Transplant Activity Worldwide 1968-2012

- Autologous
- Allogeneic

Demise of HCT for Breast Cancer

Imatinib Approved

Transplants
US Allogeneic Transplants Reported to CIBMTR Annually, 1990-2011
Despite dramatic advances in the use and success of BMT over the past 3 decades,

- Only about half of patients needing a transplant actually get one
- Only about half of patients who get a transplant become long-term survivors
- About half of survivors have chronic health problems that continue for years after transplantation
To Address Issues of Access and Outcome – *we need data.*

• **Assessment** – identify the most important problems and most promising solutions

• **Analysis** - determine efficacy – overall and for specific subgroups; monitor long-term outcomes

• **Advancement** - Optimize treatment strategies/improve outcome

• **Allocation** of resources – research and clinical care
From Where Do We Get Data?

- Phase III Clinical Trials
- Phase II Trials
- Single institution case series/reports

HCT FACES SOME UNIQUE CHALLENGES IN GETTING GOOD DATA
The Challenge of Small Numbers: Annual Numbers of HCTs vs Numbers of Selected Cancers

- Breast
- Pancreas
- HCT
- Ovary
- Stomach
- Brain
- Liver
- Sarcomas
Individual transplant centers treat relatively few patients and these patients are heterogeneous in many factors that affect outcomes.
95% Confidence Intervals for Samples Drawn from a Population Receiving a Treatment Producing 50% Survival
From Where Can We Get Data?

- Phase III Clinical Trials
- Phase II Trials
- Single institution case series/reports
- Outcomes registries
What is an Outcomes Registry?

- Organized system that uses observational study methods to collect uniform data to evaluate specified outcomes for a population defined by a particular disease, condition or exposure that serves one or more predetermined scientific, clinical, or policy purposes – US Agency for Healthcare Research and Quality
  - Provides “real world” assessments of diseases and their treatments
OUTCOMES REGISTRIES – A Part of the HCT Community Since the “Beginning” and Continuing to Grow

IBMTR – 1970; EBMT - 1974
National: US, Japan, Germany, France, etc – 1980s-90s
International: Asian-Pacific BMT Group; Eastern Mediterranean BMT Group; Eurocord – 1990s-2000s

IBMTR Established

NMDP Established

BMT CTN Funded

CIBMTR Established

Transplants
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
180 staff including, 6 PhD statisticians, 14 MS statisticians, 11 MD-MS faculty; Active program of statistical methodology research specifically focused on transplant outcomes in addition to supporting clinical studies.
Number of Transplants Registered with CIBMTR, 1985-2011

Transplants

Years

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

'85 '87 '89 '91 '93 '95 '97 '99 '01 '03 '05 '07 '09 '11
The Value of Outcome Registries: 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
The Value of Outcome Registries: Clinical Evidence of Biologic Effects (e.g. graft versus tumor effects)

RELAPSE AFTER 2,254 HLA-IDENTICAL SIB TRANSPLANTS FOR EARLY LEUKEMIA

Horowitz, Blood, 1990
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.

Transplants of Umbilical-Cord Blood or Bone Marrow from Unrelated Donors in Adults with Acute Leukemia

Vanderson Rocha, M.D., Ph.D., Myriam Labopin, M.D., Guillermo Sanz, M.D., William Arcese, M.D., Rainer Schwerdtfeger, M.D., Alberto Bosi, M.D., Niels Jacobsen, M.D., Tapani Ruutu, M.D., Marcos de Lima, M.D., Jürgen Finke, M.D., Francesco Frassoni, M.D., and Eliane Gluckman, M.D., for the Acute Leukemia Working Party of European Blood and Marrow Transplant Group and the Eurocord—Netcord Registry*

Number of transplants


Adults  Children

0 50 100 150 200 250 300 350 400 450 500

CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH
The Value of Global Outcome Registries: Understanding the Influence of HLA

Adjusted Probability of Overall Survival for AML after Transplant, 2002-2006

- HLA-id Sib (N=624)
- 7/8 MUD (N=406)
- 8/8 MUD (N=1,193)
The Value of Global Outcome Registries: 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
The Value of Outcome Registries: Understanding Long-term Outcomes

Cumulative Incidence

- Cumulative Incidence
- Upper Confidence Limit
- Lower Confidence Limit

Years

Rizzo JD, Curtis RE et al CIBMTR 2008
The Value of Outcome Registries: Understanding Health Care Delivery

Department of Health and Human Services

Advisory Council

HRSA/Division of Transplantation

Accrediting Organizations

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 Outcome Registries: Center-Specific Outcomes

Adjusted Survival Rates for Transplant Centers with 11–20 Transplants

Adjusted Survival with 95% Confidence Interval

Adjusted Survival

Transplant Center Code and Risk Score
Relative Rate of HCT in the US Caucasians vs. African-Americans

<table>
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<th>Type</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Overall HCT</td>
<td>1.45</td>
<td>1.35-1.40</td>
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<td>Autologous HCT</td>
<td>1.30</td>
<td>1.24-1.35</td>
<td>&lt;0.0001</td>
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<td>HLA-identical Sib HCT</td>
<td>1.74</td>
<td>1.46-1.74</td>
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<td>Unrelated Donor HCT</td>
<td>2.33</td>
<td>2.02-2.33</td>
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Odds Ratio
Leveraged CIBMTR outcomes registry for trial design, enhancing accrual, assisting with data collection: Paradigm for increasing trial efficiency with real time population data.
Other CIBMTR Roles in BMT CTN

• Follow-up of BMT CTN patients through CIBMTR is allowing assessment of long-term outcomes of these trials – and some secondary analyses:
  – T-depleted vs non-T-depleted transplants
  – Long-term (5+ yrs) disease-free survival after transplants for myeloma, lymphoma
  – Assessment of second cancers
  – Comparison of transplant vs non-transplant therapy for MDS
## CIBMTR PUBLICATIONS

by U24-CA76518 Funding Period

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**BUT, MOST IMPORTANTLY, IT TAKES YOUR COMMITMENT TO PROVIDING THE HIGH QUALITY DATA THAT MAKES THESE STUDIES POSSIBLE**
Trends in Transplants by Recipient Age*

* Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma
Transplantation with Reduced Intensity Conditioning

Goal: Harness anti-cancer effect of donor cells without much of the toxicity of high doses of radiation and chemotherapy
Transplantation with Reduced Intensity Conditioning

>25 CIBMTR Studies of Reduced Intensity Conditioning since 2002

7 BMT CTN Trials of Reduced Intensity Conditioning since 2002

Provided important information:

- on the success of this approach
- on what regimens work best for specific diseases
Trends in Transplants by Recipient Age*

* Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma
Trends in Transplants
Recipient Age*

* Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma
What if Jonell’s Brother Had Not Been a Match?

10 CIBMTR Studies of Reduced Intensity Conditioning with Alternative Donors

>50 CIBMTR studies evaluating how best to select an alternative donor/graft source

8 BMT CTN Trials of Reduced Intensity Conditioning include alternative adult donors or cord blood
Allogeneic Transplants after Reduced Intensity Conditioning, by Donor Type, Registered with CIBMTR

Number of Transplants

Related  Unrelated PB/BM  Unrelated CB

*Data incomplete

* 2011*
Survival after Allogeneic Transplants for MDS, 2001-2011

By Disease Status and Donor Type

- Early, sibling donor (N=631)
- Advanced, sibling donor (N=1,116)
- Advanced, unrelated donor (N=1,432)
- Early, unrelated donor (N=795)

P < 0.001
What if Jonell had been 65 Instead of 62?

- Most patients 65+ years have health insurance through Medicare

- August 2010: Medicare decided it would only cover costs of BMT 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
Why? *For Life*

Jonell and her grandson
For Our Patients and Their Families