Center for International Blood and Marrow Transplant Research

Sharing Knowledge
Sharing Hope
Center for International Blood and Marrow Transplant Research

The Year in Review –
Or, What Your Data Makes Possible

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

A research collaboration between the National Marrow Donor Program (NMDP)/Be The Match and the Medical College of Wisconsin
CIBMTR Number of Patients Registered, 1970-2015

Cumulative Patients Registered

Years

(Data are incomplete for 2015)
CIBMTR 420,000 Cases Registered, 1985-2015 >1000 Publications

Years

Transplants

0 50000 100000 150000 200000 250000 300000 350000 400000 450000

'85 '87 '89 '91 '93 '95 '97 '99 '01 '03 '05 '07 '09 '11 '13

- Allogeneic
- Autologous
- Cumulative Total

Health Services Research
QOL, Long-term Follow-up
Immunobiology*
Multicenter Clinical Trials
Technology Assessment
Prognostic factors
Descriptive

* NMDP Repository - Specimens for >33,000 donor-recipient pairs.
Facilitating Data to Knowledge

Data

• Collecting
• Organizing
• Validating
• Summarizing
• Interpreting
• Analyzing
• Decision-making

Information

• Publications
• DBtC™, Reports & Info Requests
• FN / AGNIS™

Knowledge

• Experience
• Interpretations
• Patterns
• Calculations
• Relationships
• Standardization

Observations

• Facts
Information Resources

CIBMTR® (Center for International Blood and Marrow Transplant Research) is a research collaboration between the National Marrow Donor Program/Be The Match and the Medical College of Wisconsin.

430,000 page views in 2015
Utilization of CIBMTR Web Presence and Other Information Resources, 01/01/2015 – 12/01/2015

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Survival Calculator – 1 year

- Calculates probability of 1 year survival after allogeneic transplantation for individual patients
- Uses model developed for annual center-specific outcomes analysis for US transplant centers
# 65 CIBMTR Presentations in 2015

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Peer-Reviewed Publications 2004-2015
Please note 2015 is not labeled. Includes IBMTR and NMDP publications prior to formation of CIBMTR.
It Takes a Village

CIBMTR PUBLICATIONS
by Federal U24 Grant Periods

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~40% of studies led by junior investigators (paired with senior investigators)

* First 3 years of grant period 2013-2017
CIBMTR Scientific Activities

Observational Research
- Clinical Outcomes
- Immunobiology
- Health Services
- Bioinformatics

Prospective Clinical Trial Support
- RCI BMT
- BMT CTN

Statistical Methodology

BMT CTN = Blood and Marrow Transplant Clinical Trials Network
RCI BMT = Resource for Clinical Investigations in Blood and Marrow Transplant
Working Committee Structure

- Acute Leukemia
- Autoimmune Diseases and Cellular Therapies
- Chronic Leukemia
- Donor Health and Safety
- Graft Sources and Manipulation
- Graft-vs-Host Disease
- Health Services and International Studies
- Immunobiology
- Infection and Immune Reconstitution
- Late Effects and Quality of Life
- Lymphoma
- Non-Malignant Marrow Disorders and Inborn Errors of Metabolism
- Pediatric Cancer
- Plasma Cell Disorders and Adult Solid Tumors
- Regimen-Related Toxicity and Supportive Care
CIBMTR Research

Observational Research
- Clinical Outcomes
- Immunobiology
- Health Services
- Bioinformatics
- RCI BMT
- BMT CTN

Prospective Clinical Trial Support

Statistical Methodology
Donor-Recipient Research Repository – 2015

• Unrelated Donor Repository
  – 33,919 Adult Recipient / Donor pairs
  – 3,579 Recipient / Cord pairs
  – 8,770 samples distributed to investigators during 2015

• Related Donor Repository
  – 71 centers participated in 2015
  – 4,545 Adult Recipient / Donor pairs

• More than 2 million aliquots stored
CIBMTR Research

Observational Research
- Clinical Outcomes
- Immunobiology
- Health Services

Prospective Clinical Trial Support
- RCI BMT
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Statistical Methodology
HSR Program Focus

• Center and physician practice patterns
• Disparities in access and outcomes
• Health economics research
• Quality of care
• Survivorship
CIBMTR Scientific Activities

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Statistical Methodology

BMT CTN = Blood and Marrow Transplant Clinical Trials Network
RCI BMT = Resource for Clinical Investigations in Blood and Marrow Transplant
Bioinformatics Research Goals

- Develop pipelines to analyze NGS typing data
- Investigate the role of genetic ancestry in transplantation
- Develop data standards and tools for making data portable
- Investigate HLA data from other countries
- Develop methods for HLA association studies
RCI BMT

• Study infrastructure in place for multicenter prospective Phase I/II trials and other studies requiring statistical and / or logistical support

• Offers statistical consultation, study, data and sample management, and regulatory expertise

• Not a funding mechanism
  – Provides multicenter infrastructure for PIs
  – Will assist PI seeking third party funding
Ongoing RCI BMT Studies

NMDP-sponsored IND studies

• Access and distribution of cord blood units by (10-CBA)
  – Opened to accrual October 2010
  – 2,757 enrolled
  – Open indefinitely to allow distribution and access to unlicensed cord units

• Filgrastim-mobilized PBSC for unrelated allogeneic transplant
  – Opened to accrual April 1996
  – Just under 25,000 URDs enrolled
  – Will close to accrual upon FDA licensure; another protocol will be opened to maintain access to unlicensed products

Accrual numbers as of Dec 2015
Ongoing RCI BMT Studies

Donor Studies

• Related donor safety and QOL (RDSafe)
  – 1,812 donors enrolled
  – One abstract accepted to 2015 BMT Tandem Meetings; One paper in press, others in preparation

• Long-term follow-up of unrelated donors after BM vs PBSC harvest (LTDFU)
  – 21,568 donors enrolled; closed to accrual October 2015
  – Follow-up continues through 2020

• Impact of donor statin therapy on GVHD after unrelated donor HCT (Statin)
  – 5,569 of 7,000 targeted donors enrolled

Accrual numbers as of Dec 2015
CIBMTR Research

Observational Research
- Clinical Outcomes
- Immunobiology
- Health Services
- Bioinformatics

Prospective Clinical Trial Support
- RCI BMT
- BMT CTN

Statistical Methodology
BMT CTN Centers
>125 centers have enrolled >8,600 patients since 2003

[Map of the United States with different colored dots indicating different types of centers.]

Legend:
- blue diamond = Core Centers
- orange triangle = PBMTC Centers
- green circle = Affiliate Centers
BMT CTN Trials Developed in Years 1-10

Total Subjects = 450, 1,050, 1,625, 2,150, 2,625, 3,050, 3,450, 4,300, 7,000, 7,500

2003 2004 2005 2006 2007 2008 2009 2010 2011

- 0901 Full vs. RIC - MDS/AML
- 0804 High Risk CLL
- 0902 Stress Mgmt
- 0805 Ph+ ALL
- 0803 HIV+ Lymphoma
- 0702 PIII Myeloma Follow-on
- 0801 P II/III GVHD Treatment
- 0802 PII AGVHD Treatment
- 0701 PII NST for NHL
- 0604 PII DCB-Adult
- 0603 PII Haplo-Adult
- 0601 PII Sickle Cell INST
- 0703 PIII HD (closed early)
- 0704 PIII MM maintenance
- 0502 PII NST for AML >60y
- 0402 PII GVHD prophylaxis
- 0501 III Single vs. Double CBT
- 0401 PII BEAM vs BEAM-Bexxar for Lymphoma
- 0302 PII AGVHD therapy
- 0303 PII T-depleted HCT for AML
- 0202 PII follicular NHL (closed early)
- 0201 PII Unrelated PBSC vs. Marrow
- 0101 PII Voris vs. Fluconazole
- 0102 PII Myeloma Tandem HCT

= Enrollment/follow-up complete
= Enrollment complete; ongoing F/U
= Enrollment on-going

PUBLICATIONS
★ Primary Outcome
★ Safety, Secondary Outcome, or Design
BMT CTN Trials Developed in Years 11-16

- 37 Trials Opened; 9 currently open
- 30 BMT CTN-led
- 7 NCI Group/PI-led (+)
- 3 to open soon (1201, 1401, 1501)
- 4 in development (1502, 1503, 1506, 1507)

Total Subjects = 3,450

PUBLICATIONS

- Star = Primary Outcome
- Star = Safety, Secondary Outcome, or Design

0903 Allo HIV-malignancy
1101 Haplo vs. Double Cord
1202 Biomarker Collection
1204 RIC for HLH
1302 BMT vs Chemo for MDS
1304 Early vs Late BMT for MM
1205 ETRIC
1102 BMT vs Chemo for MDS
07LT STaMINA Follow-Up
1203 PROGRESS I
1505 RECRUIT
1301

= Enrollment/follow-up complete

= Enrollment complete; ongoing F/U

= Enrollment on-going
CIBMTR Data and Clinical Trials

• Helps inform trial design, including likely accrual time frames
  – Almost all BMT CTN trials have met targeted accrual
• Complements clinical trial data
• Provides infrastructure for long-term follow-up
• Helps assess generalizability of clinical trial findings
CIBMTR Research

Observational Research
- Clinical Outcomes
- Immunobiology
- Health Services
- Bioinformatics

Prospective Clinical Trial Support
- RCI BMT
- BMT CTN

Statistical Methodology
Statistical Methodology Research Program

- Collaboration with MCW Division of Biostatistics since 1980
- Develops new statistical methodologies
- Ensures the statistical integrity of CIBMTR research activities
- Contributes to results in articles on HCT-related statistical issues for clinical audiences
- Supports Working Committee study investigators in developing scientific study protocols using CIBMTR data
Have These Studies Made A Difference?
The Value of CIBMTR: Identifying patients most likely to benefit from BMT

Probability of Overall Survival after HCT for AML not in Remission by CIBMTR Risk Score

Risk score = 0, N = 148, 42% (39-50)
Risk score = 1, N = 326, 27% (23-33%)
Risk score = 2, N = 342, 15% (11-19%)
Risk score = 3, N = 321, 6% (3-9%)

Duval, JCO, 2010
Outcomes after Transplantation of Cord Blood or Bone Marrow from Unrelated Donors in Adults with Leukemia

Mary J. Laughlin, M.D., Mary Eapen, M.B., B.S., Pablo Rubinstein, M.D., John E. Wagner, M.D., Mei-Jei Zhang, Ph.D., Richard E. Champlin, M.D., Cladd Stevens, M.D., Juliet N. Barker, M.D., Robert P. Gale, M.D., Ph.D., Hillard M. Lazarus, M.D., David I. Marks, M.D., Ph.D., Jon J. van Rood, M.D., Andromachi Scaradavou, M.D., and Mary M. Horowitz, M.D.
The Value of CIBMTR: Understanding the Influence of HLA

8/8 Match  7/8 Match  6/8 Match

S. Lee, et al.  *Blood* 2007 Showed impact of single allele mismatch at A, B, C and DRB1: *changed the paradigm for selecting adult donors*
Survival After Unrelated Donor Transplantation

Age <50 years, myeloablative conditioning, acute leukemia in remission or MDS

Odds of 1-year survival increased by 8% per year (95% CI, 7-9%) on average between 1990 and 2011.
Adjusted Probability of After Transplantation for AML, 2002-2006

- HLA-id Sib (N=624)
- 7/8 MUD (N=406)
- 8/8 MUD (N=1,193)
Numbers of Allogeneic HCTs in the US By Year and Donor Type

Excludes twins, related CB, 0-1 mism relatives

- HLA-id sibling
- Matched unrelated
- Something else
Haplo-Identical Transplantations
Hematologic Malignancy

Years of 0603/0604 trial

Number of Transplants

- Other centers
- CTN 0603 centers

Year 0603/0604 paper was published

BLOOD AND MARROW
TRANSPLANT
CLINICAL TRIALS NETWORK
Transplants from Donors Who Are Not HLA-identical Adults

![Graph showing transplants from different donors over years]

- Haplo
- Other Relative
- Single Cord
- Double Cord
- Related Cord
CIBMTR Data Facilitated Medicare Coverage for HCT for Myelodysplastic Syndromes

- Assessment of allogeneic HCT in Medicare beneficiaries with MDS (10 CMS-MDS-1)
  - Opened to accrual Dec 2010
  - 1294 patients enrolled
  - Allows reimbursement for BMT in Medicare patients

US Allogeneic Transplants for MDS in patients older than 65, 2005 - 2014
People Turn to CIBMTR to…

- **Get support when planning research**
  - Summarized data, statistical expertise, protocol development

- **Participate in CIBMTR research**
  - Propose a study, join a working committee, enroll patients

- **Access data & tissue samples for research**
  - Conduct research external to CIBMTR

- **Access reference materials**
  - Slides, guidelines, publications, education
What Makes Us So Valuable to the Transplant Community?

High quality, comprehensive data on hundreds of thousands of patients
DATA DOESN’T JUST HAPPEN

• Providing the data needed to do good clinical research is hard work
IBMTR – 1985
(year of first major NIH funding)

1970 - 1985
• 200 centers
• 1,000 transplants
• 35 publications

Mortimer M. Bortin, MD
Scientific Director

Al Rimm, PhD
Statistician

D’Etta Waldoch
Sharon Nell (now Meier)
Diane Knudsen
Data Management

Karen Witkowskki
Admin. Assistant
RECIPIENT INFORMATION

7. Name: ____________________________ 8. Male □ Female ☑

9. Date of Birth: ______________________ 10. Height: __________ Weight 55.2 kg
   Mo Day Yr

11. Race: Caucasian □ Negro □ Oriental □ Other □ specify
The Exception in 1985:
Forms Completed by a Data Professional!
What Is a Professional?

1. Person formally certified by a professional body of belonging to a specific profession by virtue of having completed a required course of studies and/or practice. And whose competence can usually be measured against an established set of standards.

2. Person who has achieved an acclaimed level of proficiency in a calling or trade.
What is a Data Professional?

Someone

• Who understands the importance of accurate, complete data and
  – Knows how to get it
  – Is committed to getting it (including developing the skills necessary to deal with recalcitrant clinicians)

• Who takes the time to understand the data because understanding increase accuracy

• Who understands that nature did not take our forms into account and that sometimes......
What is a Data Professional?

• We must squeeze square pegs into round holes – with our best judgment
What is a CIBMTR Data Professional?

• Someone committed to improving the lives of transplant patients through research and dissemination of knowledge.