causes of mortality included recurrent/ progressive disease (n=2), veno-occlusive disease (n=2), infections (n=7) and diffuse alveolar hemorrhage (n=1).

Conclusions: While HCT in LCH is feasible for patients who fail conventional therapy, transplant-related mortality is high. It is uncertain whether newer approaches in transplantation such as reduced-intensity conditioning regimens may lower transplant-related mortality.

Study # ID00-01
Title: Malignancies after HCT for primary immune deficiency disorders (PIDD).
Study Chair: Naynesh Kamani (Children’s National Medical Center)
MS Statistician: Anna Hassebroek (ahassebr@nmdp.org)
PhD Statistician: TBD
Study Status: Manuscript preparation
Purpose: To assess the incidence of malignancies in children with PIDD following allogeneic HCT and analyze risk factors for the development of malignancies.

Patients/Methods: 2,602 patients from the CIBMTR database who had undergone allogeneic HCT for PIDD, patient, disease and transplant risk factors for development of a post-HCT malignancy were analyzed, and pathology reports were retrieved and reviewed independently by a pathologist for confirmation.

Results: The incidence of malignancy was highest for severe combined immunodeficiency (SCID) patients (3.7%), with an overall incidence of 1.65% for PIDD. 24/27 patients confirmed as having developed a malignancy post-HCT had a lymphoproliferative disorder (PTLD) at a median of 2 months post-HCT. Of these, 16 had received T-cell depleted (TCD) bone marrow. Three patients developed myelodysplastic disorder MDS (median 44 months). All had undergone total body irradiation and had received T-cell depleted marrows.

Conclusions: Patients with PIDD who undergo HCT appear to be at a relatively low risk of developing malignancies compared to the historical risk of cancer in these patients. The most frequent malignancy seen is early-onset PTLD and as has been noted for other HCT recipients, the use of TCD appears to correlate with the development of PTLD post-transplantation.

Study # ID06-02
Title: Overall survival after allogeneic HCT for congenital immunodeficiency and metabolic disorders.
Study Chair: Mitch Horwitz (Duke University)
Ed Horwitz (Children’s Hospital of Philadelphia)
MS Statistician: Anna Hassebroek (ahassebr@nmdp.org)
PhD Statistician: Gisela Silva (Gsilva@mcw.edu)
Study Status: Manuscript preparation
Purpose: To compare overall survival after allogeneic HCT for congenital immunodeficiency and metabolic disorders with children of a similar age who receive HCT for acute leukemia in first or second complete remission.

Patients/Methods: 343 children (≤ 5-years) with congenital immunodeficiency (129 with severe combined immunodeficiency [SCID]; 214 with non-SCID) and 354 children with metabolic disorders were
compared to 622 age-matched children with acute leukemia and aged ≤5-years (control population).

Results: Using univariate analysis, 5-year overall survival was higher after HLA-matched sibling donor transplants for SCID (80%), non-SCID (84%) and metabolic disorders (78%), compared to the control group (51%, p<0.001). Among recipients of unrelated donor HCT, 5-year overall survival was highest after HCT for non-SCID (66%), compared to SCID (41%, p=0.002), metabolic disorders (51%, p=0.006) and control (50%, p=0.003). In multivariate analysis, donor type was the only factor associated with survival. We observed no differences in survival after unrelated donor bone marrow and cord blood HCT.

Conclusion: Prompt referral for unrelated donor HCT for these children should be encouraged, even in the absence of an HLA-matched sibling donor.

Study # ID06-03
Title: Outcomes of transplantation using various cell sources for Hurler’s Syndrome: A Eurocord-EBMT-CIBMTR collaborative study.
Study Chairs: JJ Boelens (UMC Utrecht/Wilhelmina Children’s Hospital)
                   Vanderson Rocha (Hôpital Saint-Louis)
                   Joanne Kurtzberg (Duke University)
                   Paul Orchard (University of Minnesota)
MS Statistician: Anna Hassebroek (ahassebr@nmdp.org)
PhD Statistician: NA
Study Status: Manuscript preparation
Presentation: Accepted for oral presentation at the 2010 BMT Tandem Meetings.
Purpose: To study the impact of various cell sources (Matched Sibling donor [MSD], unrelated donor [URD], unrelated cord blood [UCB] and T-cell depleted URD [TCD-URD]) on outcomes of allogeneic-HCT in Hurler’s Syndrome. Allogeneic HCT, if performed early, halts disease progression and prolongs life for patients with Hurler’s Syndrome, an otherwise lethal disease.
Patients/Methods: We analyzed 258 patients with Hurler’s Syndrome transplanted from 1995 to 2007. Median age at transplantation was 17 months, and median follow up, at 5 years. The donors were MSD (n=37; 14%), URD (n=52; 21%), UCB (n=116; 44%), TCD-URD (n=53; 21%). 97% of patients received busulfan-containing myeloablative regimens.
Results: Overall survival was higher in patients aged <20months and after MSD transplant, compared to the other sources URD, UCB and TCD-URD. 21% of surviving patients (median follow-up, 5 years) had mixed donor chimerism (<5% donor) and the remaining 69% patients had donor chimerism ≥95%. 93% of UCB transplant recipients had ≥95% donor chimerism compared to 73% after MSD, 64% after URD and 75% after TCD-URD.
Conclusion: Early referral for transplantation with a suitably matched related or unrelated donor prior to 20 months of age is recommended.

Study # ID09-01
Title: Long-term survival and late deaths after HCT for primary immunodeficiency diseases and inborn errors of metabolism
Study Chair: Mary Eapen (Medical College of Wisconsin, CIBMTR)
MS Statistician: Anna Hassebroek (ahassebr@nmdp.org)
PhD Statistician: Kwang Woo Ahn
Study Status: Manuscript preparation
Presentation: Presented as a poster at the 2009 American Society of Hematology Meeting.
Purpose: To study late mortality after HCT for severe combined immunodeficiency (SCID), non-SCID immune diseases and inborn errors of metabolism (IEM).

Patients/Methods: 960 patients (SCID, n=201; non-SCID, n=352; IEM, n=352) who survived at least 2 years after HCT and were disease-free were eligible. 70% of SCID patients received grafts from a related donor and 56% of non-SCID and IEM patients received grafts from an unrelated donor.

Results: The 7-year probabilities of overall survival were 93%, 96% and 90% for SCID, non-SCID immune diseases and IEM, respectively. No factor was associated with late deaths for SCID. For non-SCID, late deaths included more recipients of T-cell depleted grafts. For IEM, there were more late deaths after unrelated donor and mismatched related donor transplant than matched sibling donor transplant. There were 69 late deaths, with 52 occurring 2 – 6 years after transplantation and 17 after 6 years.

Conclusion: Though the risk of late deaths in this population is in excess of that for the general population for several years after transplantation, with extended follow up, the risk appears to decrease towards normal rates for patients with SCID and non-SCID surviving beyond 6-years after HCT but not for patients with IEM.

**Immune Deficiencies/Inborn Errors Working Committee Studies in Progress**

**Study # ID98-02/D00-111**
- **Title:** HCT for severe combined immunodeficiency syndrome
- **Study Chair:** Alexandra H. Filipovich (Cincinnati Children’s Hospital)
- **MS Statistician:** Anna Hassebroek (ahasbebr@nmdp.org)
- **PhD Statistician:** TBD
- **Study Status:** Data File Preparation

**Study # ID04-02/D01-68**
- **Title:** Unrelated HCT for severe Wiskott-Aldrich syndrome: analysis of outcome by graft type
- **Study Chair:** Alexandra H. Filipovich (Cincinnati Children’s Hospital)
- **MS Statistician:** Vincent He (vhe@mcw.edu)
- **PhD Statistician:** TBD
- **Study Status:** Data Collection

Go to [www.cibmtr.org](http://www.cibmtr.org) for a biannual study status update.
10.10 IMMUNO BIOLOGY WORKING COMMITTEE

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Immunobiology Working Committee Publications

Study # R02-40s/R03-63s


Presentation: Presented orally at the 2009 American Society of Hematology Meeting.

Purpose: To assess the correlation between natural killer (NK) cell alloreactivity, as determined by donor killer-cell immunoglobulin-like receptors (KIR) and recipient human leukocyte antigen (HLA), and successful HCT for acute myeloid leukemia (AML). Survival for patients with AML is limited by treatment-related mortality and relapse after unrelated donor HCT.

Patients/Methods: Donors and recipients from 209 HLA-matched and 239 mismatched T-replete unrelated donor (URD) transplantations for AML were genotyped, hypothesizing that donor KIR genotype (A/A: two A KIR haplotypes; B/x: at least one B haplotype) would affect outcomes.
Purpose: Three-year overall survival was significantly higher after transplantation from a KIR B/x donor (31% [95% CI: 26-36] vs. 20% [95% CI: 13-27]; p = 0.007). Multivariate analysis demonstrated a 30% improvement in the relative risk of relapse-free survival with B/x donors compared to A/A donors (RR 0.70 [95% CI 0.55-0.88]; p=.002). B/x donors were associated with a higher incidence of chronic GVHD (RR 1.51 [95% CI 1.01-2.18]; p=.03), but not of acute GVHD, relapse or treatment-related mortality.

Conclusions: That unrelated donors with KIR B haplotypes confer significant survival benefit to patients receiving T-replete HCT for AML. KIR genotyping of prospective donors, in addition to HLA typing, should be performed to identify HLA-matched donors with B KIR haplotypes.

Study # IB05-01s

Purpose: To confirm results of several studies in HLA-matched sibling HCT that reported an association between mismatches in minor histocompatibility antigens (mHAg) and outcomes.

Patients/Methods: 730 unrelated donor pairs matched at HLA-A, B, C, DRB1, and DQB1 were analyzed. Patients had acute and chronic leukemia and myelodysplastic syndrome (MDS), received myeloablative conditioning regimens and calcineurin inhibitor-based GVHD prophylaxis, and most received bone marrow (85%). Donor and recipient DNA samples were genotyped for mHAg including: HA-1, HA-2, HA-3, HA-8, HB-1, CD31125/563. Primary outcomes included grades III-IV acute GVHD and survival; secondary outcomes included chronic GVHD, engraftment and relapse.

Results: Single disparities at HA-1, HA-2, HA-3, HA-8, and HB-1 were not significantly associated with any of the outcomes analyzed. In HLA-A2 positive individuals, single CD31563 or multiple mHAg mismatches in the HvG vector were associated with lower risk of grades III-IV acute GVHD.

Conclusions: mHAg incompatibility at HA-1, HA-2, HA-3, HA-8, HB-1 and CD31 has no detectable effect on the outcome of HLA-matched unrelated donor HCT.

Study # R01-60

Purpose: To determine if there are particular common disparities that have detectable effects on transplant outcomes by studying the most frequent HLA-A mismatches. HLA-A mismatches were characterized to provide the foundation for a structure-based ranking system for HLA disparities.

Patients/Methods: Patients in this investigation received transplants for hematological malignancies, facilitated by the NMDP between 1990 and 2002 (n=4,226). High-resolution HLA typing was performed for HLA-A, -B, -C, -DRB1, -DQA1, -DQB1, -DPA1 and -DPB1.

Results: In 745 donor-recipient pairs with HLA-A mismatches, there were 190 different combinations of HLA alleles; 60% also had mismatches at HLA-B, -C and/or -DRB1. When HLA-B, -C, and -DRB1 were matched, an HLA-A disparity (n=282) was associated with increased mortality (odds ratio 1.32, confidence interval 1.07-1.63). The most frequent HLA-A mismatches were HLA-A*0201:0205 (n=28), HLA-A *0301:0302 (n=15), HLA-A *0201:0206 (n=15), HLA-A *0201:6801 (n=12), and HLA-A*0101:1101 (n=11,) and none of these showed statistically significant
relationships with transplant outcomes (engraftment, acute and chronic GVHD, relapse, transplant-related mortality or overall survival).

Conclusions: More than 11,000 pairs are needed to determine the risks associated with particular HLA-A disparities; structure-based strategies are a feasible alternative for studying HLA disparities.

Study # R03-57s

Journal Citation: Shah R, Selby ST, Yokley B, Slack RS, Hurley CK, Posch PE. **TNF, LTA and TGFBI genotype distributions among acute graft versus host disease (aGVHD) subsets after HLA-matched unrelated hematopoietic stem cell transplantation: a pilot study.** Tissue Antigens 2009 74(1):50-56. [PMCID not yet available]

Purpose: To determine whether polymorphisms in the regulatory region and gene of tumor necrosis factor (TNF), lymphotoxin alpha (LTA) and transforming growth factor beta 1 (TGFBI) were associated with severity of aGVHD in patients undergoing HLA-matched allogeneic HCT. Cytokine single nucleotide polymorphisms (SNPs) and consequent production levels have been associated with the development of acute GVHD.

Patients/Methods: The distribution of SNPs and their linkages was examined in 38 recipient-donor pairs with either low grade (grade 0-I) or high grade (grade III-IV) aGVHD.

Results: No significant differences were found.

Conclusions: There are trends noted in genotype distributions among aGVHD grade groups for each of these cytokines. It was calculated that at least 162 pairs for SNP genotypes and 500 pairs for allelic genotypes would be needed to show significance in the distributions.

Study # IB06-08


Purpose: To test whether mismatching between donor and recipient at MICA influences gastrointestinal (GI) GVHD. Major histocompatibility complex (MHC) class I chain-related gene A (MICA) is a polymorphic, MHC-like protein with restricted tissue expression. The highest levels of MICA are found on the GI epithelium, a major target tissue for GVHD. MICA is stress inducible and is increased after oxidative stress, infection and heat shock. MICA is a ligand for the immune-activating receptor NKG2D. NKG2D is an immune-activating receptor on NK and T-cells and NKG2D-MICA interactions lead to cell activation and cytotoxicity.

Patients/Methods: 38 well-HLA-matched donor-recipient pairs from the NMDP had allele-level typing for MICA. Half of the recipient cohort had GI GVHD and the remainder was free of GVHD.

Results: 10/58 MICA alleles (in a mainly Caucasian cohort) were identified. Tight linkage between MICA and HLA-B (in this highly HLA-matched cohort, matched for HLA-A, B, C, DRB1, DQ and DP) was observed. No effect of donor-recipient MICA mismatching on GVHD (nearly all pairs were matched [37/38]). There was no obvious association for a particular MICA allele and GVHD. A higher rate of GI GVHD for recipients having the MICA amino acid motif was found in the MICA alleles 004, 006, 009, 044 and 046 in combination with an HLA-Bw4 allele (2/19 vs. 8/19).

Conclusions: Independent of HLA-B, this study did not identify an impact of MICA matching on GI GVHD.
Immunobiology Working Committee Preliminary Results

Study # R02-40s/R03-63s

**Title:** Choosing donors with favorable KIR B genotypes for unrelated HCT results in superior relapse protection and better relapse-free survival for patients with acute myeloid leukemia (AML)

**Study Chair:** Jeffrey S. Miller (University of Minnesota-Minneapolis)

**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)

**PhD Statistician:** John P. Klein (klein@mcw.edu)

**Study Status:** Ongoing

**Purpose:** To investigate the beneficial effect of KIR B donors and develop a donor selection strategy to improve clinical outcomes after HCT for leukemia.

**Patients/Methods:** Multivariate models were used to evaluate the effect of donor KIR genotypes on clinical outcomes after unrelated donor (URD) transplants facilitated by the NMDP for AML (n=1086) and acute lymphoblastic leukemia (ALL: n=334) between 1988 and 2006.

**Results:** Compared to KIR A/A donors, using those with more KIR B gene motifs (centromeric [Cen] or telomeric [Tel]) protected against relapse and improved relapse-free survival. Most striking, Cen-B/B donors conferred significant protection against AML relapse (relative risk [RR] of relapse 0.34, 95% confidence interval (CI, 0.2-0.57), p <0.0001) with absolute relapse rates of only 15.4% compared to 37.2% for donors with 0 or 1 B-motif. Similar improvements in AML relapse (RR 0.64, [95% CI .48-0.86]; p=0.003) were seen in the 21% of donors with ≥ 2 B-motifs who were not Cen-B/B. Donor KIR genotype had no effect on rates of graft vs. host disease or treatment related mortality. No effect was observed in patients with ALL.

**Conclusion:** To capture the benefit of Cen-B and/or higher B domain content scores we propose that the ~30% of donors who have ≥ 2 B domains (includes all Cen-B/B donors) be given preference over donors with 0 or 1 KIR B domains.

Study # IB05-02s

**Title:** Effect of single Class I mismatching on unrelated donor HCT

**Study Chair:** Martin B. A. Heemskerk (Leiden University Medical Center)

**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)

**PhD Statistician:** Tao Wang (taowang@mcw.edu)

**Study Status:** Additional analysis & manuscript preparation

**Purpose:** To confirm previous findings in a larger cohort. Single highly-divergent HLA class I mismatches were associated with superior survival rates after HCT compared to other single HLA class I mismatches in our previous study. This is an International Histocompatibility Working Group study.

**Patients/Methods:** Outcomes of 654 HCTs with a single HLA class I mismatch were analyzed. Overall survival and other transplantation-related endpoints were analyzed in relation to the category of HLA class I mismatch with univariate and multivariate Cox regression analysis.

**Results:** Univariate and multivariate analysis did not identify any association between highly divergent class I mismatches and outcomes.

**Conclusions:** We were unable to confirm previous study results. However, most of the current HCTs were T-cell replete and the previous study included predominantly T-cell deplete HCTs. The study will be repeated on a large cohort of T-cell depleted HCTs. This large cohort (n=504) of T-cell depleted HCTs with similar HLA mismatch criteria has been divided into three groups according to the HLA amino acid mismatch criteria. The data were analyzed similar to the previous cohort of 654 HCTs, and analysis should be finished by the end of December 2009, after which data can be incorporated into the manuscript.
**Study # IB06-02**

**Title:** Impact of mismatches in low expression HLA loci on the outcome of unrelated HCT

**Study Chair:** Marcelo Fernandez-Vina (M. D. Anderson Cancer Center)

**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)

**PhD Statistician:** John P. Klein (klein@mcw.edu)

**Study Status:** Manuscript preparation

**Purpose:** To investigate the role of incompatibilities in the HLA DRB3/4/5, DQ and DP (low expression) loci (LEL) on the outcome of unrelated HCT. We hypothesized that the effects of these loci are weak, cumulative and only demonstrable in combination with mismatches in other loci.

**Patients/Methods:** Results of 3,853 U.S. transplants facilitated by NMDP between 1988 and 2003 were evaluated and compared to retrospective HLA high-resolution typing. Patients had acute myelogenous leukemia (AML), acute lymphoblastic leukemia (ALL), chronic myelogenous leukemia (CML), or MDS.

**Results:** In the 7/8 HLA-A, B, C, DRB1 matched group, patients with 3 or more mismatches (MM) in LEL in the GVHD vector had significantly higher risk for mortality and transplant-related mortality than the subgroups with 0MM and 1MM in LEL. No single LEL appeared to have a more pronounced effect on clinical outcome, when mismatched, versus the other LEL.

**Conclusions:** Three or more mismatches at the HLA class II LEL are associated with poor clinical outcome after 7/8 matched transplantation. Prospective evaluation of matching for the LEL may be warranted to reduce post-transplant risks in 7/8 HLA-A, B, C, DRB1 matched donor recipient pairs.

**Study # IB06-06**

**Title:** Comparison of transplant outcomes using HLA-identical siblings, single antigen mismatched related donors, phenotypically-matched related donors or HLA -A, -B, -C and -DRB1 matched unrelated donors for treatment of malignant disease in children

**Study Chair:** Peter J. Shaw (Children's Hospital at Westmead)

**MS Statistician:** Fiona Kan (fkan@nmdp.org)

**PhD Statistician:** Kwang Woo Ahn (kwooahn@mcw.edu)

**Study Status:** Manuscript preparation

**Purpose:** To reevaluate the role of transplant for leukemia using a closely matched relative when the patient does not have a matched sibling donor.

**Patients/Methods:** The outcome of 1,208 patients who received bone marrow from a matched sibling donor were compared to 266 children who had a fully matched (8/8) unrelated donor and 151 patients whose donor was a relative who was closely matched.

**Conclusions:** The best outcome for children with leukemia is seen using a matched sibling donor. When considering the risks and benefits of the procedure, a closely matched relative should be considered in the same light as an unrelated donor when a matched sibling donor is not available.

**Study # IB06-03**

**Title:** One antigen mismatch related donor vs. HLA-matched unrelated donor HCT in patients with acute leukemia: results in the era of molecular typing

**Study Chairs:** David Valcarcel (Hospital de la Santa Creu i Sant Pau, Barcelona)

Jorge Sierra (Hospital de la Santa Creu i Sant Pau, Barcelona)

**MS Statistician:** Fiona Kan (fkan@nmdp.org)

**PhD Statistician:** Tao Wang (taowang@mcw.edu)

**Study Status:** Manuscript preparation
Purpose: To compare outcomes of allogeneic HCT between a single HLA antigen-mismatched related donor (mmRD) and an HLA-A, B, C and DRB1 matched unrelated donor.

Patients/Methods: Outcomes of adult patients (≥18 years old) receiving a transplant for the treatment of AML or ALL in first or second remission from either mmRD (N=89) were compared to those receiving a transplant from an 8/8 HLA-A, B, C and DRB1 allele matched unrelated donor (URD) (N=700) in procedures performed between 1995 and 2005.

Results: Univariate comparisons (mmRD vs. URD) showed: 3-year overall survival (42% vs. 44%, p=0.65), 3-year disease free survival (41% vs. 41%, p=0.93), 3-year treatment related mortality (39% vs. 31%, p=0.14), 3-year incidence of relapse (20% vs. 28%, p=0.09), grade III-IV acute GVHD by 100 days (22% vs. 15%, p=0.15), chronic GVHD by 1 year (35% vs. 47%, p=0.03). Multivariate analyses confirmed the univariate results, only showing a difference between mmRD and URD in chronic GVHD (RR=0.58, p=0.006).

Conclusions: HCT utilizing either mmRD or 8/8 allele-URD did not significantly differ in overall survival or disease-free survival, but chronic GVHD was more frequent after unrelated HCT.

Study # I806-04
Title: Effect of age on outcome in patients undergoing related HLA mismatched/ haploidentical stem cell transplantation
Study Chair: Lujia Dong (Fu Dan University, BMT Center, Shanghai Dao-Pei Hospital)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Analysis
Presentation: Accepted for presentation as a poster at the 2010 BMT Tandem Meetings.
Purpose: To determine if outcomes of haploidentical related donor transplants are different in adults and children.
Patients/Methods: 137 CIBMTR patients (50 children, 87 adults) and 181 Chinese patients (68 children, 113 adults) transplanted from related donors with 2 or more HLA-mismatches from 2000-2005 were studied. The two cohorts were analyzed separately because of differences in patient characteristics and transplantation outcomes.
Results: In the CIBMTR cohort, four subgroups were compared (adult-no TCD [T-cell depletion]; child-no TCD; adult TCD; child-TCD) due to a significant interaction between age and TCD. With TCD, adults had a higher mortality rate than children (RR 1.75, 95% CI 1.08-2.84, p=0.02). However, the difference was not observed in patients without TCD. In the Chinese cohort, there were no significant differences between the outcomes of children and adults.
Conclusions: Adults and children have similar outcomes after haploidentical HCT. In vitro TCD in adults is associated with worse outcomes in the cohort reported to CIBMTR.

Study # I806-05
Title: Use of high-resolution HLA data from NMDP for the International Histocompatibility Working Group (IHWG) in HCT
Study Chair: Effie Petersdorf (Fred Hutchinson Cancer Research Center)
MS Statistician: Michael Haagens (mhaagens@nmdp.org)
PhD Statistician: Ted Gooley (Fred Hutchinson Cancer Research Center)
Study Status: Manuscript preparation
Purpose: To define the clinical importance of mismatching at specific HLA loci and at class I and II residues. This is an IHWG study.
Patients/Methods: 4,138 9/10 matched unrelated transplants for hematologic disorders were analyzed. The odds of GVHD and hazards of mortality associated with single HLA-A, B, C or DRB1 mismatches were
defined using multivariate analysis. Risks associated with mismatching for polymorphic residues were measured.

Results: The number of mismatched residues does not appear to have a major impact on overall survival. Donor-recipient mismatching at certain residues of class I and class II may be associated with increased risk of mortality, relapse or GVHD. Donor-recipient mismatching at certain residues of class I and class II may have a protective effect. For certain residues, the specific amino acid mismatch may matter.

Conclusions: Non-permissible HLA mismatches are likely defined more by the number than the nature of residue mismatches. Clinically important residues may be directly involved in peptide binding or T-cell receptor contact, or may be distant from these sites. Future analysis should include structural analysis.

Study # IB07-01
Title: Evaluation of HLA matching requirements for peripheral blood stem cells (PBSC) in unrelated HCT
Study Chair: Ann Woolfrey (Fred Hutchinson Cancer Research Center)
MS Statistician: Michael Haagenson (mhaagens@nmdp.org)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Manuscript preparation
Purpose: To determine the effect of HLA-A, -B, -C, -DRB1, or -DQ mismatches on outcomes after unrelated PBSC HCT.

Patients/Methods: 1,933 patients receiving unrelated PBSC HCT between 1999 and 2006 for treatment of acute myelogenous leukemia (AML), acute lymphoblastic leukemia (ALL), chronic myelogenous leukemia (CML) or myelodysplastic syndromes (MDS) were studied. Myeloablative (65%) and reduced-intensity (35%) regimens were included.

Results: No effect of HLA-DQ mismatching was found. Matching for 8/8 alleles was associated with better survival at one year (56% vs. 47%) compared with 7/8 matched pairs. Comparing 8/8 to 7/8 donor-recipient pairs mismatched at specific loci, only HLA-C antigen mismatches (n=187) were significantly associated with lower disease-free survival and increased risk for overall mortality, treatment-related mortality and GVHD grades III-IV. HLA mismatching was not associated with relapse or chronic GVHD.

Conclusions: These data suggest that when 8/8 matched PBSC donors are not available, HLA-C antigen mismatched donors should be avoided. The effects of HLA-mismatching in unrelated PBSC may be distinct from marrow, although additional studies with larger numbers of patients may increase the power to detect effects of other specific locus mismatches.

Study # IB07-02
Title: The effect of HLA mismatches at the amino acid level on HCT
Study Chair: Susana R. Marino (University of Chicago Medical Center)
MS Statistician: Michael Haagenson (mhaagens@nmdp.org)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Manuscript preparation
Purpose: To examine the effect of HLA mismatches at the amino acid sequence level on day 100 survival (D1005).

Patients/Methods: Patients received an HCT between 1988 and 2003 for acute lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, or myelodysplastic syndromes (early or intermediate stage) and were HLA-class I and DRB1 matched (n=1,507) or had a single HLA-class I mismatch at HLA-A (n=179), -B (n=88), or -C (n=333) and were DRB1 matched. A three-step
analysis approach was used. Random Forest method was used as a screening tool, followed by traditional multivariate and univariate regression methods.

Results: Four patient variables (age, disease stage, disease type, gender match) and 31 amino acid substitutions [A positions 9, 43, 62, 63, 76, 77, 95, 97, 114, 116, 152, 156, 166, and 167; HLA-B positions 116, and 156; and HLA-C positions 1, 9, 11, 21, 77, 80, 95, 97, 99, 116, 156, 163, 219, 248, and 275] were identified as predictors of death at D100 post-transplant using Random Forest techniques. Thirteen of these amino acid substitutions had been previously reported by other investigators using classical multivariate analysis.

Conclusions: Although additional studies need to be performed to confirm these findings, based on the weight of the literature, it may be prudent to avoid donors, if possible, that are mismatched with the recipient at positions 116 or 156 at either of the HLA class I loci, at position 9 at HLA-A or HLA-C, and at position 99 at HLA-C, since these mismatches are consistently associated with higher risks of early death and other adverse outcomes.

Study # IB07-05
Title: Impact of donor-recipient ethnicity on risk of acute GVHD among HLA-A, B, C, DRB1, DQB1, and DPB1 matched unrelated donor transplants.
Study Chair: Yasuo Morishima (Aichi Cancer Center)
MS Statistician: Michael Haagenson (mhaagens@nmdp.org)
PhD Statistician: Ted Gooley (Fred Hutchinson Cancer Research Center)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To define the role of recipient and donor race on clinical outcome after unrelated donor HCT. This is an IHWG study.
Patients/Methods: 5,543 10/10 T-replete transplants for leukemia or myelodysplastic syndrome (MDS) were retrospectively evaluated according to donor-recipient race. Using Asian/Pacific Islander (AA, n=2062) recipient-donor pairs as the reference group, multivariate models defined the odds of GVHD and hazards of mortality associated with transplantation for Caucasians (CC, n=2414), Blacks (BB, n=39), Hispanics (HH, n=21), and recipient-donors of mismatched race (MM, n=268).
Results: The AA (predominantly Japanese) transplants had lower risks of acute GVHD, recurrent malignancy and mortality compared to CC. Although the number of BB and HH pairs was small, mortality was significantly higher in these groups than AA.
Conclusions: Ethnicity is associated with clinical outcomes after unrelated HCT from HLA matched donors with non-T-cell depleted GVHD prophylaxis.

Study # IB07-06
Title: Human leukocyte antigen: DP epitope study
Study Chair: Bronwen Shaw (Anthony Nolan Research institute)
MS Statistician: Michael Haagenson (mhaagens@nmdp.org)
PhD Statistician: Ted Gooley (Fred Hutchinson Cancer Research Center)
Study Status: Analysis
Purpose: To define the clinical importance of HLA-DP matching and epitopes on transplant outcome. This is an IHWG study.
Patients/Methods: 5,838 HLA-A,-B,-C,-DRB1,-DQB1 allele matched pairs included 4,490 DPB1 mismatched and 1,348 12/12 matched pairs. HLA-DP mismatched pairs were defined as T-cell epitope disparate (TCED) or matched (TECM). Using the TCEM HLA-DP mismatched pairs as the reference population, the risks of GVHD, relapse, TRM and mortality were defined for the TCED pairs.
Results: Compared to the DP mismatched by the TCEM group, 10/10 TCED transplants had statistically significantly higher hazards of TRM, grades III-IV acute GVHD, and mortality, but lower relapse (ns). The 12/12 transplants had lower treatment-related mortality rates and grades III-IV GVHD, but higher relapse and comparable mortality.

Conclusions: Among 10/10 matched pairs, knowledge of the TCE match status provides new information on transplant risks. TCED patients represent a high risk transplant group, whereas TCEM patients have comparable survival compared to 12/12 matches. These data provide impetus for future exploration of the impact of TCEs in HLA (9/10) mismatched transplants.

Study # IB07-07
Title: HLA-DR15 and transplantation HCT outcome
Study Chair: Alois Gratwohl (University Hospital Basel)
MS Statistician: Michael Haagens (mhaagens@nmdp.org)
PhD Statistician: Ted Gooley (Fred Hutchinson Cancer Research Center)
Study Status: Analysis
Purpose: To test the hypothesis that the presence of HLA-DR15 influences clinical outcome after unrelated HCT. This is an IHWG Study.

Patients/Methods: 7,161 10/10 HLA-matched unrelated donor transplants were defined according to the presence of HLA-DR15. Probability of survival, disease relapse and acute GVHD in patients with or without DR15 were defined. Transplants facilitated by the Japanese Marrow Donor Program (JMDP) (N=2,569) were analyzed separately from non-JMDP transplants (N=4,952).

Results: DR15 was present in 46% of JMDP and 34% of non-JMDP transplants. In both univariate and multivariable analysis, we could not demonstrate a significant effect of DR15 on survival, rates of relapse, incidence and severity of acute GVHD, with the exception of a small reduction in rates of grade II-IV aGVHD in DR15+ patients (hazard ratio 0.89, 95% confidence interval 0.79-0.99, p=0.03).

Conclusions: In a large population of well-matched unrelated donor transplants, HLA-DR15 status did not impact on survival, risk of disease relapse, or acute GVHD incidence and severity. DR15 does not appear to confer a special susceptibility to alloimmune effects in the setting of matched unrelated donor allogeneic HSCT.

Study # R03-70s
Title: Candidate gene study to examine the impact of chemokine and chemokine receptor gene polymorphisms on the incidence and severity of acute and chronic GVHD
Study Chair: Reza Abdi (Brigham and Women's Hospital)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: Tao Wang (taowang@mcw.edu)
Study Status: Manuscript preparation
Purpose: To test the association between recipient and donor chemokine polymorphisms and transplant outcomes.

Patients/Methods: 1,370 10/10 HLA-matched URD pairs were analyzed using multivariate Cox modeling to adjust for clinical characteristics. Patients had AML, ALL, MDS or CML.

Results: Recipients homozygous for a common high-expressing CCR5 haplotype (H1/H1) had better disease-free survival (DFS, 0.74, 95% CI 0.59-0.91, p=0.005) compared with heterozygous (H1+/+) and wild type recipients (+/+). Donors homozygous for this haplotype (H1/H1) were associated with more acute GVHD (RR 1.5, 95% CI 1.1-2.0), p=0.02) and lower DFS (RR 1.3, 95% CI 1.0-1.5, p=0.03).

Conclusions: A high-expressing CCR5 haplotype (H1/H1) is associated with better DFS if present in the recipient and absent in the donor.
**Study # R04-75s**

**Title:** Functional significance of cytokine gene polymorphisms in modulating risk of post-transplant complications

**Study Chair:** Effie Petersdorf (Fred Hutchinson Cancer Research Center)

**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)

**PhD Statistician:** Ted Gooley (Fred Hutchinson Cancer Research Center)

**Study Status:** Manuscript preparation

**Purpose:** To identify the immune response gene (IRG) variants that may be associated with risks of acute GVHD, relapse and mortality after unrelated donor HCT. This is an IHWG study.

**Patients/Methods:** 43 polymorphisms descriptive of 27 IRGs were identified in 1,215 10/10 HLA-matched unrelated donor transplants and risks measured for acute GVHD, relapse, TRM and overall survival associated with donor or recipient IRG genotype and with donor-recipient IRG mismatching and with simultaneous occurrence of recipient and/or donor single nucleotide polymorphisms (SNPs) within genes involved in pathways of pathogenesis of acute GVHD.

**Results:** Statistically significant associations between donor or recipient IRG genotype and grades III-IV acute GVHD (recipient MTHFR 222, IL15RA 182; donor IFNG -1615); relapse (recipient IL6 -174, PECAM1 125, PECAM1 563, PECAM1 670; donor IL1B -511, IL10 -819, IL10 -592, IL15RA 182); overall survival (donor MTHFR 222 and TLR4 399), and TRM (donor TLR4 399) were observed. Donor-recipient mismatching for IL4 -590 and TGFβ1 Leu10Pro was associated with increased risk of relapse.

**Conclusion:** Results suggest that sequence polymorphism of IRGs is functionally relevant in unrelated donor HCT.

**Study # IB05-03s**

**Title:** Genetic polymorphisms in the genes encoding human IL-7 Receptor-α: prognostic significance in allogeneic HCT

**Study Chair:** Klaus Müller (Rigshospitalet - Copenhagen, Denmark)

**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)

**PhD Statistician:** Tao Wang (taowang@mcw.edu)

**Study Status:** Manuscript preparation

**Purpose:** To validate previous results suggesting that donor +1237G in the alpha chain for IL-7R is associated with higher TRM and more acute GVHD.

**Patients/Methods:** 590 Caucasian adults with AML, ALL, CML or MDS with early stage disease transplanted with myeloablative conditioning and 10/10 HLA matched unrelated donors were studied. All transplants were T-replete.

**Results:** Neither donor nor recipient SNP genotypes for IL-7Rα were associated with overall survival or TRM. Some univariate associations were seen between donor SNP genotypes, relapse and acute and chronic GVHD but these were not confirmed in multivariate analysis.

**Conclusions:** Results do not support an association between the 3 examined IL-7Rα SNPs and adverse transplant outcomes.

**Study # R04-74s**

**Title:** Functional significance of killer-IG-ligand genes in HLA-matched and mismatched unrelated HCT

**Study Chairs:** Katharine Hsu (Memorial Sloan-Kettering Cancer Center)

**Bo Dupont (Memorial Sloan-Kettering Cancer Center)**

**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)

**PhD Statistician:** Ted Gooley (Fred Hutchinson Cancer Research Center)

**Study Status:** Analysis
Purpose: To determine the influence of donor KIR genotypes and haplotypes on myeloablative HCT for leukemia using sample data from the NMDP and IHWG.

Patients/Methods: DNA samples from 10/10 HLA-matched (n=751) and HLA-mismatched (n=522) T-replete myeloablative HCT donor-recipient pairs were KIR genotyped. Analyses focused on influence of missing ligand, missing self, donor activating KIR, donor KIR haplotype.

Results: Among 10/10 matched HCT pairs, there was a beneficial effect of missing ligand on overall survival in AML/ MDS patients. No benefit was seen in ALL or CML patients. Lack of recipient HLA-Bw4 appears to confer a benefit on survival. The effect of missing ligand could not be attributed solely to a decrease in relapse. No benefit was seen for specific donor activating KIR or KIR haplotype (AA vs BX).

Conclusions: NK alloreactivity against AML/MDS occurs according to missing KIR ligand. Donor activating KIRDS1 plays a role in survival, likely mediated by lowering GVHD, and inhibitory KIR alleles may play a functional role in HCT outcome.

Study # R04-76s
Title: Identification of functional single nucleotide polymorphisms (SNPs) in unrelated HCT
Study Chair: Effie Petersdorf (Fred Hutchinson Cancer Research Center)
MS Statistician: Michael Haagenson (mhaagens@nmdp.org)
PhD Statistician: Ted Gooley (Fred Hutchinson Cancer Research Center)
Study Status: Manuscript preparation
Purpose: To identify novel MHC resident variations of clinical importance. This is an IHWG study.
Patients/Methods: 2,505 10/10 matched pairs from the IHWG were characterized and genotyped using the Illumina platform for 1120 Major histocompatibility antigens (MHC) SNPs. Risks associated with recipient genotype, donor genotype, and donor-recipient mismatching were defined in multivariate analysis.

Results: Minor allele frequencies for recipients and donors were comparable for the entire panel of SNPs. In all three models (recipient SNPs, donor SNPs, and donor-recipient mismatching), variation within the class I, III and II regions were found to correlate with risks of acute GVHD, relapse, treatment related mortality, disease-free survival and survival. Mapping SNPs to the nearest known gene family/locus is currently in progress.

Conclusions: HLA-matched unrelated donor-recipient pairs may differ for SNPs within the MHC. Certain genotypes, and donor-recipient mismatching for SNPs, may indicate a functional gene that influences GVHD, relapse and survival after HCT.

Study # IB06-07s
Title: Insufficient evidence for association of NOD2/CARD15 or other inflammatory bowel disease (IBD)-associated markers on GVHD or other outcomes in T-replete, unrelated donor HCT
Study Chair: Nicholas Davidson (Washington University School of Medicine)
MS Statistician: Michael Haagenson (mhaagens@nmdp.org)
PhD Statistician: Tao Wang (taowang@mcw.edu)
Study Status: Submitted
Purpose: To determine if IBD markers, NOD2/CARD15, IL23-R, and IRGM are associated with adverse outcomes following URD transplantation.
Patients/Methods: Pre-transplant samples were obtained from 390 patients and their 10/10 HLA-matched unrelated donors. Patients received T-replete transplants for early stage AML, ALL, CML, or MDS using myeloablative conditioning between 1995 and 2004. DNA genotyping was performed using Sequenom and/or Taqman assays for three NOD2/CARD15 SNPs (rs2066844, rs2066845, rs2066847), two IL23R SNPs (rs11209026, rs11465804), and two IRGM SNPs
Conclusions: Multivariate analyses adjusting for clinical variables were performed for overall and disease-free survival, transplant-related mortality, relapse, acute GVHD and chronic GVHD.

Results: None of the three IBD-associated alleles showed evidence of a statistically significant association with any of the aforementioned outcomes at p <0.01.

Conclusions: Several factors may contribute to this discrepancy from prior studies, including differences in patient characteristics, exclusion of sibling-matched donor HCTs and T-cell depletion procedures. Our findings do not support the use of IBD-associated allele mutation status in the donor/recipient selection process.

Study # IB07-08
Title: Single nucleotide polymorphisms in the P53 Pathway (P53, MDM2, ATM AND P21/WAF1) and transplant outcome after unrelated HCT
Study Chair: Bo Dupont (Memorial Sloan-Kettering Institute)
MS Statistician: Michael Haagenson (mhaagens@nmdp.org)
PhD Statistician: Ted Gooley (Fred Hutchinson Cancer Research Center)
Study Status: Manuscript preparation
Purposes: 1) To determine if tumor suppressor p53 Arg72Pro polymorphism affects post-transplantation survival; 2) To determine if genetic variations in modifiers of p53 such as ATM, MDM2 and p21/Waf1 have an impact on the effect of p53 Arg72Pro; and 3) To determine if presence of the p53 Arg72Pro allele in HLA-A*0201 positive recipients increases post-transplantation disease-free survival.

Patients/Methods: 1,065 donor-recipient paired DNA samples obtained from the NMDP Research Repository were tested. All pairs were HLA 10/10 matched.

Results: The allele frequency of the p53 Codon 72Pro is 23% in Caucasian but 67% in African-Americans. Our studies to date indicate that homozygosity for the Pro allele is a significant risk factor for overall long-term survival after HCT.

Conclusions: Arg72Pro in TP53 in recipients may be a risk factor for overall long-term survival, but not for GVHD or relapse after HCT. Arg72Pro in donor does not appear to affect HCT outcome. Homozygosity for the Pro allele is a significant risk factor for overall long-term survival after HCT. Study was expanded to include reduced-intensity conditioning regimens and HLA mismatched cases. Testing is in progress.

Study # IB07-09
Title: To develop and test a prognostic index for survival in chronic myelogenous leukemia matched unrelated donor cohorts
Study Chair: Anne Dickinson (University of Newcastle)
MS Statistician: Michael Haagenson (mhaagens@nmdp.org)
PhD Statistician: Kim Pearce (University of Newcastle)
Study Status: Manuscript preparation
Purpose: To validate previous work in HLA-matched sibling transplantation showing that cytokine SNPs were associated with decreased survival and improved prognostic accuracy when combined with the European Group for Blood and Marrow Transplantation (EBMT) risk score in CML patients.

Patients/Methods: 383 adults with CML receiving 10/10 HLA-matched URD transplants were studied. After calculation of the EBMT score (determined by clinical factors), we tested whether absence of recipient TNFRII 196R, absence of donor IL-10 ATA/ACC and presence of donor IL-1Ra allele 2 were associated with transplant outcomes.
Results: The EBMT score predicted survival in the CIBMTR validation cohort. The polymorphisms were not associated with survival with or without adjustment for EBMT score; there was also no association with outcomes: acute GVHD, chronic GVHD, relapse, transplant-related mortality, or disease-free survival. Since this was a negative study, the original CLWP (EBMT) HLA-matched sibling population was compared to the CIBMTR cohort to see if population differences could explain the results. Differences were seen in donor age, sex matching, time from diagnosis to transplant, CMV positivity, and stem cell source.

Study # R03-65s
Title: Detection of H-Y antibodies in healthy female donors: Does H-Y presensitization predict male HCT outcome
Study Chair: David Miklos (Stanford University)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Manuscript preparation
Purpose: To confirm results of prior studies showing that 50% of F→M HCT patients develop specific antibodies for any of these H-Y antigens 4-12 months after HCT, and were associated with chronic GVHD and persistent disease remission (p<0.0001).

Patients/Methods: Pre-transplant sera were collected from 289 female donors who donated unrelated bone marrow grafts for HLA-identical male recipients undergoing myeloablative HCT for AML (18%), CML (38%), ALL (24%), MDS (13%), and non-Hodgkin lymphoma (NHL) (7%). Primary immune prophylaxis was cyclosporine A (CSA) or FK506 plus methotrexate (MTX) (78%) and T-cell depletion (22%). Presence of H-Y antibodies (tested via ELISA or H-Y microarrays) was correlated with chronic GVHD and recurrent malignancy.

Results: With eight-year median follow-up, cGVHD incidence was 47%. Eighteen percent relapsed, and overall survival was 50.2% at one year and 41.8% at two years. 22.3% female donor sera diluted 1:50 tested positive for any H-Y antigen by ELISA, and UTY was the most frequent target at 18.3%. H-Y microarrays detected antibodies for any H-Y antigen in 33% of female donors. H-Y seropositivity did not correlate with donor age by quartile nor reported number of donor pregnancies: nulliparous (38.4%), one (16.3%), two (19%), and three or more (26%). Child gender data was not available. Male recipients of H-Y seropositive donors had 51.2% cGVHD incidence, 20.1% relapse, and 45.8% overall survival at two years. By Cox regression analysis, these clinical outcomes for seronegative donors did not differ significantly: 42.7% cGVHD, 17.8% relapse and 39.3% overall survival.

Conclusions: Testing for H-Y antibodies in female donors before sex-mismatched unrelated donor HCT will not predict cGVHD or relapse risk, suggesting chronic GVHD and graft-vs.-leukemia responses develop from naïve and not memory lymphocytes.

Study # R04-98s
Title: Detection of donor-directed, HLA-specific alloantibodies in recipients of unrelated HCT and their relationship to graft/patient outcome
Study Chair: Robert Bray (Emory University Hospital)
MS Statistician: Michael Haagenson (mhaagens@nmdp.org)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Submitted
Purpose: To evaluate the role of donor-directed specific alloantibodies (DSA) in unrelated donor HCT. DSAs cause graft failure in animal models of HCT.
Patients/Methods: Archived pre-transplant sera from graft failure patients (N=37) and a matched case-control cohort (N=78) were tested to evaluate the role of DSA in unrelated donor HCT. Controls were matched for disease, disease status, graft type, patient age and transplant year. Patients had AML, ALL, CML or MDS, 98% received myeloablative conditioning regimens, 100% received T-replete grafts, 97% received marrow, 94% were HLA-mismatched and 97% received calcineurin-based GVHD prophylaxis.

Results: Among the 37 failed transplants, 9 (24%) recipients possessed DSA against HLA-A, B and/or DP, compared to only 1 (1%) of 78 controls. Therefore, the presence of DSA was significantly associated with graft failure (OR 22.84; 95% CI 3.57-∞; p=0.0002).

Conclusions: These results indicate that the presence of pre-transplant DSA in recipients of unrelated donor HCT are associated with failed engraftment and should be considered in HCT donor selection.

Study # IB06-09s
Title: Detection of HLA antibody to the mismatched antigen in single antigen HLA-mismatched unrelated donor HCT: Is it associated with GVHD outcome?
Study Chair: Sally Arai (Stanford University)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Analysis
Purpose: To determine whether alloantibody to HLA is made in patients with acute GVHD.
Patients/Methods: Day 100 serum samples of 40 recipient-donor pairs of single antigen/allele HLA-mismatched unrelated donor transplants who developed acute GVHD were tested. Class I and II antibody levels to the mismatched alleles were tested using single antigen beads covering 96 different class I (A,B,C) and 56 different class II (DR,DQ,DP) alleles on a Luminex platform. Since the threshold antibody response to HLA mismatch in marrow transplantation is unknown, we applied the established scale from solid organ transplantation where ≥1,000 is positive, 500-999 is possible, and <500 is negative. The limitation of the analysis is that the beads contain every antigen but not every allele.
Results: In the 40 pairs, no anti-A, B, or C allele-specific antibodies were detected at day 100 in either GVH or HVG directions. Class II antibodies against DRB1, DQB1, DPA1 and DPB1 were detected, with the highest frequency antibody seen against DPA1.
Conclusions: Day 100 Ab to class II rather than class I allele mismatch were observed. Current studies to determine if these are de novo or preformed antibodies are being performed using pre-transplant sera from these same pairs. Future studies will look at antibody association with GVHD and disease relapse with attention to class II on B cells as a meaningful GVL target.

Study # IB06-11s
Title: Effect of non-inherited maternal antigens (NIMA) in cord blood transplantation
Study Chair: Vinod K. Prasad (Duke University Medical Center – Durham, NC)*
*Since December 2008; preceding work was done by Lee Ann Baxter-Lowe (UC-San Francisco)
MS Statistician: Fiona Kan (fkan@nmdp.org)
PhD Statistician: TBD
Study Status: Manuscript preparation
Purpose: To determine the frequency with which NIMA tolerance may favorably influence outcomes of cord blood transplants.
Patients/Methods: HLA typing of 102 maternal samples was performed to determine the feasibility of studying NIMA in cord blood transplants. Pairs were found to be 3/6 (n=22), 4/6 (n=46), 5/6 (n=26), and
6/6 (n=8) matched by high-resolution HLA-A,-B, and -DRB1 typing. High-resolution HLA typing on the mother of the cord blood donor was used to identify NIMA in the donor.

**Results:** Of the 102 pairs, 12 (11%) had NIMA mismatches. The distribution of these NIMA mismatches was similar between 3/6 (14%; 3 of 22), 4/6 (13%; 6 of 46), and 5/6 (12%; 3 of 26) HLA-matched pairs. A preliminary 80% power calculation showed that the survival rates of 50% vs. 30% for NIMA vs. non-NIMA groups would require 1,900 to 3,500 patients in each of the HLA matching categories. However, if 3/6, 4/6, and 5/6 were combined, the required sample size would be around 450-500.

**Conclusions:** The frequency of NIMA mismatches in recipients of unrelated donor cord blood transplants is 12-14% and is similar between the HLA match categories. Larger numbers (450-500) will be needed to study the impact on survival and outcomes.

**Immunobiology Working Committee Studies in Progress**

**Study # R04-80s**
**Title:** Impact of HLA matching on outcome in pediatric patients undergoing unrelated umbilical cord blood transplantation
**Study Chair:** Susana R. Marino (University of Chicago Medical Center)
**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)
**PhD Statistician:** Tao Wang (taowang@mcw.edu)
**Study Status:** Data Collection

**Study # IB06-10**
**Title:** Evaluation of the impact of exposure to NIMA during fetal life and breast feeding and to the inherited paternal antigens during pregnancy on the clinical outcome of HCT from haploidentical family members
**Study Chair:** Jon Van Rood (Europdonor Foundation)
**MS Statistician:** Fiona Kan (fkan@nmdp.org)
**PhD Statistician:** TBD
**Study Status:** Data File Preparation

**Study # IB07-03**
**Title:** Analysis of KIR ligands in reduced-intensity conditioning allogeneic HCT
**Study Chair:** Ronald Sobecks (The Cleveland Clinic)
**MS Statistician:** Erik Iverson (eiverson@nmdp.org)
**PhD Statistician:** TBD
**Study Status:** Protocol received/in development

**Study # IB08-02**
**Title:** HLA matching for unrelated HCT for non-malignant disorders
**Study Chairs:** John Horan (Children’s Healthcare of Atlanta)
Ann Woolfrey (Fred Hutchinson Cancer Center)
**MS Statistician:** Erik Iverson (eiverson@nmdp.org)
**PhD Statistician:** TBD
**Study Status:** Protocol received/in development
**Study # IB07-04**

**Title:** Employing advanced bioinformatic methods for predicting peptide specificities of HLA molecules in the characterization of permissible mismatches in HCT

**Study Chair:** Soren Buus (University of Copenhagen)

**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)

**PhD Statistician:** Ted Gooley (Fred Hutchinson Cancer Research Center)

**Study Status:** Analysis

**Purpose:** To identify a way to use bioinformatic methods to define clinically relevant major histocompatibility index epitopes. This is an IHWG study.

**Patients/Methods:** MHCNetPan (M. Nielsen, et al., PLoS ONE 2, e796, 2007) will be used to define the distance for each pairwise donor-recipient MHC class I and II allele mismatch that are most strongly associated with post-transplant risks of acute GVHD and mortality. The study population will consist of HLA 9/10 matched unrelated donor pairs.

**Study # IB08-04**

**Title:** Immune response gene polymorphisms in unrelated donor HCT in children

**Study Chair:** Klaus Muller (Rigshospitalet)

**MS Statistician:** TBD

**PhD Statistician:** TBD

**Study Status:** Protocol received/in development

**Study # IB08-08**

**Title:** Genome-wide association in unrelated donor HCT recipients and donors

**Study Chair:** Rakesh Goyal (Children’s Hospital of Pittsburgh)

**MS Statistician:** Michael Haagenson (mhaagens@nmdp.org)

**PhD Statistician:** TBD

**Study Status:** Sample typing in progress

**Study # IB09-01s**

**Title:** Clinical importance of major histocompatibility complex haplotypes in umbilical cord blood transplantation

**Study Chair:** Effie Petersdorf (International Histocompatibility Working Group)

**MS Statistician:** TBD

**PhD Statistician:** TBD

**Study Status:** Data collection

**Study # IB09-02s**

**Title:** Non-permissive HLA-DPB1 disparities based on T-cell alloreactivity

**Study Chair:** Katharina Fleischhauer (Milan)

**MS Statistician:** TBD

**PhD Statistician:** TBD

**Study Status:** Protocol received/in development

**Study # IB09-03s**

**Title:** Clinical relevance of cytokine/immune response genes in umbilical cord blood transplant

**Study Chair:** Effie Petersdorf (International Histocompatibility Working Group)

**MS Statistician:** TBD
PhD Statistician: TBD
Study Status: Data collection

**Study # IB09-04s**
Title: Donor/recipient gene polymorphisms of drug metabolism and in innate immune response post allele-matched unrelated donor HCT
Study Chair: Vanderson Rocha (Hôpital Saint Louis–Unité de Recherche Clinique)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

**Study # IB09-05s**
Title: Identification of functional SNPs in umbilical cord blood transplant
Study Chair: Effie Petersdorf (International Histocompatibility Working Group)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Data collection

**Study # IB09-03s**
Title: Clinical significance of genome-wide variation in unrelated donor HCT
Study Chair: Effie Petersdorf (International Histocompatibility Working Group)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Data collection

**Study # IB09-08**
Title: Donor/recipient birth order in matched sibling HCT
Study Chair: Christiane Dobbelstein (Hannover)
MS Statistician: Erik Iverson (eiverson@nmdp.org)
PhD Statistician: TBD
Study Status: Protocol received/in development

**Immunobiology Working Committee Planned Studies**

**Study # IB08-05/LK08-04**
Title: Lymphotoxin alpha alleles in acute myelogenous leukemia relapse
Study Chair: Philip Posch (Georgetown University)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol Development

**Study # IB08-06**
Title: KIR ligands in umbilical cord blood HCT
Study Chair: Ronald Sobecks (The Cleveland Clinic)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol Development
Study # IB09-06s
Title: Genetic polymorphisms and HCT-related mortality
Study Chair: Theresa Hahn (Roswell Park Research Institute)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Deferred

Go to www.cibmtr.org for a biannual study status update.
10.11 INFECTION AND IMMUNE RECONSTITUTION WORKING COMMITTEE

Committee Leadership

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Scientific Director: Marcie Tomblyn, MD, MS, Moffitt Cancer Center  
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Infection and Immune Reconstitution Working Committee Publications

Study # LE04-02


Purpose: To determine the role of allogeneic HCT in human immunodeficiency virus (HIV)-positive patients.

Patients/Methods: Using the CIBMTR database, we retrospectively evaluated 23 HIV-positive patients undergoing matched sibling donor (n=19) or unrelated donor (n=4) allogeneic HCT between 1987 and 2003.

Results: The median age at allogeneic HCT was 32 years. Indications for allogeneic HCT were diverse and included malignant (n=21) and nonmalignant (n=2) hematologic disorders. Nine patients (39%) underwent transplantation after 1996, the approximate year that highly active antiretroviral therapy became standard treatment. The median time to neutrophil engraftment was 16 days (range, 7 to 30 days), and the cumulative incidences of grade II-IV acute graft-versus-host disease (aGVHD) at 100 days, chronic GVHD (cGVHD), and survival at 2 years were 30% (95% confidence interval [CI] = 14% to 50%), 28% (95% CI = 12% to 48%), and 30% (95% CI = 14% to 50%), respectively. At a median follow-up of 59 months, 6 patients were alive. Survival appears to be better in the patients undergoing allogeneic HCT after 1996; 4 of these 9 patients survived, compared with only 2 of 14 of those undergoing transplantation before 1996.
Conclusions: These data suggest that allogeneic HCT is feasible for selected HIV-positive patients with malignant and nonmalignant disorders. Prospective studies are needed to evaluate the safety and efficacy of this modality in specific diseases for these patients.

**Infection and Immune Reconstitution Working Committee Preliminary Results**

**Study # GV02-02**

Title: No effect of recipient or donor Hepatitis B and/or Hepatitis C serostatus on the outcomes of related donor allogeneic HCT

Study Chairs: Marcie Tomblyn (Moffitt Cancer Center)
Karen Ballen, MD (Massachusetts General Hospital)

MS Statistician: Min Chen (minchen@mcw.edu)
PhD Statistician: Sergey Tarima (starima@mcw.edu)

Study Status: Manuscript preparation

Purpose: To evaluate available information, though limited, on allogeneic HCT in patients with prior or current hepatitis B (HBV) or C (HCV) infection as well as for recipients receiving hematopoietic cells from seropositive donors.

Patients/Methods: Transplant outcomes in 416 recipients from 121 centers who received a related-donor allogeneic HCT for either AML, ALL, CML, or NHL between 1995 and 2003 were evaluated. Of these, 161 cases had markers of ongoing or previous viral hepatitis in the recipient (n = 89), the donor (n = 35), or both (n = 37), compared to 256 matched seronegative controls. Cases were positive for either HBV (n = 100), HCV (n = 46), or both (n = 15).

Results: With a median follow-up of 5.9 years for cases and 6.7 years for controls, there were no significant differences in the incidence of treatment-related mortality, survival, and GVHD, whether comparing recipient and/or donor positivity for infections with HBV and HCV. The frequencies of hepatic toxicities as well as causes of death between cases and controls were similar.

Conclusions: Infection with HBV or HCV in either the recipient or the donor should not be considered a contraindication to transplant

Addendum: After initial manuscript submission, the editors of Blood and Biology of Blood and Marrow Transplantation suggested the study be split into two manuscripts, which is in progress.

**Study # R04-90**

Title: Decreased infections in recipients of unrelated donor HCT from donors with an activating killer immunoglobulin-like (KIR) receptor B genotype

Study Chairs: Jo-Anne Young (University of Minnesota)
Marcie Tomblyn (Moffitt Cancer Center)
Mukta Arora (University of Minnesota)
Jeffrey Miller (University of Minnesota)
Daniel Weisdorf (University of Minnesota)

MS Statistician: Mike Haagens (mhaagens@nmdp.org)
PhD Statistician: John P. Klein

Study Status: Manuscript submitted

Purpose: To evaluate the hypothesis that recipients of an URD with an activating KIR (B/x) genotype would have decreased infectious complications due to enhanced natural killer (NK) cell function.

Patients/Methods: We compared the infectious complications in 116 recipients of a graft from a donor with an A/A KIR (n = 44) genotype and a B/x KIR (n = 72) genotype. All recipients participated in the
prospective NMDP infection project collecting infection data from conditioning until six months post-transplant.

Results: The cohort with a B/x donor had fewer initial bacterial infections by day 180 (A/A: 86% [95% CI, 75 – 95]; B/x: 68% [95% CI, 57 – 78]; p = 0.02). There was no difference in the incidence of viral or fungal infections. When accounting for multiple infections, fewer bacterial infections were seen in the B/x cohort (A/A: 3.55/patient; B/x: 2.63/patient; p = 0.09). During the study period, only 19 patients had no infections; of these, 15 had received cells from a B/x KIR donor.

Conclusion: Donor KIR genotype had no impact on other transplant outcomes including TRM, GVHD, or survival. The role of donor KIR genotype on infection complications is intriguing and warrants further investigation.

Infection and Immune Reconstitution Working Committee Studies in Progress

Study # LE04-01
Title: Cytomegalovirus (CMV) infection and mortality after HCT
Study Chair: Michael Boeckh (Fred Hutchinson Cancer Research Center)
MS Statistician: Min Chen (minchen@mcw.edu)
PhD Statistician: TBD
Study Status: Data collection

Study # IN05-02
Title: Atypical mold infections in HCT patients
Study Chairs: Marcie Tomblyn (Moffitt Cancer Center)
Steven Trifilio (Northwestern Memorial Hospital)
Charles Bennett (Northwestern University)
MS Statistician: Min Chen (minchen@mcw.edu)
PhD Statistician: TBD
Study Status: Data Analysis

Study # IN06-01
Title: Rate of breakthrough of pneumocystis jiroveci pneumonia as a function of prophylaxis regimens.
Study Chairs: Kirsten Williams (Johns Hopkins Hospital)
Allen Chen (Johns Hopkins Hospital)
Allison George Agwu (Johns Hopkins Hospital)
Thomas J. Walsh (National Institute of Health)
MS Statistician: Tanya Pedersen (tpederse@nmdp.org)
PhD Statistician: TBD
Study Status: Data collection

Study # IN07-01
Title: Blood stream infection by vancomycin-resistant enterococcus in patients undergoing allogeneic HCT
Study Chairs: Mark Robien (University of Washington, Seattle)
Genovefa A Papanicolaou MD (Memorial Sloan-Kettering Cancer Center)
MS Statistician: Min Chen (minchen@mcw.edu)
PhD Statistician: TBD
Study Status: Data collection
| Study # | IN07-02 | Title: Epidemiology of infections in children after HCT  
Study Chair: Ashok Srinivasan (St. Jude Children’s Research Hospital)  
Randall T. Hayden (St. Jude Children’s Research Hospital)  
MS Statistician: Min Chen (minchen@mcw.edu)  
PhD Statistician: TBD  
Study Status: Protocol received/in development |
| Study # | IN07-03 | Title: Incidence of herpes zoster disease after HCT  
Study Chair: Michelle R. Salvaggio (University of Oklahoma Health Sciences Center)  
Jennifer Holter, MD (University of Oklahoma Health Sciences Center)  
George Selby, MD (University of Oklahoma Health Sciences Center)  
MS Statistician: Min Chen (minchen@mcw.edu)  
PhD Statistician: TBD  
Study Status: Protocol received/in development |
| Study # | IN08-01 | Title: Ablative vs. non-ablative HCT for early infection in acute myelogenous leukemia in complete remission  
Study Chair: Celalettin Ustun (Medical College of Georgia)  
MS Statistician: Min Chen (minchen@mcw.edu)  
PhD Statistician: TBD  
Study Status: Protocol received/in development |
| Study # | IN09-01 | Title: Outcomes of allogeneic HCT for patients with and without pre-existing fungal infections  
Study Chairs: Richard T. Maziarz (Oregon Health & Science University)  
Aleksandra Ciszewski (Oregon Health & Science University)  
MS Statistician: Min Chen (minchen@mcw.edu)  
PhD Statistician: TBD  
Study Status: Protocol received/in development |

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10.12 INTERNATIONAL STUDIES WORKING COMMITTEE

Committee Leadership

Co-Chair: Philip Rowlings, MBBS, MD, Newcastle Mater Hospital  
E-mail: phil_rowlings@yahoo.com.au

Co-Chair: David Gomez-Almaguer, MD, Hospital Universitario  
E-mail: dr_gomez@infosel.net.mx

Co-Chair: Mahmoud Aljurf, MBBS, King Faisal Specialist Hospital  
E-mail: maljurf@kfshrc.edu.sa

Statistician: Kathleen A. Sobocinski, MS, CIBMTR Statistical Center Milwaukee  
E-mail: ksobo@mcw.edu

Statistician: John P. Klein, PhD, Medical College of Wisconsin  
E-mail: klein@mcw.edu

Scientific Director: Marcelo Pasquini, MD, MS, Medical College of Wisconsin  
E-mail: mpasquin@mcw.edu

International Studies Working Committee Studies in Progress

Study # IS08-01
Title: Hematopoietic cell transplantation activity survey in the Americas: WBMT Global Survey 2008
Study Chairs: Willem Bujan (Hospital Mexico)  
Marcelo Pasquini (CIBMTR, Milwaukee)  
Helen Baldomero (Basel Kantonsspital)
MS Statistician: Kathleen Sobocinski (ksobo@mcw.edu)
PhD Statistician: TBD  
Study Status: Protocol received/in development

Study # IS09-02
Title: Comparison of the effect of stem cell source on the outcome of HLA-matched sibling donor transplants for severe aplastic anemia based on transplant region
Study Chair: Rajat Kumar (University of Manitoba)
MS Statistician: Kathleen Sobocinski (ksobo@mcw.edu)
PhD Statistician: TBD  
Study Status: Protocol received/in development
### International Studies Working Committee Planned Studies

**Study # IS09-01**  
**Title:** Outcome of autologous hematopoietic progenitor cell transplantation in patients with multiple myeloma, comparison of patients from North vs. South America  
**Study Chair:** Gustavo Milone (Angelica Ocampo-Hospital and Research Center-Fundaleu Uirburu)  
**MS Statistician:** Kathleen Sobocinski (ksobo@mcw.edu)  
**PhD Statistician:** TBD  
**Study Status:** Protocol Development

**Study # IS09-03**  
**Title:** Global trends in hematopoietic stem cell transplantation  
**Study Chair:** Mahmoud Aljurf (King Faisal Specialist Hospital and Research Center)  
**MS Statistician:** Kathleen Sobocinski (ksobo@mcw.edu)  
**PhD Statistician:** TBD  
**Study Status:** Protocol Development

**Study # IS09-04**  
**Title:** Hematopoietic stem cell transplantation in Latin America  
**Study Chair:** Laura Rodriguez-Romo (Hospital Universitario)  
**MS Statistician:** Kathleen Sobocinski (ksobo@mcw.edu)  
**PhD Statistician:** TBD  
**Study Status:** Protocol Development

**Study # IS09-05**  
**Title:** Non-ablative stem cell allogeneic transplanting in chronic myelogenous leukemia in developing countries  
**Study Chair:** Guillermo J. Ruiz-Delgado (Centro de Hematologia y Medicina Interna de Puebla)  
**MS Statistician:** Kathleen Sobocinski (ksobo@mcw.edu)  
**PhD Statistician:** TBD  
**Study Status:** Protocol Development

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**Go to www.cibmtr.org for a biannual study status update.**
10.13 LATE EFFECTS AND QUALITY OF LIFE WORKING COMMITTEE

Committee Leadership

Co-Chair: Brian Bolwell, MD, Cleveland Clinic Foundation  
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Co-Chair: David Jacobsohn, MD, Children’s Memorial Hospital  
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Co-Chair: Mohamed Sorror, MD, Fred Hutchinson Cancer Center  
E-mail: msorror@fhcrc.org

Statistician: Zhiwei (Jerry) Wang, MS, CIBMTR Statistical Center Milwaukee  
E-mail: zwang@mcw.edu

Statistician: Ruta Bajorunaite, PhD, CIBMTR Statistical Center Milwaukee  
E-mail: ruta@mcw.edu

Scientific Director: Navneet S. Majhail, MD, MS, University of Minnesota  
E-mail: majha001@umn.edu

Late Effects and Quality of Life Working Committee Publications

Study # LE98-07a  

Purpose: To evaluate patterns of post-traumatic lymphoproliferative disorders (PTLD) among recipients of allogeneic HCT.

Patients/Methods: 26,901 patients transplanted between 1968 and 1996 for leukemia or severe aplastic anemia in 271 U.S. and international centers were included in the study.

Results: We confirmed that PTLD risks were strongly associated with T-cell depletion, anti-thymocyte globulin use, unrelated or HLA-mismatched grafts and acute and chronic GVHD. New findings included elevated risks of PTLD for age ≥50 years at transplant and second transplantation. Lower risks were found for T-cell depletion methods that remove both T- and B-cells compared with other methods. The cumulative incidence of PTLD was low (0.2%) for patients with no major risk factors but increased to 8.1% with ≥ 3 risk factors.

Conclusions: Subgroups of allogeneic HCT recipients at increased risk for PTLD were identified. Prospective monitoring of Epstein-Barr virus activation and early treatment intervention may be beneficial to these patients.

Study # LE99-01a  
Journal Citation: Bishop MM, Lee SJ, Beaumont JL, Andrykowski MA, Rizzo JD, Sobocinski KA, Wingard JR. The preventive health behaviors of long-term survivors of cancer and hematopoietic stem cell
transplantation compared to matched controls. Biol Blood Marrow Transplant. 2009 Sep 22. [Epub ahead of print].

**Purpose:** To examine the current health and secondary prevention behaviors of long-term HCT survivors compared with matched controls without cancer and to identify socio-demographic and clinical factors associated with appropriate preventive practices.

**Patients/Methods:** HCT survivors (n = 662) were drawn from 40 North American transplant centers. Peer-nominated acquaintances of survivors matched on sex, age, education, and marital status served as controls (n = 158).

**Results:** HCT survivors had similar health and screening behaviors as matched controls. Socio-demographic factors were associated with health prevention behaviors in expected ways. Some differences between disease group and type of transplant were found.

**Conclusions:** Despite higher levels of engagement with health care providers, HCT survivors had health behaviors that were similar to matched controls and to behaviors reported by cancer survivors who did not undergo HCT. There remains considerable room for improvement. These findings support the need for further education of both HCT survivors and health practitioners.

**Study # LE99-01b**

**Citation (pending):** Bishop MM, Brady MJ, Beaumont JL, Curbow B, Rizzo JD, Wingard JR. Post-traumatic growth and spiritual well-being: separate, related, or overlapping constructs? It Depends. Journal of Psychosocial Oncol In press.

**Purpose:** To study the relationship between spiritual well-being, religious coping, and post-traumatic growth. We examined the underlying factor structure of these constructs, as well as the differences in the relationships between these constructs for long-term cancer survivors and their partners. People’s capacity to experience positive change after negative events is well-documented, as is the importance of spirituality for many of those individuals.

**Patients/Methods:** Participants (177 survivor-spouse pairs) completed the Post-Traumatic Growth Inventory, Brief Coping with Problems Experienced, religion subscale, and Functional Assessment of Chronic Illness Therapy Spiritual Well-Being Scale, and a single item of perceived spirituality.

**Results:** Principle components analyses indicated three distinct factors, “Growth,” “Faith,” and “Meaning.” The Spiritual Change subscale of the Post-traumatic Growth Index loaded equally on both “Growth” and “Faith.” Correlations between the various constructs indicated that spiritual well-being correlated with post-traumatic growth only in survivors, not spouses. Furthermore, the Faith spiritual well-being subscale was related to all Post-traumatic Growth Index subscales, whereas Meaning/Peace subscale was not.

**Conclusions:** Although traumatic for both, the post-cancer post-traumatic growth experience may be qualitatively different for survivors and spouse/partners.

**Study # LE00-02a**


**Purpose:** To describe long-term outcomes of autologous HCT for advanced Hodgkin (HL) and non-Hodgkin lymphoma (NHL).

**Patients/Methods:** The study included recipients of autologous HCT for HL (N=407) and NHL (N=960) from 1990-1998 who were in continuous complete remission for at least two years post-HCT. Median follow-up was 104 months for HL and 107 months for NHL.
Results: Overall survival at 10 years was 77% for HL, 78% for diffuse large-cell NHL, 77% for follicular NHL, 85% for lymphoblastic/Burkitt’s NHL, 52% for mantle-cell NHL and 77% for other NHL. On multivariate analysis, mantle-cell NHL had the highest relative-risk for late mortality (RR=2.87) while the risks of death for other histologies were comparable. Relapse was the most common cause of death. Relative mortality compared to age, race and gender adjusted normal population remained significantly elevated and was 14.8 (6.3-23.3) for HL and 5.9 (3.6-8.2) for NHL at 10-years post-HCT.

Conclusions: Recipients of autologous HCT for HL and NHL who remain in remission for at least two years have favorable subsequent long-term survival but remain at risk for late relapse. Compared to the general population, mortality rates continue to remain elevated at 10 years post-transplantation.

Study # 98-05

Purpose: To evaluate long-term risk of secondary malignancy among allogeneic transplant recipients and determine the associated risk factors.

Patients/Methods: 28,874 allogeneic transplant recipients, including 189 solid malignancies, were studied in a multi-institutional cohort.

Results: Overall, transplant recipients developed new solid cancers at twice the rate expected based on general population rates (observed-to-expected ratio 2.1; 95% confidence interval 1.8, 2.5), with risk increasing over time (P trend<0.001). Risk reached 3-fold among patients followed ≥15-years post-transplant. New findings showed that the risk of developing a non-squamous cell carcinoma (non-SCC) following conditioning radiation was highly dependent on age at exposure. Among patients irradiated at ages under 30 years, the relative risk of non-SCC was nine times that of non-irradiated patients, while the comparable risk for older patients was 1.1 (P interaction <0.01).

Conclusions: Chronic GVHD and male sex were the main determinants for risk of SCC. Allogeneic transplant survivors, particularly those irradiated at young ages, face increased risks of solid cancers, supporting strategies to promote lifelong surveillance among these patients.

Late Effects and Quality of Life Working Committee Preliminary Results

Study # LE00-02b
Title: Long-term survival and late relapse after autologous HCT for acute myeloid leukemia
Study Chair: Navneet Majhail (University of Minnesota)
MS Statistician: Jerry Wang (zwang@mcw.edu)
PhD Statistician: Ruta Bajorunaite (ruta@mcw.edu)
Study Status: Submitted

Purpose: To describe long-term outcomes of autologous HCT.

Patients/Methods: Study included 315 patients with acute myeloid leukemia (AML) in first or second complete remission (CR) who underwent autologous transplant from 1990-1998 and were in continuous CR for at least two years after HCT. Patients were predominantly transplanted in CR1 (78%) and had good or intermediate cytogenetic risk disease (74%).

Results: Overall survival at 10 years after HCT was 94% and 80% for patients receiving HCT in CR1 and CR2, respectively. Older age at transplantation and poor cytogenetic risk disease were
independent predictors of late mortality and adverse disease-free survival. Karnofsky performance score <90 at transplant increased the risks of late non-relapse mortality and use of hematopoietic growth factors to promote engraftment increased the risks of relapse. The relative mortality of these 2-year survivors was comparable to that of age-, race- and gender-matched normal population.

Conclusions: Patients who receive an autologous HCT for AML in CR1 or CR2 and remain in remission for at least two years post-transplant have very favorable subsequent long-term survival. Their mortality rates are similar to that of the general population.

Study # LE07-03
Title: Long-term survival and late deaths after allogeneic HCT
Study Chair: John Wingard (University of Florida)
MS Statistician: Jerry Wang (zwang@mcw.edu)
PhD Statistician: Ruta Bajorunaite (ruta@mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To investigate the long-term survival, evaluate risk factors for late mortality, and compare the long-term survival among allogeneic HCT recipients who had survived in CR for at least two years following transplantation to that of the general population.

Patients/Methods: Our study cohort consisted of 10,632 patients who received a myeloablative allogeneic HCT through 2003 and included patients who had survived in CR for two years after transplant. Diagnoses included AML, ALL, MDS, lymphoma and severe aplastic anemia.

Results: Older age at HCT and chronic GVHD increased the risks of late mortality for all diseases. Some risk factors were associated with increased mortality for specific diseases only. At 15 years after HCT, the relative mortality of patients who had received HCT for AML, ALL, MDS and SAA remained significantly higher than in age-, race- and gender-matched normal populations. Mortality rates for lymphoma patients were not significantly different than those of the matched general population after eight years post-HCT.

Conclusions: Recipients of myeloablative allogeneic HCT who remain in remission for at least two years have favorable subsequent long-term survival. Older age at HCT and chronic GVHD are important risk factors for late deaths.

Study # LE08-01
Title: Risk of second solid cancers after myeloablative allogeneic HCT using busulfan-cyclophosphamide conditioning
Study Chair: Navneet Majhail (University of Minnesota)
MS Statistician: Jerry Wang (zwang@mcw.edu)
PhD Statistician: Ruta Bajorunaite (ruta@mcw.edu)
Study Status: Manuscript preparation
Presentation: Accepted for oral presentation at the 2010 BMT Tandem Meetings.
Purpose: To evaluate the risks of second solid cancers in a population of allogeneic HCT recipients who had received non-total body irradiation (TBI)-based conditioning.

Patients/Methods: This study cohort consisted of 4,349 pediatric and adult recipients of allogeneic HCT using busulfan-cyclophosphamide (Bu-Cy) conditioning from 1986-2005 for acute myeloid leukemia in first complete remission (AML CR1) or chronic myeloid leukemia in first chronic phase (CML CP1).

Results: The overall rate of solid cancers among HCT recipients was significantly higher than the expected general population rates (observed to expected ratio [O/E] 1.4; 95% confidence intervals 1.1-1.8). Significantly elevated risks were observed for tumors of the lip (O/E 25.7),
Conclusions: Recipients of allogeneic HCT for AML CR1 and CML CP1 using Bu-Cy conditioning are at risk of developing solid cancers, especially those with older age, chronic GVHD and recipients of peripheral blood grafts. The incidence for solid cancers continues to increase with time and life-long cancer surveillance is warranted in this population.

Study # LE07-04
Title: Pregnancy after hematopoietic cell transplantation
Study Chair: Allison Loren (University of Pennsylvania)
MS Statistician: Jerry Wang (zwang@mcw.edu)
PhD Statistician: Ruta Bajorunaite (ruta@mcw.edu)
Study Status: Manuscript preparation
Presentation: Accepted for oral presentation at the 2010 BMT Tandem Meetings.
Purpose: To describe the characteristics of patients who became pregnant or fathered a child after HCT. To use this data to build follow-up questionnaires to learn more about fertility and pregnancy after HCT
Patients/Methods: The study cohort included 181 pregnancies that were reported to the CIBMTR between 2002 and 2007 among female HCT recipients (N=84) or partners of male HCT recipients (N=98).
Results: 182 pregnancies were reported to the CIBMTR among female HCT recipients (N=84) or partners of male HCT recipients (N=98). Transplant types included autologous HCT (20 women, 13 men), myeloablative allogeneic HCT (50 women, 80 men) and non-myeloablative allogeneic HCT (14 women, 5 men). Conditioning regimen used total body irradiation in 16% women and 20% men. Bu-Cy conditioning was used in 6% women and 40% men. Fifteen men reported the use of cryopreserved sperm to facilitate pregnancy.
Conclusions: Some HCT recipients retain fertility, including patients who have received myeloablative conditioning. Appropriate patients should be counseled about fertility before and after HCT. Outcomes of pregnancy after HCT need prospective evaluation.

Late Effects and Quality of Life Working Committee Studies in Progress

Study # LE99-01c
Title: Clinical and demographic variables as predictors of long-term quality of life
Study Chair: John Wingard (University of Florida)
MS Statistician: Kathy Sobocinski (ksobo@mcw.edu)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Ongoing

Study # LE06-01
Title: Genetic susceptibility to transformed myelodysplastic syndromes/acute myelogenous leukemia after autologous HCT in non-Hodgkin lymphoma
Study Chair: Timothy Fenske (Medical College of Wisconsin)
MS Statisticians: Kathy Sobocinski (ksobo@mcw.edu)
Jerry Wang (zwang@mcw.edu)
PhD Statistician: TBD
Study Status: Tissue analysis
Study # LE07-01
Title: Second cancers after allogeneic non-myeloablative HCT
Study Chairs: Olle Ringdén (Karolinska University Hospital Huddinge)
Navneet Majhail (University of Minnesota)
MS Statistician: Jerry Wang (zwang@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # LE07-02
Title: Duration of chronic GVHD and later effects in HCT survivors
Study Chair: Navneet Majhail (University of Minnesota)
MS Statistician: Jerry Wang (zwang@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # LE09-01
Title: New malignancies after autologous HCT in children
Study Chair: Karina E. Danner-Koptik (Children’s Memorial Hospital)
MS Statistician: Jerry Wang (zwang@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # LE09-03
Title: Survey of physician practice patterns regarding fertility preservation
Study Chair: Alison Loren (University of Pennsylvania)
MS Statistician: Jerry Wang (zwang@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

Late Effects and Quality of Life Working Committee Planned Studies

Study # LE05-01
Title: Incidence of bronchiolitis obliterans after reduced-intensity HCT
Study Chair: Shin Mineishi (University of Michigan Cancer Center)
MS Statistician: Jerry Wang (zwang@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol Development

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10.14 LYMPHOMA WORKING COMMITTEE

**Committee Leadership**

| Co-Chair: | Hillard M. Lazarus, MD, Case Western Reserve University  
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| Co-Chair: | Ginna Laport, MD, Stanford University Medical Center  
| E-mail: | glaport@stanford.edu |
| Co-Chair: | Silvia Montoto, MD, London School of Medicine and Dentistry  
| Email: | Silvia.Montoto@cancer.org.uk |
| Statistician: | Jeanette Carreras, MPH, CIBMTR Statistical Center Milwaukee  
| E-mail: | jcarrera@mcw.edu |
| Statistician: | Mei-Jie Zhang, PhD, CIBMTR Statistical Center Milwaukee  
| E-mail: | meijie@mcw.edu |
| Scientific Director: | Parameswaran Hari, MD, MS, Medical College of Wisconsin  
| E-mail: | phari@mcw.edu |

**Lymphoma Working Committee Publications**

### Study # D98-10


**Purpose:** To analyze the outcomes of patients receiving unrelated donor allogeneic HCT for NHL.

**Patients/Methods:** 283 patients received unrelated donor allogeneic HCT for NHL facilitated by the CIBMTR/NMDP between 1991 and 2004.

**Results:** Factors adversely associated with overall survival included increasing age, decreased performance status, and refractory disease. Follicular lymphoma and peripheral T-cell lymphoma improved survival compared to aggressive B-cell lymphomas. Factors adversely associated with progression-free survival included performance status, histology and disease status at transplant. T-cell depletion was associated with decreased treatment related mortality.

**Conclusions:** Long-term failure-free survival is possible following unrelated donor HCT for NHL, although early mortality was high in this large cohort.

### Study # LY03-01

**Conclusions:**

**Purpose:**
To determine whether pre-transplant exposure to rituximab affects outcomes following autologous HCT for diffuse large B-cell lymphoma (DLBCL).

**Patients/Methods:**
994 patients who underwent autologous HCT for DLBCL between 1996 and 2003 were analyzed according to whether rituximab was (n=176) or was not (n=818) administered prior to autologous HCT.

**Results:**
In univariate analysis, platelet and neutrophil engraftment, and non-relapse mortality were not affected by exposure to rituximab. Despite the rituximab group containing older and more heavily treated patients, progression-free survival and overall survival at 1 and 3 years was superior in the rituximab exposed group. In multivariate analysis, pretransplant rituximab, age <55, and fewer than 3 lines of chemotherapy were all associated with improved progression-free and overall survival.

**Conclusions:**
Pre-transplant rituximab is associated with less progression and improved survival following autologous HCT for DLBCL, with no evidence of impaired engraftment or increased non-relapse mortality.

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**Study # LY04-02**


**Purpose:**
To compare clinical outcomes after autologous HCT versus myeloablative HLA-identical sibling allogeneic HCT for patients with DLBCL.

**Patients/Methods:**
Outcomes were compared in DLBCL patients age ≥ 18 years receiving autologous HCT (n=837) versus myeloablative allogeneic HCT (n=79) between 1995 and 2003 and reported to the CIBMTR.

**Results:**
In multivariate analysis, transplant-related mortality (TRM) was a 3.91 times higher significant risk factor of death in the allogeneic HCT arm, especially in the early post-transplant period (relative risk [RR] 5.11, 95% confidence interval [CI] 2.63-9.94, p<0.0001), with no effect on progression/relapse compared to the autologous HCT arm. Five-year progression-free and overall survivals were better in autologous HCT, (43% vs 22% and 49% vs 22%, respectively). Beyond 12 months post-transplant, outcomes were similar between groups.

**Conclusions:**
Myeloablative allogeneic HCT increases the risk of early TRM and has no effect on progression/relapse compared to autologous HCT, which is associated with superior survival. Chemosensitive disease at time of transplant does not affect the outcome.

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**Study # LY05-03**


**Purpose:**
To study the outcomes and determine prognostic factors for patients with relapsed/refractory Hodgkin lymphoma (HL) undergoing a reduced-intensity or nonmyeloablative conditioning (RIC/NST) unrelated donor allogeneic HCT.
Patients/Methods: 143 patients underwent RIC/NST for relapsed/refractory HL. Patients were heavily pretreated, 96% had received at least three chemotherapy regimens, and 89% had failed previous autologous HCT.

Results: With median follow-up of 25 months, probabilities of transplant-related mortality were 15% at 100 days and 33% at 2 years. Probabilities of progression-free survival were 30% at 1 year and 20% at 2 years; probabilities of overall survival were 56% at 1 year and 37% at 2 years. The incidence of acute GVHD grade 2-4 was 60%. Disease relapse/progression and GVHD were the most common causes of death.

Conclusions: Unrelated donor RIC/NST can salvage some patients with refractory(relapsed HL. Future studies should aim to reduce incidence of acute GVHD and relapse/progression.

Lymphoma Working Committee Preliminary Results

Study # LY04-01
Title: Alternative donor transplantation using reduced intensity or non-myeloablative conditioning for children with non-Hodgkin lymphoma

Study Chair: Gregory Hale (St. Jude Children’s Research Hospital)

MS Statistician: Smriti Shrestha (sshresth@mcw.edu)

PhD Statistician: Jennifer Le-Rademacher (jlerade@hpi.mcw.edu)

Study Status: Manuscript preparation

Presentation: Presented as a poster at the 2009 American Society of Hematology Meeting.

Purpose: To describe outcomes following RIC or non-myeloablative HCT using alternative donors (unrelated or mismatched family), and determine prognostic factors associated with outcomes.

Patients/Methods: We analyzed the outcomes of 248 (61% male) adult recipients of HCT for NHL from alternative donors after RIC/NMA conditioning reported to the CIBMTR from 1997 to 2004.

Results: The following factors were associated with higher risk of treatment failure (or lower PFS): high-grade histology, use of anti-thymocyte globulin (ATG), and chemotherapy resistant disease at HCT. Older age, shorter interval from diagnosis to HCT, non-total body irradiation conditioning regimens or T-cell depletion and HLA mismatched unrelated donors were all associated with higher risk of death.

Conclusions: In NHL patients without sibling donor options, alternative donor HCT with RIC/NST conditioning results in favorable long-term survival although advanced age, histology and resistant disease status remain concerning factors. Higher grade NHL, use of ATG or T-cell depletion and greater HLA mismatch were associated with inferior outcomes. Lack of an available sibling donor should not be a barrier to allogeneic HCT in the appropriate patient.

Study # LY04-03
Title: Outcomes of autologous versus allogeneic HCT for patients with non-Hodgkin lymphoma with pre-existing central nervous system (CNS) involvement

Study Chair: Richard Maziarz (Oregon Health Sciences University)

MS Statistician: Jerry Wang (zwang@mcw.edu)

PhD Statistician: TBD

Study Status: Analysis

Presentation: Accepted for oral presentation at the 2010 BMT Tandem Meetings.

Purpose: To assess the results of previous, retrospective single institutional and registry analyses that suggested that pre-existing CNS involvement was not a contraindication for allogeneic HCT for patients with NHL.
Patients/Methods: We analyzed the outcomes of 151 (64% male) adult recipients of allogeneic HCT with NHL and CNS involvement identified at any time prior to transplant and compared them to 4,688 patients undergoing allogeneic HCT with no CNS lymphoma involvement during the years 1990-2005.

Results: No statistically significant differences in outcomes non-relapse mortality, relapse, disease-free survival or overall survival were identified between the two groups. Patients with CNS remission (96/151) at time of allogeneic HCT had significantly superior survival compared with those with active CNS disease (55/151) at transplant.

Conclusions: Excellent long-term survival is possible after allogeneic HCT in NHL patients with prior CNS involvement despite adverse baseline prognostic factors. However, best outcomes are in patients who achieve a CNS remission prior to transplant.

Study # LY06-02
Title: Nonmyeloablative allogeneic HCT in patients who experience relapse after autologous HCT for lymphoma
Study Chair: César Freytes (University of Texas Health Science Center)
MS Statistician: Jeanette Carreras (jcarrera@mcw.edu)
PhD Statistician: Mei-Jie Zhang (mei-jie@mcw.edu)
Study Status: Manuscript preparation
Purpose: To determine the outcome of patients with lymphoma who undergo nonmyeloablative (NST) allogeneic HCT after a previous autologous HCT failure.
Patients/Methods: 267 patients who underwent NST HCT after an autologous HCT failure performed between 1997 and 2006 were analyzed. Excluded were patients with planned second transplants, patients younger than 21 and cord blood transplants.
Results: TRM at 1 year was 39% and 45%, respectively. Overall survival at 1 and 5 years was 44% and 28%. PFS was 30% and 19% at 1 and 5 years, respectively. Factors associated with a higher risk of progression or death included poor performance status, time interval between transplants of two years or less, not receiving a TBI-containing regimen and primary induction failure.
Conclusions: NST after autologous HCT failure is associated with substantial TRM but selected patients can attain prolonged remissions.

Study # LY06-03
Title: HLA identical sibling transplantation versus HLA- matched unrelated donor transplantation in patients with follicular lymphoma (FL)
Study Chairs: Anna Sureda (Hospital de la Santa Creu i Sant Pau)
Harry Schouten (University Hospital Maastricht)
MS Statistician: Marcelo Pasquini (mpasquin@mcw.edu)
PhD Statistician: Mei-Jie Zhang (mei-jie@mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To determine if improvements in HLA-matching have improved the safety of unrelated donor (URD) HCT. Allogeneic HCT is potentially curative in FL, but wide adoption of this treatment is limited by its toxicity and donor availability.
Patients/Methods: We compared the outcomes of 702 recipients of allogeneic HCT for FL (198 URD and 504 sibling donors) from 171 centers worldwide reporting to the CIBMTR or EBMT from 1997 to 2005.
Results: Significant risk factors associated with worse outcomes included poor performance status at transplantation and extensive pre-transplant therapy (> 4 lines of therapy or prior autologous
HCT). Additionally, in vivo T-cell depletion was associated with a higher risk of relapse/progression and treatment failure.

Conclusions: This study shows that URD HCTs are performed later in the treatment course for FL, in higher risk patients, most commonly with RIC, and are associated with worse PFS and OS compared to HLA identical sibling HCT.

Study # LY06-06
Title: A prognostic model for prolonged event-free survival after autologous or allogeneic transplantation for relapsed and refractory Hodgkin disease.
Study Chairs: Philip McCarthy (Roswell Park Cancer institute)
Theresa Hahn (Roswell Park Cancer institute)
MS Statistician: Jeanette Carreras (jcarrera@mcw.edu)
PhD Statistician: Mei-Jie Zhang (mei-jie@mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented as a poster at the 2009 American Society of Hematology Meeting.
Purpose: To determine if prognostic risk score models for HL patients receiving allogeneic HCT effectively predict post-transplant outcomes based on factors measured at the time of allogeneic HCT.
Patients/Methods: We performed a comparison of three such models from Dana-Farber Cancer Institute (DFCI), Roswell Park Cancer Institute (RPCI) and the University of Minnesota (UMinn) in an independent multicenter dataset of 597 relapsed or refractory HL patients receiving allogeneic HCT from 1996-2004.
Results: The UMinn model high risk group had a higher PFS than either of the other two models’ high risk groups, and the intermediate group in this model was not significantly different from the high risk group. The relative incremental change in R² was 26% higher for the DFCI than the RPCI model and 120% higher for the RPCI than the UMinn model.
Conclusions: From the Brier score and R² values, the DFCI model had marginal superiority over RPCI model, while both performed better than the UMinn model.

Lymphoma Working Committee Studies in Progress

Study # LY05-01
Title: Effectiveness of donor leukocyte infusion (DLI) in the management of relapsed lymphoma after allogeneic stem cell transplantation.
Study Chair: Marcie Tomblyn (H. Lee Moffitt Cancer Center and Research Institute)
MS Statistician: Jeanette Carreras (jcarrera@mcw.edu)
PhD Statistician: TBD
Study Status: Data File Preparation

Study # LY06-05
Title: Comparison of autologous vs. allogeneic HCT for T-cell non-Hodgkin lymphoma
Study Chairs: Sonali Smith (University of Chicago Medical Center)
Koen Van Besien (University of Chicago Medical Center)
Linda Burns (University of Minnesota Medical Center)
MS Statistician: Vincent He (vhe@mcw.edu)
PhD Statistician: Jennifer Le-Rademacher (jlerade@hpi.mcw.edu)
Study Status: Data File Preparation
**Study # LY07-02**
*Title:* Transplantation outcomes in the mycosis fungoides and Sezary syndrome patients  
*Study Chair:* Mary Jo Lechowicz (Emory University School of Medicine)  
*MS Statistician:* Manza Agovi (magovi@mcw.edu)  
*PhD Statistician:* NA  
*Study Status:* Analysis

**Study # LY08-01**
*Title:* Outcome of allogeneic and autologous HCT for Burkitt and Burkitt-like lymphoma  
*Study Chair:* James Gajewski (Oregon Health and Science University)  
*MS Statistician:* Jeanette Carreras (jcarrera@mcw.edu)  
*PhD Statistician:* TBD  
*Study Status:* Data file preparation

**Study # LY08-02**
*Title:* Outcome of patients with mantle cell lymphoma treated with autologous vs. allogeneic HCT  
*Study Chair:* Timothy Fenske (Medical College of Wisconsin)  
*MS Statistician:* Jeanette Carreras (jcarrera@mcw.edu)  
*PhD Statistician:* TBD  
*Study Status:* Data file preparation

**Study # LY08-03**
*Title:* Comparison of reduced and standard conditioning in allogeneic transplantation in patients with B-cell non-Hodgkin lymphoma  
*Study Chairs:* Ulrike Bacher (Universitats Kranken Haus)  
Tatjana Zabelina (University Medical Center Hamburg)  
Axel Rolf Zander (University Medical Center Hamburg)  
*MS Statistician:* Jeanette Carreras (jcarrera@mcw.edu)  
*PhD Statistician:* TBD  
*Study Status:* Data file preparation

**Study # LY09-01**
*Title:* Clinical outcomes of HCT in patients with diffuse large B-cell lymphoma transformed from chronic lymphocytic leukemia, follicular lymphoma or Waldenstrom macroglobulinemia  
*Study Chairs:* Baldeep Wirk (University of Florida)  
John Wingard (University of Florida)  
*MS Statistician:* TBD  
*PhD Statistician:* TBD  
*Study Status:* Protocol received/in development

**Study # LY09-03**
*Title:* A retrospective review of involved field radiotherapy pre- or post-high dose chemotherapy and autologous HCT in refractory or relapsed patients with Hodgkin lymphoma  
*Study Chair:* Heather J. Miller (Scripps Cancer Center)  
James Mason (Scripps Cancer Center)  
*MS Statistician:* TBD  
*PhD Statistician:* TBD  
*Study Status:* Protocol received/in development
Lymphoma Working Committee Planned Studies

**Study # LY09-02**
Title: Comparison of nonmyeloablative allogeneic HCT as upfront salvage therapy for relapsed lymphoma compared to a strategy of utilizing nonmyeloablative allogeneic HCT after autologous transplant failure
Study Chair: Cesar O. Freytes (University of Texas Health Science Center)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol development

**Study # LY09-04**
Title: Outcomes of patients with non-Hodgkin lymphoma with pre-existing parenchymal CNS involvement treated with autologous HCT versus standard chemotherapy and radiation therapy approaches
Study Chairs: Richard T Maziarz (Oregon Health & Science University)
Nancy Doolittle (Oregon Health & Science University)
MS Statistician: Wael Saber (wsaber@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol development

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10.15  NON-MALIGNANT MARROW DISORDERS WORKING COMMITTEE

Committee Leadership

Co-Chair: Mark Walters, MD, Children's Hospital of Oakland  
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Co-Chair: Joachim Deeg, MD, Fred Hutchinson Cancer Research Center  
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Statistician: Jeanette Carreras, MPH, CIBMTR Statistical Center Milwaukee  
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Statistician: Jennifer Le-Rademacher, PhD, CIBMTR Statistical Center Milwaukee  
E-mail: jlerade@hpi.mcw.edu

Scientific Director: Mary Eapen, MD, MS, Medical College of Wisconsin  
E-mail: meapen@mcw.edu

Non-Malignant Marrow Disorders Working Committee Publications

Study # AA03-01


Purpose: To identify patient, disease and treatment-related factors that were associated with survival following a second HLA-matched sibling transplant for severe aplastic anemia.

Patients/Methods: 166 patients who received second transplants between 1986 and 2004 were analyzed. The indication for the second transplants was graft failure.

Results: The analysis yielded two prognostic factors: inter-transplant interval (surrogate for primary and early secondary graft failure) and performance status. The 8-year probabilities of overall survival when second transplants were ≤3 and >3 months from first transplant in patients with performance scores of 90-100% were 56% and 76%, respectively. Corresponding probabilities in patients with lower performance scores were 33% and 61%. Repeated graft failure was the most frequent cause of treatment failure.

Conclusions: Second transplants are effective for patients with good performance status who suffer late secondary graft failure. New strategies are needed for other patients.
Non-Malignant Marrow Disorders Working Committee Preliminary Results

**Study # AA03-02**

**Title:** Bone marrow transplantation from HLA-identical siblings for thalassemia

**Study Chair:** Mitchell Sabloff (Ottawa Hospital)

**MS Statistician:** Jerry Wang (zwang@mcw.edu)

**PhD Statistician:** Brent Logan (blogan@mcw.edu)

**Study Status:** Manuscript preparation

**Presentation:** Presented as a poster at the 2009 American Society of Hematology Meeting.

**Purpose:** To report on the current experience of BMT for thalassemia outside Italy, and describe the characteristics and transplant outcomes in children after HLA-identical sibling HCT for thalassemia.

**Patients/Methods:** Patients aged ≤20 years at HCT who received a myeloablative HLA-matched sibling HCT for thalassemia between 1995 and 2001 were eligible for the survey (n=179)

**Results:** A multivariate analysis showed that age at BMT ≥10 years (relative risk [RR] 2.16, 95% confidence interval [CI] 1.1 – 4.23, p=0.025) and baseline hepatomegaly (RR 5.57, 95% CI 2.14 – 14.49, p<0.001) were associated with higher risk of mortality. Younger patients without hepatomegaly fared the best and older patients with hepatomegaly, the worst.

**Conclusions:** This series confirms reports from large single center series that the results after HLA-matched sibling BMT for thalassemia major are optimized when performed in young children before the development of risk factors for poor outcome.

**Study # AA05-01**

**Title:** Risk factors for graft failure and mortality after human leukocyte antigen (HLA)-matched sibling donor HCT for severe aplastic anemia (SAA) in Brazil

**Study Chair:** Ricardo Pasquini (Hospital de Clinicas-Federal University)

**MS Statistician:** Jeanette Carreras (jcarrera@mcw.edu)

**PhD Statistician:** Mei-Jie Zhang (meijie@mcw.edu)

**Study Status:** Manuscript preparation

**Purpose:** To report the risk factors for HLA-matched sibling donor transplant for SAA in Brazil.

**Patients/Methods:** Transplant outcomes in 269 SAA patients were reported who received their HLA-matched HCT at a single center in Brazil between 1990 and 2003.

**Results:** Graft failure rates were higher after cyclophosphamide (Cy) conditioning; the highest rate (60%) was seen in patients who received ≥16 red blood cell transfusions. Among patients who received ≥16 red blood cell transfusions [Busulfan/cyclophosphamide (Bu+Cy) or Cy alone conditioning], overall survival rates were lower: 67% and 56%, respectively. When comparing Bu+Cy and Cy alone in these heavily transfused patients, use of Bu+Cy appears to confer a survival advantage (p=0.05).

**Conclusions:** Graft failure rate is lowest after Bu+Cy in patients who received ≥16 red blood cell transfusions (RBCT). Mortality rates were higher in patients who received ≥16 RBCT regardless of conditioning regimen. Early referral for transplant and judicious use of RBCT prior to transplantation is encouraged.

**Study # AA07-01**

**Title:** Outcomes of marrow transplantation in patients >40 years with acquired aplastic anemia (AA) using matched sibling donors

**Study Chair:** Vikas Gupta (Princess Margaret Hospital)

**MS Statistician:** Jeanette Carreras (jcarrera@mcw.edu)
Conclusions: To determine whether age has an impact on the outcomes of patients with acquired AA undergoing transplantation using matched sibling donors.

Patients/Methods: The impact of age on outcomes in 1,563 patients with AA undergoing matched sibling donor transplantation and compared in three age groups (<20 years (n=818), 20-40 years (n=618) and >40 years (n=127)) were evaluated.

Results: Patients >40 years comprised a significantly higher proportion of patients who had: received >50 transfusions, had prior exposure to immunosuppressive therapy, poor performance scores, a longer time to transplant and received grafts from peripheral blood. The 5-year probabilities of adjusted survival were 81% (95% CI 78-84), 72% (95% CI 68-74) and 53% (95% CI 45-60) in patients aged <20 years, 20-40 years and >40 years, respectively (p<0.001).

Conclusions: Poor platelet recovery, increased risk of GVHD, a longer interval from diagnosis to transplantation, and poor performance scores at transplantation may explain some of the reasons for inferior outcomes in patients >40 years.

Study # AA08-01
Title: The role of the HLA DRB1 antigen, DR15, in patients with severe aplastic anemia (SAA) undergoing HLA-matched HCT
Study Chair: Minoo Battiwalla (Roswell Park Cancer institute)
MS Statistician: Jeanette Carreras (jcarrera@mcw.edu)
PhD Statistician: Tao Wang (taowang@hpi.mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To determine whether the presence of DR15 could impact clinical outcomes after allogeneic stem cell transplant in severe aplastic anemia.
Patients/Methods: We studied 1,422 patients with SAA (30% were DR15+) who were transplanted in 1990-2006 to determine whether the presence of HLA DR15 affected clinical outcomes.
Results: Proportions of patients who had received prior immunosuppressive therapy were similar among those with and without DR15. In multivariate analysis, after adjustment for significant factors, neutrophil recovery at day 28 (odds ratio [OR] 1.02, p=0.905), platelet recovery at day 100 (OR 0.95, p=0.776), secondary graft failure at 2 years (OR 0.66, p=0.123), acute (hazard ratio [HR] 0.88, p=0.345) and chronic (HR 1.09, p=0.519) graft-versus-host disease and overall mortality (HR 1.22, p=0.102) risks were similar in patients with and without DR15.
Conclusions: The presence of DR15 did not impact clinical outcomes after HLA-identical sibling transplantation for SAA.

Study # AA08-02
Title: Unrelated donor umbilical cord blood transplantation (UCBT) for sickle cell disease and thalassemia
Study Chair: Vanderson Rocha (Hôpital Saint Louis–Unité de Recherche Clinique)
MS Statisticians: Mary Eapen (meapen@mcw.edu)
Vanderson Rocha (vanderson.rocha@sls.aphp.fr)
Study Status: Manuscript preparation
Purpose: To describe the outcomes after unrelated UCBT for patients with sickle cell disease (SCD) and thalassemia (Thal) major.
Patients/Methods: Outcomes following UCBT for Thal major (N=31) and SCD (N=17) performed in 1996 to 2008 were assessed. All but three patients received a single cord blood unit.
Results: Estimated probability of survival at two years was 71%. It was 94% for patients with SCD and 57% for those with Thal. For those patients receiving an HLA-matched transplant, two-year survival rate was 90%, one HLA mismatch 79%, and it was 65% for those receiving 2 HLA mismatched grafts.

Conclusions: These data suggest interesting results in spite of low rates of sustained donor engraftment, mainly for those patients receiving a lower nucleated cell dose. It constitutes the basis for a multi-center prospective trial with a more homogenous conditioning regimen and more stringent criteria of cord blood selection based on cell dose and HLA.

Non-Malignant Marrow Disorders Working Committee Studies in Progress

**Study # AA02-03**
- **Title:** Allogeneic transplantation with fludarabine-based conditioning regimens for paroxysmal nocturnal hemoglobinuria
- **Study Chair:** Judith Marsh (St. George’s Hospital)
- **MS Statistician:** Jeanette Carreras (jcarrera@mcw.edu)
- **PhD Statistician:** TBD
- **Study Status:** Data collection

**Study # AA07-03**
- **Title:** Chronic GVHD and overall survival after unrelated donor HCT for SAA: comparison of outcomes after peripheral blood and bone marrow grafts
- **Study Chair:** Mary Eapen (CIBMTR, Medical College of Wisconsin)
- **MS Statistician:** Jeanette Carreras (jcarrera@mcw.edu)
- **PhD Statistician:** TBD
- **Study Status:** Protocol received/in development

**Study # AA09-01**
- **Title:** Outcome of allogeneic HCT in patients with Fanconi anemia who present with myelodysplasia, clonal abnormalities and/or leukemia
- **Study Chair:** Mouhab Ayas (King Faisal Specialist Hospital)
- **MS Statistician:** Wael Saber (wsaber@mcw.edu)
- **PhD Statistician:** TBD
- **Study Status:** Protocol received/in development

**Study # AA09-02**
- **Title:** Outcomes of HCT in patients with Dyskeratosis Congenita
- **Study Chair:** Shahinaz Gadalla (National Cancer Institute)
- **MS Statistician:** Jeanette Carreras (jcarrera@mcw.edu)
- **PhD Statistician:** TBD
- **Study Status:** Data collection

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10.16 PEDIATRIC CANCER WORKING COMMITTEE

**Committee Leadership**

<table>
<thead>
<tr>
<th>Role</th>
<th>Name</th>
<th>Title/Institution</th>
<th>Email</th>
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**Pediatric Cancer Working Committee Publications**

**Study #PC05-01**


**Purpose:** To determine the role of HSCT for patients aged ≤18 years with refractory or recurrent NHL.

**Patients/Methods:** Burkitt (n=41), lymphoblastic (n=53), diffuse large B-cell (n=52) and anaplastic large cell lymphoma (n=36), receiving autologous (n=90) or allogeneic (n=92) HCT in 1990-2005 were identified and analyzed.

**Results:** Characteristics of allogeneic and autologous HCT recipients were similar. Event-free survival (EFS) rates were lower for patients not in complete remission at HCT, regardless of donor type. Adjusting for disease status, 5-year EFS rates were similar after allogeneic and autologous HCT for diffuse large B-cell (50% vs. 52%), Burkitt (31% vs. 27%) and anaplastic large cell lymphoma (46% vs. 35%). However, EFS was higher for lymphoblastic lymphoma, after allogeneic HCT (40% vs. 4%, p<0.01).

**Conclusion:** HCT can salvage refractory/recurrent pediatric NHL. Outcomes were inferior if not in complete remission (CR) at HCT. Outcomes were similar for donor source, except for lymphoblastic lymphoma, where allogeneic was significantly better.
Pediatric Cancer Working Committee Preliminary Results

Study # PC08-02
Title: Outcomes after reduced-intensity conditioning (RIC) HCT for acute lymphoblastic leukemia (ALL) in children and adolescents
Study Chair: Michael Verneris (University of Minnesota)
MS Statistician: Vincent He (vhe@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Submitted
Purpose: To determine outcomes after RIC HCT for pediatric ALL.
Patients/Methods: Pediatric ALL patients transplanted with RIC between 1995 and 2005 were described and analyzed.
Results: The median age at transplant was 12 years and 47% had performance scores <90%. For 13%, the disease status was first complete remission (CR), ≥CR2 in 60% of patients and 22% had active disease at time of transplant. Matched related donors were available for a third of patients and about half of whom received bone marrow and the others, peripheral blood progenitor cells (PBPC). Sixty percent of unrelated transplant recipients received PBPC. The day-100 probability of grade II-IV acute GVHD was 37% and the three-year probability of chronic GVHD, 26%. At three years, the probability of transplant related mortality (TRM) was 40%, relapse 37%, and disease-free survival (DFS) 30%.
Conclusions: These data indicate long-term DFS can be achieved using RIC regimens in children with ALL. These findings must be validated in a larger population.

Pediatric Cancer Working Committee Studies in Progress

Study # D98-071
Title: Analysis of engraftment and outcome of unrelated donor HCT for pediatric myelodysplastic syndrome
Study Chair: Paul Woodard (Exelixis, Inc.)
MS Statistician: Vincent He (vhe@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Analysis

Study # PC05-02
Title: Outcomes after unrelated HCT for children with advanced acute lymphocytic leukemia in third clinical remission
Study Chair: Eneida Nemecek (Oregon Health and Science University)
MS Statistician: Vincent He (vhe@mcw.edu)
PhD Statistician: Kristin Ellis (kellis@mcw.edu)
Study Status: Analysis
Presentation: Accepted for presentation as a poster at the 2010 BMT Tandem Meetings.

Study # PC09-01
Title: Outcomes in children with T-cell acute lymphoblastic leukemia following allogeneic HCT
Study Chair: Michael Burke (University of Minnesota)
MS Statistician: Vincent He (vhe@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development
Pediatric Cancer Working Committee Planned Studies

**Study # PC09-02**

**Title:** Does the intensity of prior chemotherapy affect transplant outcomes for children with acute lymphoblastic leukemia who receive an allogeneic HCT in second complete remission?

**Study Chair:** Bruce Camitta (Medical College of Wisconsin)

**MS Statistician:** Vincent He (vhe@mcw.edu)

**PhD Statistician:** TBD

**Study Status:** Protocol development

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10.17  PLASMA CELL DISORDERS WORKING COMMITTEE

Committee Leadership

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Co-Chair: Sagar Lonial, MD, Emory University Hospital  
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Plasma Cell Disorders Working Committee Publications

Study # MM04-01


Purpose: To compare the International Staging System (ISS) and Durie-Salmon Staging (DSS) systems for predicting outcomes after upfront autologous HCT.

Patients/Methods: Outcomes of 729 patients with MM transplanted between 1995 and 2002 were analyzed.

Results: With a median follow-up of 56 months, the univariate probabilities (95% confidence interval) of non-relapse mortality, relapse, progression-free survival (PFS) and overall survival (OS) at five years were 7%, 68%, 25% and 52%, respectively. The median overall survival for stages I, II, III by DSS and ISS were 82, 68, 50 and 64, 68, 45 months, respectively. The concordance between the two staging systems was only 36%. Staging systems were formally compared using Cox models fit with DSS and ISS stages. Relative risks of PFS and OS were significantly different for stages I vs. II and II vs. III for DSS but only for stages II vs. III for ISS.

Conclusion: Although both systems were predictive of PFS and OS, the DSS was superior in formal statistical comparison using the Brier Score. However, neither system was strongly predictive of outcomes indicating the need for newer schemes incorporating other prognostic markers.
Study # MM06-03/HS06-01


Purpose: To describe the influence of race on outcomes of autologous HCT for MM. Blacks are twice as likely to develop and die from multiple myeloma (MM) and are less likely to receive an autologous HCT for MM than whites.

Patients/Methods: We compared transplant outcomes among black (n=303) and white (n=1892) recipients of autologous HCT for MM transplanted from 1995 to 2005.

Results: The black cohort was more likely to be female, had better Karnofsky performance scores but lower hemoglobin and albumin levels at diagnosis. Black recipients were younger and more likely to be transplanted later in their disease course. Black and white recipients had similar probabilities of five-year OS and PFS as well as cumulative incidences of disease progression and non-relapse mortality. In multivariate analyses, race was not associated with any of these endpoints.

Conclusion: Black recipients of autologous HCT for MM have similar outcomes to whites, suggesting that the reasons underlying lower rates of autologous HCT in blacks need to be studied further to ensure equal access to effective therapy.

Plasma Cell Disorders Working Committee Preliminary Results

Study # MM02-03/MM03-01

Title: The graft-versus-myeloma effect in patients receiving non-myeloablative conditioning

Study Chairs: Olle Ringdén (Karolinska University Hospital)
John Barrett (NHLBI/NIH)

MS Statistician: Smriti Shrestha (sshresth@mcw.edu)
PhD Statistician: Gisela Tunes da Silva (tunes@ime.usp.br)
Mei-Jie Zhang (meijie@mcw.edu)

Study Status: Manuscript preparation

Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Accepted for presentation as a poster at the 2010 BMT Tandem Meetings.

Purpose: To determine whether non-myeloablative (NMA) conditioning and reduced-intensity conditioning (RIC) used to reduce the risk of transplant-related mortality (TRM) depend on a graft-versus-myeloma effect.

Patients/Methods: We analyzed the outcomes of 177 HLA-identical sibling HCT between 1997 and 2005 following NMA (n=120) or RIC (n=57). Median age was 50 years and 62% were Durie-Salmon Stage III.

Results: Rate of acute GVHD (grades I-IV) was 42% at 100 days and of chronic GVHD at three years was 55%. At three years, TRM, relapse, PFS and OS were 21%, 44%, 35% and 56%, respectively. Multivariate analysis showed that acute GVHD was associated with an increased risk of TRM (relative risk [RR]=2.38, p=0.018). Chronic GVHD significantly decreased relapse in the non-immunoglobulin G myeloma subgroup (RR=0.11, p=0.004). PFS was improved in patients with chronic GVHD (RR=0.60, p=0.049).

Conclusion: Chronic GVHD decreased relapse and improved PFS, suggesting a beneficial graft-versus-myeloma effect following NMA and RIC.
Study # MM05-01
Title: Clinical outcome of patients with immunoglobulin D (IgD) and immunoglobulin M (IgM) MM undergoing autologous HCT: A CIBMTR retrospective study
Study Chairs: Donna Reece (Princess Margaret Hospital)
David Vesole (Loyola University Medical Center)
MS Statistician: Smriti Shrestha (sshresth@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Manuscript preparation
Purpose: To assess the outcome of patients with the rarer immunoglobulin subtypes, IgD and IgM MM. The CIBMTR conducted a retrospective analysis of MM patients undergoing autologous HCT between 1995-2005 to describe the characteristics and results of these patients.
Patients/Methods: Retrospective analysis of 3,578 patients identified 36 (1%) with IgD and 11 (0.3%) with IgM MM. Probabilities of PFS and OS, as well as the day-100 mortality and the cumulative incidence of TRM and relapse/progression were calculated. Although the small sample size precluded multivariate statistical analysis, the outcomes were compared with patients autologous transplanted for IgG and IgA MM.
Results: Relapsed/progressive MM was the most common cause of death; TRM was low. The three-year PFS and OS were 38% and 69% for IgD MM, and 47% and 68% for IgM MM, respectively.
Conclusion: The outcomes of patients with IgD and IgM MM treated with autologous HCT are similar to the more common immunological subtypes.

Study # MM05-02
Title: Effect of obesity on outcome in patients with MM undergoing autologous HCT
Study Chairs: Dan Vogl (University of Pennsylvania School of Medicine)
Edward Stadtmauer (Hospital of the University of Pennsylvania)
MS Statistician: Waleska S. Pérez (wperez@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Manuscript preparation
Purpose: To determine whether obesity affects outcomes of high-dose autologous HCT using a melphalan-based conditioning for patients with MM.
Patients/Methods: 1,087 patients were identified who received high-dose melphalan, with or without total body irradiation (TBI), as part of initial therapy. Patients were categorized by body mass index (BMI) as normal, overweight, obese, or severely obese. Overall survival and progression-free survival were analyzed.
Results: There was no clear effect of BMI on outcomes among patients receiving melphalan alone. In the subgroup of patients who received TBI as part of conditioning, a higher BMI was associated with longer progression-free survival.
Conclusion: The reason for the restriction of this effect to TBI-containing conditioning regimens requires further investigation. The current common strategy of reducing melphalan doses (i.e. calculating based on ideal or adjusted body weight) does not appear to impair outcomes for obese patients. Obesity should not exclude patients from consideration of autologous HCT.

Study # MM08-01
Title: Examination of time trends in allogeneic HCT for multiple myeloma
Study Chair: Shaji Kumar (Mayo Clinic)
MS Statistician: Peigang Li (peigang@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To analyze the trends in practice of allogeneic HCT for MM over time.

Patients/Methods: A total of 1,211 patients undergoing allogeneic HCT for MM were analyzed in three cohorts based on year of allogeneic HCT: 1989-1994 (n=346), 1995-2000 (n=285), and 2001-2005 (n=580).

Results: Patients transplanted in the 2001-2005 cohort were older. There was decreasing use of myeloablative regimens (82% vs. 62% vs. 9%) and bone marrow grafts (99%, 62% and 13%) over time. There was increasing use of autologous HCT prior to allogeneic HCT. The proportion of unrelated allogeneic HCTs increased over time (5% vs. 21% vs. 33%). The 100-day mortality rate decreased steadily over successive time periods; 35%, 29% and 19% respectively. Similarly, the TRM at five years remained steady between the first two periods, but decreased in the last period (40 & 48% vs. 29%). The incidence of chronic GVHD increased in the later cohort.

Conclusion: While the TRM has decreased significantly in the last cohort, this did not translate into an improvement in survival primarily because of increased risk of relapse. Long term (>10 years) progression-free and overall survival has remained unchanged over the past two decades.

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**Study # MM08-02**

Title: HLA specificities and predisposition to the development of multiple myeloma
Study Chair: Meral Bekzac (Ankara University School of Medicine)
MS Statistician: Peigang Li (peigang@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Manuscript preparation
Purpose: To compare the HLA-A,-B and -DRB1 2-digit allele and haplotype frequencies of patients with MM to the normal population.

Patients/Methods: HLA-A, B and DRB1 allele frequencies among 1,803 U.S. Caucasian patients were compared to A-B-DRB1 frequencies in HLA-typed healthy U.S. Caucasian controls (N= 433838) from the NMDP database.

Results: B*44 was observed less frequently among the patients (a protective effect) frequency (f): 0.126 vs 0.145 (p= 0.005, Odds Ratio (OR): 0.848). HLA-B*07 was more common (a predisposing effect) among patients (OR: 1.135, p=0.047). Similar predisposing and protective haplotype associations were observed with A*02-B*07-DRB1*04 and A*02-B*44-DRB1*04 respectively.

Conclusion: A protective effect was observed on the risk of developing MM with B*44 and a predisposing effect with B*07. Similar predisposing and protective haplotype associations were observed with A*02-B*07-DRB1*04 and A*02-B*44-DRB1*04 respectively. A revised analysis using a gender-matched control group repeated the previous findings confirming the impact of B*44.

---

**Study # MM09-01**

Title: Plasma cell leukemia: Outcomes with autologous or allogeneic HCT
Study Chairs: Anuj Mahindra (Massachusetts General Hospital)
Matt Kalaycio (Cleveland Clinic)
Jorge Vela (Hospital de Especialidades Centro Médico)
David Vesole (Loyola University Medical Center)
MS Statistician: Peigang Li (peigang@mcw.edu)
PhD Statistician: Mei-Jie Zhang (meijie@mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To determine the potential for long-term disease control using HCT in primary plasma cell leukemia (PPCL).
Patients/Methods: A retrospective review of 160 patients with PPCL who received autologous (n=107), allogeneic (n=52) or syngeneic (n=1) HCT and were reported to the CIBMTR between 1995 and 2006 was performed.

Results: The relapse rate at three years was 29% (95% confidence interval [CI], 14%-48%) in the allogeneic group and 24% (95% CI, 4%-54%) in the autologous group. Non relapse mortality at three years was 40% (95% CI, 23%-59%) in the allogeneic group and 11% (95% CI, 0-36%) in the autologous group. Progression-free survival at three years was 31% (95% CI, 27%-65%) in the allogeneic group and 65% (95% CI, 32%-91%) in the autologous group; overall survival was 46% (95% CI, 40%-93%) in the allogeneic group and 70% (95% CI, 40%-93%) in the autologous group.

Conclusion: The remarkable overall survival of patients after autologous HCT in this analysis is noteworthy and indicates that autologous HCT is a safe and acceptable treatment option for patients with PPCL.

Plasma Cell Disorders Working Committee Studies in Progress

Study # MM02-01/D01-117
Title: Comparison of second autologous transplant vs. related or unrelated non-myeloablative allogeneic HCT in patients with multiple myeloma who relapse after autologous transplantation
Study Chairs: Cesar Freyles (University of Texas Health Science Center)
               David Vesole (Loyola University Medical Center)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Data collection

Study # MM06-04
Title: Impact of pre-transplant therapy and depth of disease response prior to autologous peripheral blood stem cell transplantation in multiple myeloma
Study Chairs: Ravi Vij (Washington University School of Medicine)
               Shaji Kumar (Mayo Clinic)
               Donna Reece (Princess Margaret Hospital)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Data file preparation

Study # MM08-03
Title: Effect of renal failure after autologous HCT for multiple myeloma
Study Chairs: Baldeep Wirk (University of Florida)
               John Wingard (University of Florida)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # MM09-02
Title: Outcome of salvage second autologous stem cell transplantation in relapsed multiple myeloma
Study Chairs: Ayman Saad (Medical College of Wisconsin)
               Laura Michaelis (Loyola University Chicago)
               David Vesole (Loyola University Chicago)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

**Study # MM09-03**
Title: Comparison of early transplantation (< 12 months from diagnosis) to delayed transplantation after relapse (> 12 months) in multiple myeloma patients treated with novel induction therapy
Study Chairs: Leona Holmberg (Fred Hutchinson Cancer Center)
David Vesole (Loyola University Chicago)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

**Study # MM09-04**
Title: Clinical outcomes of donor lymphocyte infusions for relapsed, persistent or progressive multiple myeloma after allogeneic HCT
Study Chairs: Baldeep Wirk (University of Florida)
John Wingard (University of Florida)
MS Statistician: TBD
PhD Statistician: TBD
Study Status: Protocol received/in development

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10.18 REGIMEN-RELATED TOXICITY/SUPPORTIVE CARE WORKING COMMITTEE

Committee Leadership

Co-Chair: Karen Ballen, MD, Massachusetts General Hospital
E-mail: kballen@partners.org

Co-Chair: Vincent T. Ho MD, Dana-Faber Cancer Institute
E-mail: vtho@partners.org

Co-Chair: Kenneth R. Cooke, MD, Case Western Reserve University School of Medicine
E-mail: Kenneth.cooke@UHhospitals.org

Statistician: Manza Agovi-Johnson, MPH, CIBMTR Statistical Center Milwaukee
E-mail: magovi@mcw.edu

Statistician: Brent Logan PhD, CIBMTR Statistical Center Milwaukee
E-mail: blogan@mcw.edu

Scientific Director: Marcelo Pasquini, MD, MS, CIBMTR, Medical College of Wisconsin
E-mail: mpasquin@mcw.edu

Regimen-Related Toxicity/Supportive Care Working Committee Publications

Study # LE03-01

Purpose: To compare major transplant outcomes of patients with chronic myeloid leukemia (CML) who were non-smokers (NS) and past or current smokers (PCS). The effect of smoking on allogeneic transplant outcome is uncertain.

Patients/Methods: 2,193 NS and 1,108 PCS patients who received matched sibling or unrelated donor allogeneic transplants for CML in first chronic phase were evaluated. After comparing outcomes, we looked for dose effects and identified low and high dose smoking groups (>10 pack years, >1 pack per day). Outcomes were adjusted for known prognostic variables including the EBMT risk score.

Results: In multivariate analyses of sibling allogeneic transplant recipients, relapse risk was higher (RR 1.67, p=0.003) in smokers than NS, but dose effects were not consistent. High-dose smokers experienced 50% transplant-related mortality (TRM) compared to a 28% risk in the NS group, and the RR was 1.57 (p=0.005) on multivariate analysis. Overall survival at five years was 68% in NS vs. 50% in the high dose smoking group (p=0). Smoking did not affect outcomes in unrelated donor recipients.

Conclusions: High-dose smoking significantly reduces overall survival in patients having sibling allogeneic transplants for CML. Physicians can use these data to counsel patients who smoke about
transplant risk. A prospective study with detailed demographic, pulmonary function test and quality of life data would improve understanding of this issue.

Regimen-Related Toxicity/Supportive Care Committee Preliminary Results

Study # SC03-01/R02-26
Title: Obesity does not preclude safe and effective myeloablative HCT for acute myelogenous leukemia (AML) in adults
Study Chair: Willis Navarro (National Marrow Donor Program)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: Brent Logan (blogan@mcw.edu)
Study Status: Manuscript preparation
Purpose: To evaluate the impact of obesity, increasingly common in the U.S. and frequently associated with co-morbid medical conditions, on increased risk in HCT
Patients/Methods: Adult patients receiving myeloablative unpurged autologous or allogeneic HCT for AML in first or second complete remission, primary induction failure, or first relapse from 1995 to 2004 were included. Four weight groups were defined by body mass index (BMI): underweight <18; normal=18-25; overweight >25-30; and obese >30.
Results: Relative risk (normal = 1.0) in the related allogeneic HCT underweight group: death 1.86; TRM 2.22, treatment failure 2.08; obesity-related allogeneic HCT: 1.23, 1.32, and 1.19, respectively. There was no difference in autologous HCT and unrelated allogeneic HCT.
Conclusions: There were no significant differences in outcomes by weight group for autologous HCT or unrelated HCT groups. For related allogeneic HCT, obese recipients had modestly increased, and underweight, substantially increased risk of death, treatment failure and TRM. Obesity alone should not preclude HCT when appropriate.

Study # RT05-03
Title: Second unrelated donor transplantation as a rescue strategy for 122 patients with primary non-engraftment: results from the CIBMTR
Study Chair: Jeffery Schriber (City of Hope Medical Center)
MS Statistician: Manza Agovi (magovi@mcw.edu)
Study Status: Submitted
Purpose: To describe the outcomes of patients who receive a second unrelated donor transplant for primary non-engraftment.
Patients/Methods: Records of 14,136 patients transplanted from 1990-2005 and reported to CIBMTR were reviewed. 981 failed to engraft (absolute neutrophil count >500mm3) without evidence of disease. Of these, 122 received a second unrelated HCT.
Results: 98 patients used the same donor as the first for their second transplant; 28 of these used cryopreserved products and 70 used fresh original donor cells. By day 28, 43% had engrafted, and this increased to 48% at day 100. The 30- and 100-day mortality rates were 39% and 75%. TRM at one year was 86% (confidence interval [CI] 79-92). Disease-free survival (DFS) at one year was 7% (CI 2-12) and overall survival at one year was 11% (CI 6-17). Ten patients remained alive with a median survival of 77 months post-transplant. The primary causes of death were graft failure (33%), organ failure (22%), infection (15%), GVHD (14%) and disease (6%). There were no differences in survival comparing same versus new donor, fresh versus cryopreserved cells or small versus large initial graft. Patients who had a T-cell-depleted graft for their first transplant had a worse overall survival (OS) at one year (4 vs 16%) than those who had a T-cell replete graft.
Conclusions: Second transplant is feasible, however it has a high early mortality rate and a small minority of patients remains alive and disease-free at one year post-transplant. Further efforts are needed to try to identify groups that might benefit from such therapy or to see if earlier identification and treatment can change this natural history.

Study # D98-70
Title: Comparative analysis of busulfan (Bu) and cyclophosphamide (Cy) versus cyclophosphamide and total body irradiation (TBI) in full intensity unrelated donor HCT for acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML) and myelodysplasia (MDS)
Study Chair: Joseph Uberti (Kermanos Cancer institute)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: Sergey Tarima (starima@mcw.edu)
Study Status: Submitted
Purpose: To compare the clinical outcomes and toxicities of patients who received Cy/TBI regimens with those receiving BuCy regimens for unrelated HCT in patients with AML, CML and MDS.
Patients/Methods: Clinical outcomes were compared in 1,593 patients with AML, MDS and CML who received myeloablative regimens of either BuCy, standard dose Cy/TBI (1,000-1,260 cGy) or high-dose Cy/TBI (1,320-1,500 cGy) prior to a T-cell replete unrelated donor HCT facilitated by the NMDP between 1991 and 1999.
Results: Patients who received high-dose Cy/TBI regimens were slightly younger, more likely to receive a mismatched transplant and more likely to have intermediate or advanced disease compared to patients in the BuCy or standard dose TBI group. The rate of neutrophil and platelet engraftment was significantly higher in the standard dose CY/TBI group, compared to the high dose Cy/TBI or Bu/Cy group. The risk of developing grade II-IV aGVHD was also significantly higher among patients who received TBI-based regimens compared to the BuCy regimen (P=0.003). Overall survival, disease-free survival, TRM and relapses were not significantly different between any of the regimens.
Conclusions: BuCy, standard-dose Cy/TBI and high dose Cy/TBI regimens have equivalent efficacy profiles in terms of the major outcomes overall survival, disease-free survival, TRM and relapse in patients undergoing T-replete unrelated donor marrow transplantation for AML, CML and MDS.

Study # RT06-02
Title: A longitudinal study of transplant-related mortality (TRM) to determine how innovations in clinical care over the past two decades have affected the safety of myeloablative allogeneic HCT
Study Chair: John Horan (Emory University/Children’s Healthcare of Atlanta)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: Brent Logan (blogan@mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To estimate the combined effect of the many advances that have been introduced in transplant care since the 1980s on the incidence of TRM.
Patients/Methods: Patients younger than 50 years who received a matched related or an unrelated transplant, using a bone marrow or peripheral blood graft, for AML in first (CR1) or second (CR2) complete remission from 1985 through 2004. Only patients who received myeloablative conditioning with a BuCy or TBI-Cy based regimen were eligible. The incidence of TRM was determined for four consecutive five-year periods for HLA-matched sibling donors, and the later three for unrelated donor (URD) separately by donor type and disease status at transplant.
Results: Adjusting for changes in patient and disease characteristics over time in the multivariate analysis, there was a significant drop in TRM over time in three of the four groups. In the matched related donor patients, the relative risk for TRM in 2000-2004 (compared to 1985-1989) was 0.5 (95% CI, 0.37-0.66, p<0.001) and 0.25 (0.15-0.44, p<0.001) for the CR1 and CR2 groups, respectively. In the unrelated donor patients, the relative risk for TRM in 2000-2004 (compared to 1990-1994) was 0.73 (95% CI, 0.5-1.06 p=0.095) for the CR1 group and was 0.58 (95% CI, 0.42-0.79, p<0.001) for the CR2 group.

Conclusions: For patients with AML, there has been a marked reduction in the incidence of TRM over time in matched related transplants performed in a first or second CR. There has also been a significant reduction in TRM in unrelated donor transplants for AML performed in a second CR.

Study # RT05-02
Title: Lower body mass index (BMI) prior to transplantation as an indicator of increased risk for morbidity and mortality during the first 100 days after the transplantation process
Study Chair: Collin Barker (BC Children’s Hospital)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: Brent Logan (blogan@mcw.edu)
Study Status: Manuscript preparation
Presentation: Presented orally at the 2009 American Society of Hematology Meeting.
Purpose: To evaluate the impact of BMI on pediatric patients undergoing HCT for severe aplastic anemia (SAA). Outcomes of interest are 100-day mortality and incidence of severe acute GVHD and overall survival.
Patients/Methods: Records of 1,281 pediatric patients (860 HLA identical siblings and 421 matched unrelated donors) aged 2-19 years transplanted from 1990-2005 for SAA and reported to the ABMTR and NMDP were reviewed. Five BMI/weight status categories were used: <5 percentile, 5-25 percentile, 25-75 percentile, 75-95 percentile, and >95percentile. Primary endpoints were 100-day mortality and incidence of severe acute GVHD and overall survival. Secondary endpoints were age at transplant, Karnofsky score at transplantation, donor recipient mismatch, donor recipient CMV status, ethnicity, gender, patient region, primary transfusion number, time from diagnosis to transplant, TBI dose, donor type, year of transplant, GVHD prophylaxis, HLA match for URD, and cause of death, and assessed using multivariate analysis.
Results: The 100-day mortality rate was significantly higher for the obese group (BMI > 95%) as well as the overall survival at 6 months, 1 year, and 2 years post transplantation (P<0.001). Grade III-IV acute GVHD was also significantly higher in the obese group compared to the other weight groups (P<0.001). The relative risk of death decreased over time from 1990 to 2005. African-Americans had a worse outcome, irrespective of their BMI, compared to Caucasians.
Conclusions: Childhood obesity negatively impacts the outcomes of overall survival, 100-day mortality and grade III-IV acute GVHD in children undergoing HCT for SAA. The overall risk of death from HCT in this patient group is decreasing over time.

Study # RT06-01s
Title: Evaluation of TGF-B1 promoter and signal peptide polymorphisms as risk factors for renal dysfunction in HCT patients treated with cyclosporine A
Study Chair: Riddhishkumar Shah, MD, PhD, Georgetown University Medical Center,
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: Brent Logan (blogan@mcw.edu)
Study Status: Manuscript preparation
Purpose: To evaluate the impact of single nucleotide polymorphisms (SNPs) associated with increased TGF-β1 production on the risk of cyclosporine A (CsA)-induced renal dysfunction.

Patients/Methods: The study included cytomegalovirus (CMV)-negative recipients who received their CMV-negative allogeneic HCT from 2000 to 2004, and who were treated with CsA. Patients with aplastic anemia and CsA exposure of more than 30 days before transplant were excluded. Patients were genotyped for -1550, -509 and +869 SNPs. Renal dysfunction was measured by serum creatinine collected at five time points: at preconditioning, days 30, 100, 180 and 365 following transplant.

Results: There was no clear association of the three TGF-β1 SNPs and the development of renal insufficiency post-transplant, regardless of the definition of this event.

Conclusions: The frequency of TGF-β1 high expression SNPs was low compared to the other polymorphisms which could have reduced our ability to detect a small impact on renal function post-transplant.

Regimen-Related Toxicity/Supportive Care Working Committee Studies in Progress

Study # RT05-01
Title: Role of gemtuzumab ozogamicin in the development of hepatic veno-occlusive disease
Study Chair: Shannon Smiley (Roswell Park Cancer institute)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # RT07-01
Title: Interaction between co-morbidities and aging, and their combined impact on HCT outcomes
Study Chair: Mohamed Sorror (Fred Hutchinson Cancer Research Center)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: TBD
Study Status: Data collection

Study # RT08-01
Title: End stage renal disease in HCT
Study Chairs: Hariprasad Trivedi (Medical College of Wisconsin)
Parameswaran Hari (Medical College of Wisconsin)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: John P. Klein (klein@mcw.edu)
Study Status: Protocol received/in development

Study # RT08-02
Title: Effect of prior splenectomy on myeloid engraftment after ablative allogeneic HCT
Study Chair: Gorgun Akpek (University of Maryland School of Medicine)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

Study # RT09-01
Title: Primary graft failure following allogeneic HCT for the treatment of hematological malignancies
Study Chairs: Richard Olsson (Karolinska University Hospital)
Olle Ringden (Karolinska University Hospital)
Sonali Chaudhury (Northwestern University School of Medicine)
Study # RT09-02
Title: Effects of body mass in children with leukemias
Study Chairs: Richard Aplenc (Hospital for Sick Children)
Nancy Bunin (The Children’s Hospital of Philadelphia)
MS Statistician: Manza Agovi (magovi@mcw.edu)
PhD Statistician: TBD
Study Status: Protocol received/in development

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### 10.19 SOLID TUMORS WORKING COMMITTEE

#### Committee Leadership

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<th>Role</th>
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<th>Institution</th>
<th>Email Address</th>
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<td>University of Minnesota</td>
<td><a href="mailto:arora005@umn.edu">arora005@umn.edu</a></td>
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#### Solid Tumors Working Committee Publications

**Study # ST99-03**


**Purpose:** To describe the clinical outcomes in patients with rhabdomyosarcoma after autologous HCT. The five-year survival for relapsed rhabdomyosarcoma patients is 15-20% and only 5% for those with alveolar/undifferentiated subtypes.

**Patients/Methods:** Sixty-two patients received autologous HCT. Treatment-related mortality (TRM), progression-free survival (PFS) and overall survival (OS) were evaluated for subgroups: poor risk histology (alveolar/undifferentiated, n=34) vs. good risk (embryonal/botryoid, n=21); patients in first remission (REM1, n=38) vs. patients who relapsed (REL, n=21).

**Results:** 73% were <20 yrs in age, 50% had alveolar histology, 67% were in REM1 and 92% were chemosensitive at autologous HCT. The TRM at one year was 5% (95% confidence interval [CI], 1-12); the five-year PFS and OS were 29% (95% CI, 18-41) and 32% (95% CI, 21-44). There were no significant differences in five-year PFS and OS between those with poor risk vs. good risk histology (p=0.6; p=0.9), those with poor risk histology transplanted in REM1 vs. REL (34% vs. 33%; p=0.9), or those with good risk histology transplanted in REM1 vs. REL (38% vs. 25%; p=0.2).

**Conclusions:** Autologous HCT for rhabdomyosarcoma is typically done for patients with chemosensitive disease. When performed after relapse, long-term survival is seen in approximately one third of patients, seemingly better than previous reports of standard dose salvage for those with poor risk histologies.
### Solid Tumors Working Committee Studies in Progress

**Study #ST00-02**
- **Title:** Allogeneic HCT for renal cell cancer (RCC)
- **Study Chairs:**
  - A John Barrett (National Heart, Lung and Blood institute)
  - Olle Ringdén (Karolinska University Hospital Huddinge)
- **MS Statistician:** TBD
- **PhD Statistician:** TBD
- **Study Status:** Data collection

**Study # ST02-02**
- **Title:** Allogeneic HCT for colorectal cancer
- **Study Chair:** Olle Ringdén (Karolinska University Hospital Huddinge)
- **MS Statistician:** TBD
- **PhD Statistician:** TBD
- **Study Status:** Data collection

**Study # ST06-01**
- **Title:** Autologous HCT for desmoplastic tumors
- **Study Chair:** Edward Stadtmauer (University of Pennsylvania Health System)
- **MS Statistician:** Jerry Wang (zewang@mcw.edu)
- **PhD Statistician:** TBD
- **Study Status:** Data collection

**Study # ST07-01/PC07-01**
- **Title:** Allogeneic HCT for neuroblastoma
- **Study Chairs:**
  - Gregory Hale (St. Jude Children’s Research Hospital)
  - Stephen Grupp (Children’s Hospital of Philadelphia)
- **MS Statistician:** Vincent He (vhe@mcw.edu)
- **PhD Statistician:** TBD
- **Study Status:** Data collection

### Solid Tumors Working Committee Planned Studies

**Study # ST09-01**
- **Title:** HCT trends for metastatic solid tumors in North America and Europe
- **Study Chairs:**
  - Richard Childs, MD, NHLBI
  - Didier Blaise, MD, Institut Paoli Calmettes
  - Stephen Grupp (Children’s Hospital of Philadelphia)
- **MS Statistician:** TBD
- **PhD Statistician:** TBD
- **Study Status:** Protocol development

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## APPENDIX A1: CIBMTR PARTICIPATING INTERNATIONAL CENTERS

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**KEY:**
- MUD = Matched unrelated donor
- TED = Transplant Essential Data;
- CRF = comprehensive Report Form
- MED-A = (EBMT equivalent of TED)
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**KEY:**
- MUD = Matched unrelated donor
- TED = Transplant Essential Data
- CRF = comprehensive Report Form
- MED-A = (EBMT equivalent of TED)

**Form Type Submission:**
- TED
- CRF
- N/A
APPENDIX C1: WORKING COMMITTEE LEADERSHIP

For detailed information on any studies being conducted within a particular Working Committee, please contact any leader of that committee. The bolded name identifies the coordinating statistician for that committee.

### Acute Leukemia Working Committee

**Co-chairs**
- Martin Tallman, MD, Northwestern University: m-tallman@northwestern.edu
- John DiPersio, MD, PhD, St. Louis Children’s Hospital: jdipersi@im.wustl.edu
- Donald Bunjes, MD, Universitätsklinikum Ulm: donald.bunjes@uniklinik-ulm.de

**Scientific Director**
- Waleska S. Pérez, MPH, CIBMTR Statistical Center Milwaukee: wperez@mcw.edu

**Statisticians**
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### Autoimmune Diseases Working Committee

**Co-chairs**
- Harold Atkins, MD, FRCP, Ottawa Hospital: hatskins@ohri.ca
- Paolo Muraro, MD, PhD, Imperial College-Hammersmith Hospital: p.muraro@imperial.ac.uk

**Scientific Director**
- Marcelo Pasquini, MD, MS, Medical College of Wisconsin: mpasquin@mcw.edu

**Statisticians**
- Manza Agovi-Johnson, MPH, CIBMTR Statistical Center Milw: magovi@mcw.edu
- Kwang Woo Ahn, PhD, CIBMTR Statistical Center Milwaukee: kwoooahn@mcw.edu

### Cellular Therapies Working Committee

**Co-chairs**
- Joshua Hare, MD, University of Miami: jhare@med.miami.edu
- Helen Heslop, MD, Baylor College of Medicine: hheslop@bcm.tmc.edu
- Armand Keating, MD, Princess Margaret Hospital: armand.keating@uhn.on.ca

**Scientific Director**
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**Statisticians**
- Kathleen Sobocinski, MS, CIBMTR Statistical Center Milw: ksobo@mcw.edu
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### Chronic Leukemia Working Committee

**Co-chairs**
- Jeffrey Szer, MD, Royal Melbourne Hospital: jeff.szer@mh.org.au
- Jorge Cortes, MD, MD Anderson Cancer Center: jcortes@mdanderson.org
- Richard Maziarz, MD, Oregon Health and Science University: maziarzr@ohsu.edu

**Scientific Director**
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- Xiaochun Zhu, MS, CIBMTR Statistical Center Milwaukee: xzhu@mcw.edu
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### Donor Health and Safety Working Committee

**Co-chairs**
- Susan Leitman, MD, National Institutes of Health: sleitman@dtm.cc.nih.gov
- David Stroncsek, MD, National Cancer Institute: dstroncsek@dtm.cc.nih.gov
- Steven Goldstein, MD, Abramson Cancer Center-University of Pennsylvania: steven.goldstein@uphs.upenn.edu

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**Consumer Advocacy Committee (CAC) Representatives**
- Arthur Flatau, PhD, Association of Cancer Online Resources: flatau@acm.org
- Madhuri Mistry, Asians for Miracle Marrow Matches: mmistry@ltsc.org
Graft Sources and Manipulation Working Committee

Co-chairs
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Mary Laughlin, MD, Ireland Cancer Center: mary.laughlin@case.edu
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Graft-Vs-Host Disease Working Committee

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### Infection and Immune Reconstitution Working Committee

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- Paul Szabolcs, MD, Duke University Medical Center: szabo001@mc.duke.edu

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### International Studies Working Committee

**Co-chairs**
- Philip Rowlings, MBBS, MD, Newcastle Mater Hospital: phil_rowlings@yahoo.com.au
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- Brian Bolwell, MD, Cleveland Clinic Foundation: bolwebb@ccf.org
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- Richard Boyajian, RN, Dana Farber Cancer Institute: rboyajian@partners.org
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### Lymphoma Working Committee

**Co-chairs**
- Hillard Lazarus, MD, Case Western Reserve University: hml@po.cwru.edu
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**Statisticians**
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### Non-Malignant Marrow Disorders Working Committee

**Co-chairs**
- Mark Walters, MD, Children’s Hospital of Oakland: mwalters@mail cho.org
- Mouhab Ayas, MD, King Faisal Specialist Hospital: mouhab@kfshrc.edu.sa
- Joachim Deeg, MD, Fred Hutchinson Cancer Research Center: jdeeg@fhcrc.org

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- Mary Eapen, MD, MS, Medical College of Wisconsin: meapen@mcw.edu

**Statisticians**
- Jeanette Carreras, MPH, CIBMTR Statistical Center Milwaukee: jcarrera@mcw.edu
- Jennifer Le-Rademacher, PhD, CIBMTR Statistical Center Milw: jlerade@mcw.edu
## Pediatric Cancer Working Committee

**Co-chairs**
- Stella Davies, MBBS, PhD, Cincinnati Children’s Hospital: stella.davies@cchmc.org
- Paul Carpenter, MD, Fred Hutchinson Cancer Research Center: pcarpent@fhcrc.org
- Adriana Seber, MD, Instituto de Oncologia Pediatrixica: adrianaseber@graacc.org.br

**Scientific Director**
- Mary Eapen, MD, MS, Medical College of Wisconsin: meapen@mcw.edu

**Statisticians**
- Vincent He, MS, CIBMTR Statistical Center Milwaukee: vhe@mcw.edu
- Mei-Jie Zhang, PhD, CIBMTR Statistical Center Milwaukee: meijie@mcw.edu

## Plasma Cell Disorders Working Committee

**Co-chairs**
- Gustavo Milone, MD, Angelica Ocampo-Fundaleu: gmilone@fundaleu.org.ar
- Angela Dispenzieri, MD, Angela Dispenzieri, MD, Mayo Clinic Hospital: dispenzieri.angela@mayo.edu
- Sagar Lonial, MD, Emory University Hospital: sloni01@emory.edu

**Scientific Director**
- Parameswaran Hari, MD, MS, Medical College of Wisconsin: phari@mcw.edu

**Statisticians**
- Peigang Li, MS, CIBMTR Statistical Center Milwaukee: peigang@mcw.edu
- Mei-Jie Zhang, PhD, CIBMTR Statistical Center Milwaukee: meijie@mcw.edu

## Regimen-Related Toxicity/Supportive Care Working Committee

**Co-chairs**
- Karen Ballen, MD, Massachusetts General Hospital: kballen@partners.org
- Vincent T. Ho, MD, Dana-Faber Cancer Institute: vtho@partners.org
- Kenneth Cooke, MD, University Hospitals Case Medical Center: kenneth.cooke@uhhospitals.org

**Scientific Director**
- Marcelo Pasquini, MD, MS, Medical College of Wisconsin: mpasquin@mcw.edu

**Statisticians**
- Manza Agovi, MPH, CIBMTR Statistical Center Milwaukee: magovi@mcw.edu
- Brent Logan, PhD, CIBMTR Statistical Center Milwaukee: blogan@hpi.mcw.edu

## Solid Tumors Working Committee

**Co-chairs**
- Didier Blaise, MD, Institut Paoli Calmettes: blaised@marseille.fnclcc.fr
- Edward Stadtmauer, MD, Hospital of the University of Pennsylvania: stadtmau@uphs.upenn.edu
- Naoto Ueno, MD, MD Anderson Cancer Center: nueno@mdanderson.org

**Scientific Director**
- Mukta Arora, MD, MS, University of Minnesota: arora005@umn.edu

**Statisticians**
- Xiaochun Zhu, MS, CIBMTR Statistical Center Milwaukee: xzhu@mcw.edu
- Kwang Woo Ahn, PhD, CIBMTR Statistical Center Milwaukee: kwooahn@mcw.edu
## APPENDIX C2: WORKING COMMITTEE CHAIR CHANGES (effective as of 03/01/2010)

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<td>Incoming Chair: Steven Pavletic, MD, FACP</td>
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<td>Incoming Chair: none</td>
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<td>Outgoing Chair: Jeffrey Szer, MD</td>
<td>Incoming Chair: Matt Kalaycio, MD</td>
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<td>Donor Health and Safety</td>
<td>Outgoing Chair: Susan Leitman, MD</td>
<td>Incoming Chair: Michael Lankiewicz, MD</td>
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<td>Graft Sources and Manipulation</td>
<td>Outgoing Chair: Adrian Gee, PhD</td>
<td>Incoming Chair: Daniel Fowler, MD</td>
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<tr>
<td>Graft-Vs-Host Disease</td>
<td>Outgoing Chair: Steven Pavletic, MD</td>
<td>Incoming Chair: Corey Cutler, MD, MPH, FRCPC</td>
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<td>Health Policy and Psychosocial Issues</td>
<td>Outgoing Chair: none</td>
<td>Incoming Chair: none</td>
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<td>Immune Deficiencies/Inborn Errors</td>
<td>Outgoing Chair: Mitchell Horwitz, MD</td>
<td>Incoming Chair: Harry Malech, MD</td>
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<td>Outgoing Chair: Effie Petersdorf, MD</td>
<td>Incoming Chair: Carlheinz Müller, MD</td>
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<td>Outgoing Chair: JoAnne Young, MD</td>
<td>Incoming Chair: Michael Boeckh, ARND</td>
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<td>Outgoing Chair: none</td>
<td>Incoming Chair: none</td>
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<td>Late Effects and Quality Of Life</td>
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<td>Incoming Chair: Christine Duncan, MD</td>
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<td>Incoming Chair: David Maloney, MD</td>
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<td>Incoming Chair: Shalini Shenoy, MD</td>
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<td>Pediatric Cancer</td>
<td>Outgoing Chair: Stella Davies, MBBS, PhD</td>
<td>Incoming Chair: Carrie L. Kitko, MD</td>
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<td>Outgoing Chair: none</td>
<td>Incoming Chair: none</td>
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<tr>
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<td>Outgoing Chair: Karen Ballen, MD</td>
<td>Incoming Chair: Philip McCarthy, MD</td>
</tr>
<tr>
<td>Solid Tumors</td>
<td>Outgoing Chair: Didier Blaise, MD</td>
<td>Incoming Chair: Michael Bishop, MD</td>
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APPENDIX D1: CIBMTR ADVISORY and EXECUTIVE COMMITTEE MEMBERS

### Elected Members

<table>
<thead>
<tr>
<th>Role</th>
<th>Name</th>
<th>Institution</th>
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<tbody>
<tr>
<td><em>Chair</em></td>
<td>Stella Davies, MBBS, PhD</td>
<td>Cincinnati Children’s Hospital, Cincinnati, OH</td>
</tr>
<tr>
<td><em>Chair-Elect</em></td>
<td>Thomas Shea, MD</td>
<td>University of North Carolina at Chapel Hill, NC</td>
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### Vice Chairs

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<tr>
<th>Region</th>
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<tr>
<td><em>North America</em></td>
<td>Mark Litzow, MD</td>
<td>Mayo Clinic, Rochester, MN</td>
</tr>
<tr>
<td><em>Europe</em></td>
<td>Jane Apperley, MD</td>
<td>Imperial College School of Medicine, England</td>
</tr>
<tr>
<td><em>Central/South America</em></td>
<td>Carmem Maria Sales-Bonfim, MD</td>
<td>Federal University of Parana Hospital, Brazil</td>
</tr>
<tr>
<td><em>Asia/Africa/Australia</em></td>
<td>Mammen Chandy, MD</td>
<td>Christian Medical Center Hospital, India</td>
</tr>
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### Members at Large

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<tr>
<th>Region</th>
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<th>Institution</th>
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<tr>
<td>North America</td>
<td>Corey Cutler, MD, MPH</td>
<td>Dana-Farber Cancer Institute, Boston, MA</td>
</tr>
<tr>
<td></td>
<td>Allison Loren, MD</td>
<td>Hospital of the University of Pennsylvania, Philadelphia, PA</td>
</tr>
<tr>
<td></td>
<td>Jane Liesveld, MD</td>
<td>University of Rochester Medical Center, Rochester, NY</td>
</tr>
<tr>
<td></td>
<td>Brenda Sandmaier, MD</td>
<td>Fred Hutchinson Cancer Center, Seattle, WA</td>
</tr>
<tr>
<td></td>
<td>Marcos De Lima, MD</td>
<td>MD Anderson Cancer Center, Houston, TX</td>
</tr>
<tr>
<td>Non North America</td>
<td>Robert Soiffer, MD</td>
<td>Dana Farber Cancer Institute, Boston, MA</td>
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<tr>
<td></td>
<td>Jorge Sierra, MD</td>
<td>Hospital Santa Creu I Sant Pau, Barcelona, Spain</td>
</tr>
<tr>
<td></td>
<td>Ricardo Pasquini, MD</td>
<td>Hospital Nossa Senhora das Gracas, Brazil</td>
</tr>
<tr>
<td></td>
<td>Peter Shaw, MD</td>
<td>The Children’s Hospital at Westmead, Westmead, Australia</td>
</tr>
<tr>
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<td>Jonas Mattsson, MD</td>
<td>Huddinge University Hospital, Sweden</td>
</tr>
<tr>
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<td>Peter Dregger, MD</td>
<td>University of Heidelberg, Germany</td>
</tr>
<tr>
<td></td>
<td>Judith Marsh, MD</td>
<td>St. George’s Hospital, London, England</td>
</tr>
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### Appointed Members

<table>
<thead>
<tr>
<th>Role</th>
<th>Member</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Patient/Family Representatives</em></td>
<td>Andrea Feldmar, Co-Chair</td>
<td>Consumer Advocacy Committee</td>
</tr>
<tr>
<td></td>
<td>Susan K. Stewart, Co-Chair</td>
<td>Consumer Advocacy Committee</td>
</tr>
<tr>
<td><em>Donor Representative</em></td>
<td>Thomas H. Price, MD</td>
<td>Medical Director, Puget Sound Blood Center</td>
</tr>
<tr>
<td><em>Collection Center Representative</em></td>
<td>Zbigniew Szczepiorkowski, MD</td>
<td>Medical Director, Dartmouth-Hitchcock Medical Center</td>
</tr>
<tr>
<td><em>Bioethicist</em></td>
<td>Raquel Schears, MD, MPH, FACEP</td>
<td>Mayo Clinic, Rochester, MN</td>
</tr>
<tr>
<td><em>Business Representative</em></td>
<td>Alan Leahigh, Executive Vice President, Executive Admin., Inc., Chicago, IL</td>
<td>ASBMT</td>
</tr>
</tbody>
</table>

* CIBMTR Executive Committee Members

---

2. Term expires 2/28/2010. New member: Ricardo Pasquini, MD, Hospital de Clinicas, Curitiba, Brazil
3. Term expires 2/28/2010. New member: Koen van Besien, MD, University of Chicago Hospitals, Chicago, IL
4. Term expires 2/28/2010. New member: Hillard Lazarus, MD, University Hospitals Case Medical Center, Cleveland, OH
5. Term expires 2/28/2010. New member: Bart Scott, MD, Fred Hutchinson Cancer Research Center, Seattle, WA
6. Term expires 2/28/2010. New member: Yoshito Atsuta, MD, PhD, Nagoya Daini Hospital Red Cross, Nagoya, Japan
7. Term expires 2/28/2010. New member: Jürgen Finke, MD, Freiburg University Medical Center, Freiberg, Germany
8. Term expires 2/28/2010. New member: Tracey O’Brien, MD, Sydney Children’s Hospital, Sydney, Australia
Ex Officio Members

*Executive Director  Jeffrey Chell, MD, NMDP, Minneapolis, MN
*Chief Scientific Director  Mary M. Horowitz, MD, MS, CIBMTR, Milwaukee, WI
*Chief Statistical Director  John P. Klein, PhD, CIBMTR, Milwaukee, WI
*Associate Scientific Director Data Operations  J. Douglas Rizzo, MD, MS, CIBMTR, Milwaukee, WI
*Associate Scientific Director CIBMTR-Minneapolis  Dennis Confer, MD, NMDP, Minneapolis, MN
*Research Advisor  Daniel Weisdorf, MD, University of Minnesota, Minneapolis, MN
*NMDP/HRSA Project Officer  Shelley Tims, MPH
*NMDP/Navy Project Officer  Robert Hartzman, MD, Capt. MC, USN (ret)
*MCW/HRSA Project Officers  Robert Baitty, MPP
                    Randall Gale, MPH
*MCW/NCI Project Officer  Roy Wu, PhD
*MCW/NHLBI Project Officer  Nancy DiFronzo, PhD
*MCW/NIAID Project Officer  Linda Griffith, MD, PhD
*Nominating Committee Chair  Philip McCarthy, MD, Roswell Park Memorial, Buffalo, NY

* CIBMTR Executive Committee Members

1 Term expires 2/28/2010. New Chair to be determined.
APPENDIX D2: CIBMTR NOMINATING COMMITTEE

Chair:
Philip McCarthy, MD\(^1\)  Roswell Park Memorial, Buffalo, NY

Members:
Gregory Hale, MD\(^2\)  St. Jude Children’s Research Hospital, Memphis, TN
Mary Territo, MD\(^3\)  University of California (UCLA) Adults, Los Angeles, CA
Steve Devine, MD  Ohio State Medical Center, James Cancer Center, Columbus, OH
David Porter, MD  University of Pennsylvania, Abramson Cancer Center, Philadelphia

\(^1\) Term expires 2/28/2010. New member: Neena Kapoor, MD, Children’s Hospital Los Angeles, Los Angeles, CA
\(^2\) Term expires 2/28/2010. New member: Ginna Laport, MD, Stanford University, Stanford, CA
\(^3\) Term expires 2/28/2010. New member: Jeffrey Szer, MD, Royal Melbourne Hospital City Campus, Melbourne, Australia
**APPENDIX E: NMDP HISTOCOMPATIBILITY ADVISORY GROUP**

Carolyn K. Hurley, PhD, Diplomate ABHI  
Georgetown University Medical Center

Craig Kollman, PhD  
Jaeb Center for Health Research

Carlheinz Müller, MD, PhD  
Central German Bone Marrow Registry (ZKRD)

Harriet Noreen CHS  
University of Minnesota-Fairview

Ann Woolfrey, MD  
Fred Hutchinson Cancer Center

Neng Yu, MD, Diplomate ABHI  
American Red Cross Blood Services, NE Division

Pablo Rubinstein, MD  
New York Blood Center

Edward Snyder, MD  
Yale University Medical Center

Robert J. Hartzman, MD, Capt, MC, USN (Ret.)  
(Navy Representative) C.W. Bill Young Cell Transplantation Program

Robert Baitty, MPP  
Health Resources & Services Administration, HHS

James Bowman, MD  
Health Resources & Services Administration, HHS

**CIBMTR Staff**

Brent Logan, PhD  
CIBMTR, Milwaukee Campus

Mary Eapen, MD, MS  
CIBMTR, Milwaukee Campus

**NMDP Staff**

Michelle Setterholm, BS, CHS  
National Marrow Donor Program

Dennis Confer, MD  
National Marrow Donor Program

Martin Maiers, MS  
National Marrow Donor Program

Stephen Spellman, MBS  
National Marrow Donor Program

Willis Navarro, MD  
National Marrow Donor Program
APPENDIX F: CLINICAL TRIALS ADVISORY COMMITTEE (CTAC)

Dennis Confer, MD  CIBMTR-Minneapolis Campus
Steven Devine, MD  Ohio State University Medical Center
Rebecca Drexler  CIBMTR-Minneapolis Campus
Mary Eapen, MD, MS  CIBMTR-Milwaukee Campus
Andrea Feldmar  CIBMTR Consumer Advocacy Committee
Steve Forman, MD\(^1\)  City of Hope
Sergio Giralt, MD  MD Anderson Cancer Center
Mary Horowitz, MD, MS  CIBMTR-Milwaukee Campus
Naynesh Kamani, MD  Children’s National Medical Center
Hillard Lazarus, MD  Case Western Reserve University, Ireland Cancer Center; Chair
Brent R. Logan, PhD  CIBMTR-Milwaukee Campus
Richard Maziarz, MD  Oregon Health & Science University
Kirk Schultz, MD  Pediatric Blood and Marrow Transplant Consortia
Ed Stadtmauer, MD  University of Pennsylvania
Sue Stewart  CIBMTR Consumer Advocacy Committee
Willis Navarro, MD  RCI BMT Scientific Director, University of Minnesota
Daniel Weisdorf, MD  CIBMTR Senior Research Advisor, University of Minnesota
John Wingard, MD  University of Florida

\(^1\) Term expires 2/28/2010. New member is Scott Rowley, MD, Hackensack University Medical Center, Hackensack, NJ
## APPENDIX G: CONSUMER ADVOCACY COMMITTEE (CAC)

### Co-Chairs

<table>
<thead>
<tr>
<th>Name</th>
<th>Organization</th>
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<tbody>
<tr>
<td>Andrea Feldmar, LCPC</td>
<td>Patient Focused-Initiatives Committee, National Marrow Donor Program</td>
</tr>
<tr>
<td>Susan Stewart</td>
<td>Blood &amp; Marrow Transplant Information Network</td>
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### Members

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<tr>
<td>Richard Boyajian, RN</td>
<td>Dana-Farber Cancer Institute</td>
</tr>
<tr>
<td>Arthur Flatau, PhD</td>
<td>Association of Cancer Online Resources</td>
</tr>
<tr>
<td>Winona Hollins-Hauge, MSW, LICSW</td>
<td>Washington State Commission on African American Affairs and Governor's Interagency Council on Health Disparities</td>
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<tr>
<td>Myra Jacobs, MA, CFRE</td>
<td>National Bone Marrow Transplant Link</td>
</tr>
<tr>
<td>Madhuri Mistry</td>
<td>Asians for Miracle Marrow Matches</td>
</tr>
<tr>
<td>Nancy O’Connor, RN, BSN</td>
<td>University Medical Center (retired)</td>
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<tr>
<td>Barry Schatz</td>
<td>Cardinal Bernardin Cancer Center, Loyola University Medical Center</td>
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### Scientific Director

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<thead>
<tr>
<th>Name</th>
<th>Institution</th>
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<tr>
<td>J. Douglas Rizzo, MD, MS</td>
<td>CIBMTR – Milwaukee Campus</td>
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### Ex-Officio Members

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<thead>
<tr>
<th>Name</th>
<th>Institution</th>
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<tbody>
<tr>
<td>Robyn Ashton, RN, MSN</td>
<td>Health Resources and Services Administration</td>
</tr>
<tr>
<td>Robert Baitty, MPH</td>
<td>Health Resources and Services Administration</td>
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<tr>
<td>Jeffrey Chell, MD</td>
<td>National Marrow Donor Program</td>
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<tr>
<td>Dennis Confer, MD</td>
<td>CIBMTR – Minneapolis Campus</td>
</tr>
<tr>
<td>Rebecca Drexler, BS, AAS</td>
<td>CIBMTR – Minneapolis Campus</td>
</tr>
<tr>
<td>Anna Hassebroek, MPH</td>
<td>CIBMTR – Minneapolis Campus</td>
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<tr>
<td>Darlene Haven, BS</td>
<td>National Marrow Donor Program</td>
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<tr>
<td>Mary Horowitz, MD, MS</td>
<td>CIBMTR – Milwaukee Campus</td>
</tr>
<tr>
<td>Stephanie Lee, MD, MPH</td>
<td>Fred Hutchinson Cancer Center</td>
</tr>
<tr>
<td>Elizabeth Murphy, EdD, RN</td>
<td>(NMDP liaison) National Marrow Donor Program</td>
</tr>
<tr>
<td>Tanya Pedersen</td>
<td>CIBMTR – Minneapolis Campus</td>
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<tr>
<td>Kathy Sobocinski, MS</td>
<td>CIBMTR – Milwaukee Campus</td>
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<tr>
<td>Shelley Tims, MPH</td>
<td>Health Resources and Services Administration</td>
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<tr>
<td>Paula Watry</td>
<td>CIBMTR – Milwaukee Campus</td>
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## APPENDIX H: HEALTH SERVICES RESEARCH PROGRAM ADVISORY GROUP

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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<tbody>
<tr>
<td>Jeffrey Chell, MD</td>
<td>CEO, NMDP, and Executive Director, CIBMTR</td>
</tr>
<tr>
<td>Mary M. Horowitz, MD, MS</td>
<td>Executive Director and the Chief Scientific Director of CIBMTR</td>
</tr>
<tr>
<td>Dennis Confer, MD</td>
<td>Associate Scientific Director of CIBMTR-Minneapolis</td>
</tr>
<tr>
<td>J. Douglas Rizzo, MD, MS</td>
<td>Associate Scientific Director for Data Operations</td>
</tr>
<tr>
<td>Elizabeth Murphy</td>
<td>Vice President, Office of Patient Advocacy, NMDP</td>
</tr>
<tr>
<td>Steven Joffe, MD</td>
<td>Co-chair, CIBMTR Health Policy Working Committee</td>
</tr>
<tr>
<td>Susan Parsons, MD</td>
<td>Co-chair, CIBMTR Health Policy Working Committee</td>
</tr>
<tr>
<td>Nancy Omondi, MBA, MS</td>
<td>Manager, Health Services Research, Patient Services, NMDP</td>
</tr>
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APPENDIX I: EXTERNAL REVIEW PANEL PARTICIPANTS

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
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</thead>
<tbody>
<tr>
<td>Frederick R. Appelbaum, MD</td>
<td>Fred Hutchinson Cancer Research Center (Panel Co-Chair)</td>
</tr>
<tr>
<td>Robert L. Baitty</td>
<td>HRSA Division of Transplantation</td>
</tr>
<tr>
<td>Craig A. Beam, PhD</td>
<td>University of Illinois, Chicago</td>
</tr>
<tr>
<td>Smita Bhatia, MD, MPH</td>
<td>City of Hope National Medical Center</td>
</tr>
<tr>
<td>Carmem Maria Sales-Bonfim</td>
<td>Federal University of Parana Hospital, Brazil</td>
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<tr>
<td>James Bowman, MD, FACS</td>
<td>HRSA, Division of Transplantation</td>
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<tr>
<td>Richard E. Champlin, MD</td>
<td>MD Anderson Cancer Center</td>
</tr>
<tr>
<td>Nelson J. Chao, MD</td>
<td>Duke University Medical Center</td>
</tr>
<tr>
<td>Stella M. Davies, MBBS, PhD</td>
<td>Cincinnati Children’s Hospital Medical Center</td>
</tr>
<tr>
<td>Nancy L. DiFronzo, PhD</td>
<td>NHLBI</td>
</tr>
<tr>
<td>Arthur R. Derse, MD, JD</td>
<td>Medical College of Wisconsin</td>
</tr>
<tr>
<td>David M. Dilts, PhD, MBA</td>
<td>Oregon Health &amp; Science University</td>
</tr>
<tr>
<td>Craig Earle, MD, MSc</td>
<td>Institute for Clinical Evaluative Sciences, Toronto</td>
</tr>
<tr>
<td>Michael J. Eckrich, MD</td>
<td>Vanderbilt University Medical Center</td>
</tr>
<tr>
<td>Ephraim Fuchs, MD, MBA</td>
<td>Johns Hopkins Medicine</td>
</tr>
<tr>
<td>Edmund A. Gehan, PhD</td>
<td>Georgetown University Medical Center</td>
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<tr>
<td>Robert J. Hartzman, MD, Capt, USN (ret)</td>
<td>C.W. Bill Young Cell Transplantation Program, Naval Medical Research Center</td>
</tr>
<tr>
<td>Helen Heslop, MD</td>
<td>Baylor College of Medicine</td>
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<tr>
<td>David H. Howard, PhD</td>
<td>Emory University</td>
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<tr>
<td>Steven Joffe, MD, MPH</td>
<td>Dana-Farber Cancer Institute</td>
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<tr>
<td>Armand Keating, MD, FRCPC</td>
<td>Princess Margaret Hospital (Panel Co-Chair)</td>
</tr>
<tr>
<td>Richard A. Larson, MD</td>
<td>University of Chicago</td>
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<tr>
<td>John Levine, MD, MS</td>
<td>University of Michigan Medical Center</td>
</tr>
<tr>
<td>Robert D. Lorentz, PhD</td>
<td>Software, Electronics and Mechanical Systems Lab, 3M Corporation</td>
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<tr>
<td>J. Alejandro Madrigal, MD, PhD, DSc</td>
<td>Royal Free &amp; University College Medical School, London</td>
</tr>
<tr>
<td>William D. Merritt, PhD</td>
<td>NIH-NCI</td>
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<tr>
<td>James L. Omel, MD</td>
<td>Patient Advocate, Retired Physician</td>
</tr>
<tr>
<td>Thomas H. Price, MD</td>
<td>Puget Sound Blood Center</td>
</tr>
<tr>
<td>Vanderson Rocha, MD</td>
<td>Hopital Saint-Louis, Paris</td>
</tr>
<tr>
<td>Andromachi Scaradavou, MD</td>
<td>New York Blood Center, National Cord Blood Program</td>
</tr>
<tr>
<td>Jonathan S. Serody, MD</td>
<td>University of North Carolina at Chapel Hill</td>
</tr>
<tr>
<td>Thomas Shea, MD</td>
<td>University of North Carolina at Chapel Hill</td>
</tr>
<tr>
<td>Martin S. Tallman, MD</td>
<td>Northwestern University</td>
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<tr>
<td>Anat R. Tambur, PhD</td>
<td>Northwestern University</td>
</tr>
<tr>
<td>John E. Wagner, MD</td>
<td>University of Minnesota</td>
</tr>
<tr>
<td>Edmund K. Waller, MD, PhD</td>
<td>Emory University Hospital</td>
</tr>
</tbody>
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### APPENDIX J: LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ABMTR</td>
<td>Autologous Bone Marrow Transplant Registry</td>
</tr>
<tr>
<td>AGNIS</td>
<td>A Growable Network Information System</td>
</tr>
<tr>
<td>aGVHD</td>
<td>Acute graft-versus-host disease</td>
</tr>
<tr>
<td>AID</td>
<td>Autoimmune disease</td>
</tr>
<tr>
<td>ALL</td>
<td>Acute lymphoblastic leukemia</td>
</tr>
<tr>
<td>AML</td>
<td>Acute myeloid (myelogenous) leukemia</td>
</tr>
<tr>
<td>AP</td>
<td>Accelerated phase</td>
</tr>
<tr>
<td>APC</td>
<td>Antigen-presenting cells</td>
</tr>
<tr>
<td>APBMT</td>
<td>Asia-Pacific Blood and Marrow Transplant Group</td>
</tr>
<tr>
<td>ASBMT</td>
<td>American Society of Blood &amp; Marrow Transplantation</td>
</tr>
<tr>
<td>ASH</td>
<td>American Society of Hematology</td>
</tr>
<tr>
<td>ATG</td>
<td>Anti-thymocyte globulin</td>
</tr>
<tr>
<td>AYA</td>
<td>Adolescents and young adults</td>
</tr>
<tr>
<td>BM</td>
<td>Bone marrow</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>BMT CTN</td>
<td>Blood &amp; Marrow Transplant Clinical Trials Network</td>
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<tr>
<td>BP</td>
<td>Blast phase</td>
</tr>
<tr>
<td>Bu</td>
<td>Busulfan</td>
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<tr>
<td>CAC</td>
<td>Consumer Advocacy Committee</td>
</tr>
<tr>
<td>caDSR</td>
<td>Cancer Data Standards Registry and Repository</td>
</tr>
<tr>
<td>CALGB</td>
<td>Cancer and Leukemia Group B</td>
</tr>
<tr>
<td>CDE</td>
<td>Common Data Element</td>
</tr>
<tr>
<td>Cen</td>
<td>Centromeric</td>
</tr>
<tr>
<td>cGVHD</td>
<td>Chronic graft-versus-host disease</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
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<tr>
<td>CIBMTR</td>
<td>Center for International Blood &amp; Marrow Transplant Research</td>
</tr>
<tr>
<td>CITI</td>
<td>Collaborative IRB Training Initiative Program</td>
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<tr>
<td>CML</td>
<td>Chronic myeloid (myelogenous) leukemia</td>
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<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
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<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CPI</td>
<td>Continuous Process Improvement</td>
</tr>
<tr>
<td>CR</td>
<td>Complete remission</td>
</tr>
<tr>
<td>CRC</td>
<td>Clinical Research Coordinator</td>
</tr>
<tr>
<td>CRF</td>
<td>Comprehensive Report Form</td>
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<tr>
<td>CRID</td>
<td>CIBMTR Recipient Identification Number</td>
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<tr>
<td>CSA</td>
<td>Cyclosporine A</td>
</tr>
<tr>
<td>Cy</td>
<td>Cyclophosphamide</td>
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<tr>
<td>DBTC</td>
<td>Data Back to Centers</td>
</tr>
<tr>
<td>DCC</td>
<td>Data and Coordinating Center</td>
</tr>
<tr>
<td>DFCI</td>
<td>Dana-Farber Cancer Institute</td>
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<tr>
<td>DFS</td>
<td>Disease-free survival</td>
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<td>DLBCL</td>
<td>Diffuse large B-cell lymphoma</td>
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<td>DIC</td>
<td>Donor-leukocyte infusion</td>
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<td>DSA</td>
<td>Donor-directed specific alloantibodies</td>
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<td>DSS</td>
<td>Durie-Salmon Staging System</td>
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<td>DTA</td>
<td>Data Transmission Agreement</td>
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<td>EBMT</td>
<td>European Group for Blood and Marrow Transplantation</td>
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<td>ETL</td>
<td>Extract, Transform and Load</td>
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<td>FACT</td>
<td>Foundation for Accreditation of Cellular Therapy</td>
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<td>FHCRC</td>
<td>Fred Hutchinson Cancer Research Center</td>
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<td>GCM</td>
<td>Global Contact Management</td>
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<td>G-CSF</td>
<td>Granulocyte colony-stimulating factor</td>
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<td>GVHD</td>
<td>Graft-versus-host disease</td>
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<td>GVL</td>
<td>Graft-versus-leukemia effect</td>
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<tr>
<td>HBV</td>
<td>Hepatitis B virus</td>
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<td>HCV</td>
<td>Hepatitis C virus</td>
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<td>HDC</td>
<td>High dose chemotherapy</td>
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<tr>
<td>HCT</td>
<td>Hematopoietic stem cell transplantation</td>
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<td>HHS</td>
<td>(U.S. Dept. of) Health and Human Services</td>
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<tr>
<td>HIPAA</td>
<td>Health Insurance Portability and Accountability Act</td>
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<td>HL</td>
<td>Hodgkin lymphoma</td>
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<td>HLA</td>
<td>Human leukocyte antigen</td>
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<td>HR</td>
<td>Hazard ratio</td>
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<td>HRSA</td>
<td>Health Resources and Services Administration</td>
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<td>HSR</td>
<td>Health Services Research</td>
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<td>IBD</td>
<td>Inflammatory bowel disease</td>
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<td>IBMTR</td>
<td>International Bone Marrow Transplant Registry</td>
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<td>IgD</td>
<td>Immunoglobulin D</td>
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<td>IgM</td>
<td>Immunoglobulin M</td>
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<td>IHWG</td>
<td>International Histocompatibility Working Group</td>
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<td>IM</td>
<td>Imatinib mesylate</td>
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<tr>
<td>IRB</td>
<td>Institutional Review Board</td>
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<td>IRG</td>
<td>Immune response gene</td>
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<td>ISS</td>
<td>International Staging System</td>
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<td>IT</td>
<td>Information Technology</td>
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<td>IV</td>
<td>Intravenous</td>
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<td>JACIE</td>
<td>Joint Accreditation Committee of ISCT and EBMT</td>
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<td>JMDP</td>
<td>Japanese Marrow Donor Program</td>
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<tr>
<td>KIR</td>
<td>Killer-cell immunoglobulin-like receptors</td>
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<td>LCH</td>
<td>Langerhans cell histiocytosis</td>
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<td>LEL</td>
<td>Low expression loci</td>
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<td>LFS</td>
<td>Leukemia-free survival</td>
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<td>LTA</td>
<td>Lymphotoxin alpha</td>
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<td>MA</td>
<td>Myeloablative</td>
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<td>Term</td>
<td>Definition</td>
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<tr>
<td>MCW</td>
<td>Medical College of Wisconsin</td>
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<td>MDACC</td>
<td>MD Anderson Cancer Center</td>
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<td>MDS</td>
<td>Myelodysplastic syndrome</td>
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<tr>
<td>mHAg</td>
<td>Minor histocompatibility antigens</td>
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<td>MHC</td>
<td>Major histocompatibility complex</td>
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<td>MICA</td>
<td>MHC class I chain-related gene A</td>
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<tr>
<td>MM</td>
<td>Multiple myeloma</td>
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<tr>
<td>mmRD</td>
<td>Mismatched related donor</td>
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<td>MS</td>
<td>Multiple sclerosis</td>
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<td>MSD</td>
<td>Matched sibling donor</td>
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<td>MTX</td>
<td>Methotrexate</td>
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<tr>
<td>NCI</td>
<td>National Cancer Institute</td>
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<tr>
<td>NK</td>
<td>Natural killer cell</td>
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<td>NHL</td>
<td>Non-Hodgkin lymphoma</td>
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<tr>
<td>NIAID</td>
<td>National Institute of Allergy and Infectious Diseases</td>
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<td>NIMA</td>
<td>Non-inherited maternal antigens</td>
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<td>NMA</td>
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<td>NMIDP</td>
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<td>NRM</td>
<td>Non-relapse mortality</td>
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<tr>
<td>O/E</td>
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<td>OPA</td>
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<tr>
<td>OR</td>
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<tr>
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<td>PBMC</td>
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<td>PBPC</td>
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<td>PBSC</td>
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<td>PCS</td>
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<td>Ph-ALL</td>
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<td>Primary immune deficiency disorder</td>
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<td>PLL</td>
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