Center for International Blood and Marrow Transplant Research

........Sharing Knowledge

Sharing Hope.............
Celebrating 10 Years
2004-2014
A Little History……

Reported Human Bone Marrow Transplants, 1958-1968

Bortin, Transplantation, 1970
Transplant Activity Worldwide 1968-2014

Autologous
Allogeneic

International Bone Marrow Transplant Registry Established
In the Beginning……

First Advisory Committee of the International Bone Marrow Transplant Registry

Don Thomas
George Mathe
George Santos
Bob Good
Fritz Bach

Mort Bortin

JJ Bergan, JL Fahey, Bob Levey, GN Rogentine
First 200 Patients Reported to IBMTR
1968-73, 11 Countries, 35 Centers
82 with Malignancy; 108 with SCID/Marrow Failure
Paper Forms

RECIPIENT INFORMATION

7. Name: ____________________________ 8. Male ☐ Female ☒

9. Date of Birth: ____________________
   Mo  Day  Yr
10. Height: _______________ Weight 55.2 kg

11. Race:  Caucasian ☐ Negro ☐ Oriental ☐ Other ☐
     specify
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
Diane Knudsen
Data Management

Karen Gurgul
Admin. Assistant
Transplant Activity Worldwide 1968-2014

- Autologous
- Allogeneic

IBMTR

Autologous Blood and Marrow Transplant Registry Established
IBMTR: A Few Key Contributions

- 1972-85 – Success of BMT in aplastic anemia, AML, CML, other diseases
- 1985-90 – Risk factors for graft failure, GVHD, organ toxicity, relapse
- 1990 – Graft versus leukemia effects without graft-versus-host disease
- 1994 – Advantage of BMT over chemotherapy for children with relapsed ALL
- 1997 – Solid tumors in long-term survivors
- 2002 – MDS after autotransplants
Allotransplants 1980-87: ~14,000 worldwide*; 78% for blood cancers; 98% related donors

Data on 10,000 of these transplants were reported to IBMTR
The First Unrelated Donor Transplants

• 1973 – Memorial Sloan-Kettering: 5 year old boy with severe immunodeficiency syndrome.
  – Donor found in Denmark through the Blood Bank at Rigshospitalet in Copenhagen.

• 1979 – Fred Hutchinson Cancer Center: First unrelated donor for leukemia

• USE LIMITED BY THE DIFFICULTY IN FINDING AN UNRELATED PERSON WITH SAME HLA-TYPE
The National Marrow Donor Program

1973  First unrelated donor transplants
1974  Anthony Nolan Bone Marrow Register
1979  Laura Graves: unrelated transplant for AML
1986  National Bone Marrow Donor Registry established
1987  Two transplants completed

Today:  World’s largest registry
        >12 million donors
        >200,000 CBUs
        >60,000 Transplants completed

The Success of NMDP must be coupled to 28 years of uninterrupted Federal support
Transplant Activity Worldwide 1968-2014

- IBMTR Established
- 1st NIH Funding for IBMTR
- NMDP Established
- Dennis Confer becomes medical director of NMDP
A Commitment to Research

The New England Journal of Medicine

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Volume 328 MARCH 4, 1993 Number 9

ANALYSIS OF 462 TRANSPLANTATIONS FROM UNRELATED DONORS FACILITATED BY THE NATIONAL MARROW DONOR PROGRAM


Abstract  Background and Methods. Allogeneic bone marrow transplantation is curative in a substantial number of patients with hematologic cancers, marrow-failure disorders, immunodeficiency syndromes, and certain metabolic diseases. Unfortunately, only 25 to 30 percent of potential recipients have HLA-identical siblings who can act as donors. In 1986 the National Marrow Donor Program was created in the United States to facilitate the graft-versus-host disease was 64 percent, and the probability of chronic graft-versus-host disease at one year was 55 percent. The rate of disease-free survival at two years among patients with leukemia and good prognostic factors was 40 percent and among patients at higher risk, 19 percent. Twenty-nine percent of the patients with aplastic anemia were alive at two years, and the rate of two-year disease-free survival among patients with myelo-
NMDP Research – A Few Key Contributions

• Multiple studies characterizing and categorizing HLA alleles
• Physical and psychosocial effects of donation on unrelated donors
• Algorithms predicting likelihood of finding a matched unrelated donor
• 2004 – Importance of matching at HLA-C
Two successful research organizations

NMDP

NMDP Research Operations

IBMTR/ABMTR

Medical College of Wisconsin
Transplant Activity Worldwide
1968-2014

- Transplants
- Autologous
- Allogeneic

- IBMTR Established
- 1st NIH Funding for IBMTR
- NMDP Established
- ABMTR Established
- BMT Clinical Trials Network Funded
BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK

- A national clinical trials network
  - Established Sept 2001
  - Re-competed July 2010
  - Funded through 2017

- Goals:
  - Evaluate promising BMT therapies and novel cell products in high quality multicenter studies
  - Improve safety and efficacy of BMT and cellular therapy
  - Enhance understanding of the biology and effectiveness of BMT
US Transplants on Cooperative Group Trials: Impact of the BMT CTN

- 80% of BMT CTN transplants – allotransplants vs 10% cooperative group
2004 Affiliation Agreement created a research collaboration between NMDP and the Medical College of Wisconsin.
Key Measures of Success

- Number of research proposals from the transplant community that are offered and accepted
- Number of Abstracts completed
- Number/Quality of Publications
- Number of Physicians/Transplant Centers participating in studies
A research collaboration between NMDP/Be The Match and Medical College of Wisconsin
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
CIBMTR 420,000 Cases Registered, 1985-2013 > 900 Publications

- 1st NIH Funding for IBMTR
- NMDP Established
- Descriptive
- Prognostic factors
- Technology Assessment
- Multicenter Clinical Trials
- Immunobiology*
- *NMDP Repository - Specimens for >33,000 donor-recipient pairs.
- Health Services Research
- QOL, Long-term Follow-up
- BMT CTN Funded
- NMDP & IBMTR join to form CIBMTR

Transplants

0 50000 100000 150000 200000 250000 300000 350000 400000 450000

Years

NMDP Repository - Specimens for >33,000 donor-recipient pairs.
Proposals to CIBMTR Working Committees
ASH and BMT Tandem Abstracts Presented

FY09 FY10 FY11 FY12 FY13 FY14

ASH
Tandem
Total

CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH
Peer-reviewed Publications, 2004-2014
9 trials this grant cycle
0903: Allo for HIV-malignancy
1101: Haplo vs Double Cord
1202: Biomarker collection
1204: RIC for HLH
1102: BMT vs Chemo for MDS

- 34 Trials Opened
  (8 currently open)
- 28 BMT CTN-led
- 6 NCI Group-led (+)
- 3 to open soon (1301, 1302, 1401)
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.

Graph showing the number of transplants for adults and children from 1992 to 2011, with a significant increase in the number of transplants over time.
The Value of CIBMTR: Understanding the Influence of HLA

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

Probability of Survival, %

HLA-id Sib (N=624)
7/8 MUD (N=406)
8/8 MUD (N=1,193)

Months
The Value of CIBMTR: Understanding Effect of Allele-level Matching at A, B, C, DRB1 in Cord Blood Transplantation

Likely to change the paradigm for cord selection

P < 0.001

Eapen, Blood, 2013
The Value of CIBMTR: Understanding Long-term Outcomes
The Value of CIBMTR: Understanding and Improving Health Care Delivery

Department of Health and Human Services

Advisory Council

Accrediting Organizations

HRSA/Division of Transplantation

Cord Blood Banks

Cord Blood Coordinating Center

Outcomes Database

Bone Marrow Coordinating Center

Infrastructure

Public Interface

= HRSA Contract Organizations

= Other New Organizations or Relationships

Blood Stem Cell Single Point of Access

Access Point for Stem Cell Sources

Patient Advocacy Services

Referring Physicians

Patients

Transplant Centers

Stem Cell Therapeutic and Research Act of 2005: C. W. Bill Young Program Structure
The Value of CIBMTR: Facilitating Transplants for Myelodysplasia (MDS)

- Most patients 65+ years have health insurance through Medicare which did not cover BMT for MDS

- August 2010: Medicare decided it would cover costs of BMT but ONLY if patients enrolled in an IRB-approved study that will provide CMS with data to determine the value of the procedure in the Medicare population

- CIBMTR leveraged existing infrastructure to propose a study using EXISTING data collection mechanisms and CIBMTR observational protocol (already IRB approved at US centers)
US Allogeneic Transplants for MDS in patients older than 65, 2005 - 2013
The Value of CIBMTR: Center-Specific Outcomes

<table>
<thead>
<tr>
<th>Transplant Center Code and Risk Score</th>
<th>Adjusted Survival</th>
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<tbody>
<tr>
<td>305 1</td>
<td>0%</td>
</tr>
<tr>
<td>310 1</td>
<td>10%</td>
</tr>
<tr>
<td>312 2</td>
<td>20%</td>
</tr>
<tr>
<td>407 5</td>
<td>30%</td>
</tr>
<tr>
<td>425 2</td>
<td>40%</td>
</tr>
<tr>
<td>436 2</td>
<td>50%</td>
</tr>
<tr>
<td>441 1</td>
<td>60%</td>
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<tr>
<td>443 2</td>
<td>70%</td>
</tr>
<tr>
<td>448 5</td>
<td>80%</td>
</tr>
<tr>
<td>481 4</td>
<td>90%</td>
</tr>
<tr>
<td>513 4</td>
<td>100%</td>
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<tr>
<td>580 5</td>
<td></td>
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<tr>
<td>582 5</td>
<td></td>
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<tr>
<td>589 4</td>
<td></td>
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<tr>
<td>593 4</td>
<td></td>
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Adjusted Survival Rates for Transplant Centers with 11–20 Transplants

Adjusted Survival with 95% Confidence Interval
Relative Rate of HCT in the US Caucasians vs. African-Americans

<table>
<thead>
<tr>
<th></th>
<th>Overall HCT</th>
<th>Autologous HCT</th>
<th>HLA-identical Sib HCT</th>
<th>Unrelated Donor HCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds Ratio</td>
<td>1.45</td>
<td>1.30</td>
<td>1.74</td>
<td>2.33</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.35</td>
<td>1.24</td>
<td>1.75</td>
<td>2.02</td>
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<tr>
<td>P-value</td>
<td>P&lt;0.0001</td>
<td>P&lt;0.0001</td>
<td>P&lt;0.0001</td>
<td>P&lt;0.0001</td>
</tr>
</tbody>
</table>

Joshua, Cancer, 2010
Key Measures of Success

- Number of research proposals from the transplant community that are offered and accepted – much higher
- Number of Abstracts completed - higher
- Number/Quality of Publications - higher
- Number of Physicians/Transplant Centers participating in studies - higher
### People Turn to CIBMTR to…

<table>
<thead>
<tr>
<th>Get support when planning research</th>
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<tbody>
<tr>
<td>• Summarized data, statistical expertise, protocol development</td>
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<table>
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<th>Participate in CIBMTR research</th>
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<td>• Propose a study, join a working committee, enroll patients</td>
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<table>
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<tr>
<th>Access data &amp; tissue samples for research</th>
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<tbody>
<tr>
<td>• Conduct research external to CIBMTR</td>
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<table>
<thead>
<tr>
<th>Access reference materials</th>
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<tbody>
<tr>
<td>• Slides, guidelines, publications, education</td>
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Here’s to the Next 10 Years!!!!

CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH