The Role of Outcomes Registries in Blood and Marrow Transplantation
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Cape Town, South Africa
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Worldwide Network for Blood and Marrow Transplantation

World Health Organization
A Little History……

Reported Human Bone Marrow Transplants, 1958-1968

Bortin, Transplantation, 1970
Transplant Activity Worldwide 1968-2014

International Bone Marrow Transplant Registry Established

Autologous vs. Allogeneic Transplant Activity Over Time

Transplants

'68 '70 '72 '74 '76 '78 '80 '82 '84 '86 '88 '90 '92 '94 '96 '98 '00 '02 '04 '06 '08 '10 '12
First Advisory Committee of the International Bone Marrow Transplant Registry

Don Thomas
George Mathe
George Santos
JJ Bergan, JL Fahey, Bob Levey, GN Rogentine
Dirk van Bekkum
Bob Good
Fritz Bach

In the Beginning……
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; LABMT - emerging

IBMTR Established
NMDP Established
NMDP & IBMTR join to form CIBMTR
First 200 Patients Reported to IBMTR
1968-73, 11 Countries, 35 Centers
82 with Malignancy; 108 with SCID/Marrow Failure
International Bone Marrow Transplant Registry - 1985

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
Key Contributions

Transplants Can Be Done Safely and Can Cure

- Bortin MM, Buckner CD. Major complications of marrow harvesting for transplantation. Experimental Hematology. 1983

Disease Specific Outcomes

- Bortin MM, Rimm AA. **Severe combined immunodeficiency disease:** characterization of the disease and results of transplantation. Transplantation Proceedings. 1977
- Bortin MM, Rimm AA. Allogeneic bone marrow transplantation for of 144 patients with **severe aplastic anemia**. JAMA. 1981
Key Contributions

Risk Factors

• Bortin MM, Rimm AA. **Factors influencing success and failure** of human marrow transplantation: a review from the International Bone Marrow Transplant Registry. Experimental Hematology Today. 1979

• Bortin MM, Kay HEM, Gale RP, Rimm AA. **Factors associated with interstitial pneumonitis** after bone-marrow transplantation for acute leukaemia. Lancet. 1982

• Bortin MM, Gale RP, Kay HEM, Rimm AA. Bone marrow transplantation for acute myelogenous leukemia. **Factors associated with early mortality**. JAMA. 1983

HLA Associations

• Rimm AA, Bortin MM. **HLA antigens and SCID**. Lancet. 1977

• D’Amaro JD, van Rood JJ, Rimm AA, Bortin MM. **HLA associations in Italian and non-Italian Caucasoid aplastic anaemia patients**. Tissue Antigens. 1983

• D’Amaro JD, van Rood JJ, Bach FH, Rimm AA, Bortin MM. **HLA C associations with acute leukaemia**. Lancet. 1984
Why are Large Registries Still Necessary? SMALL NUMBERS
Annual Numbers of HCTs vs Numbers of Selected Cancers in the US

- Breast
- Pancreas
- HCT
- Ovary
- Stomach
- Brain
- Liver
- Sarcomas
Distribution of Allotransplant Volumes Among 162 US Centers Reporting Data to CIBMTR in 2012

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

Sample Size, N

Probability, %

- 70% Publish
- 40% Don’t publish

Sample Size, N
CIBMTR 420,000 Cases Registered, 1985-2013 > 900 Publications

- 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.
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%)

The Value of Outcome Registries: Identifying patients most likely to benefit from BMT

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.

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*
The Value of Outcome Registries: Understanding the Influence of HLA

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

- HLA-id Sib (N=624)
- 7/8 MUD (N=406)
- 8/8 MUD (N=1,193)
Early and ongoing collaboration with cooperative groups to synergize and avoid duplication (intensified since 2005)

Total Subjects =

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<tr>
<td>Total</td>
<td>450</td>
<td>1,050</td>
<td>1,625</td>
<td>2,150</td>
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<td>3,050</td>
<td>3,450</td>
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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
1205: Patient-friendly Consent
1304: Early vs Late BMT for MM
1203: GVHD proph in RIC BMT
1301: CNI-free GVHD proph (soon)

PUBLICATIONS

- Primary Outcome
- Safety, Secondary Outcome, or Design
- Submitted, Primary Outcome

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

BMT CTN

ECOG

CALBG

SWOG

COG

BMT CTN Steering Committee

Developed Infrastructure

CIBMTR

EMMES

NMDP

DCC

BMT CTN

0901 PIII Vori vs. Fluconazole
0201 PIII Unrelated PBSC vs. Marrow
0102 PIII Myeloma Tandem HCT
0202 PIII follicular NHL (closed early)
0601 PIII Unrelated Tx for aplastic anemia
0603 PIII Unrelated Pb in Adult
0604 PIII DCB in Adult
0701 PII Sickle Cell NST
0703 PII HD
0704 PII ETN for IPS
0502 PII T-depleted HCT for AML
0303 PIII T-depleted HCT for AML
0302 PII AGVHD therapy
0401 PIII BEAM vs BEAM-Bexar for Lymphoma
0301 PII Unrelated Tx for aplastic anemia
0402 PII GVHD prophylaxis
0501 PII Single vs. Double CBT
0403 PII MM maintenance
0402 PII MM maintenance
0702 PII AGVHD Treatment
0805 PII AGVHD Treatment
Pregnancy outcomes after peripheral blood or bone marrow transplantation: a retrospective survey

N Salooja, R M Szydlo, G Socie, B Rio, R Chatterjee, P Ljungman, M T Van Lint, R Powles, G Jackson, M Hinterberger-Fischer, H J Kolb, J F Apperley, for the Late Effects Working Party of the European Group for Blood and Marrow Transplantation
The Value of Outcome Registries: Influencing National Public Policy

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

• August 2010: Medicare, in part because of existing CIBMTR data, 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 used its infrastructure to open a study using EXISTING data collection mechanisms (minimal additional work of transplant centers)
US Allogeneic Transplants for MDS in patients older than 65, 2005 - 2013
The Value of Global Outcome Registries: Understanding Trends in Use, Practice and Outcomes
The Value of Global Outcomes Registries: Understanding Macro-Economic Influences on Survival Globally

LEUKEMIA-FREE SURVIVAL

Years after allo-HSCT

Probability

1st percentile
2nd percentile
3rd percentile
4th percentile
5th percentile

Association of Human Development Index with rates and outcomes of hematopoietic stem cell transplantation for patients with acute leukemia (Giebel at al, Blood 2010)
Why Should a Registry be Considered When BMT is Just Developing in a Country or a Region?
Because to Develop a Therapy Effectively, We Need DATA

- **Assessment** – identify the most important problems and most promising solutions
- **Analysis** - determine efficacy – overall and for specific subgroups/regions; monitor long-term outcomes
- **Advancing best practices** - Optimize treatment strategies/improve outcome in the real world with real resource constraints
- **Allocation** of resources – research and clinical care
Data Are Needed:

• At the center level
  – Quality improvement
  – Understanding costs and resource needs (and making the case for them to hospital and local authorities)
  – Scientific study
• At the national level
  – Understanding access, costs and resource needs (and making the case for them)
  – To advance best practices
Data Are Needed:

• At the regional level
  – Facilitate research relevant to regional issues
  – The process of sharing data also creates opportunities for professional, educational and scientific collaboration in a community that faces similar challenges and affords the potential for sharing expertise and resources

• At the global level
  – To understand differences and commonalities in access, practice and outcomes
  – To advance the science and practice of HCT
  – To communicate with regulatory and funding bodies about needs
Because building a culture of evaluating and understanding outcomes is critical for
- effective quality management systems to improve patient care
- building an effective clinical research infrastructure to improve patient care

When numbers of transplants in individual centers and countries are small, sharing data allows examination of important issues with greater power.
• High prevalence of non-malignant hematopoietic disorders
  – Development and evaluation of regimens that ensure engraftment and minimize GVHD
  – Studies of BMT vs non-BMT therapy; HLA-id sib vs haplo or other alternative graft sources
• Extremely diverse distribution of HLA and other genetic determinants of outcomes – insight into permissive vs non-permissive matches/variations
• Examination of cost-effective approaches to both autologous and allogeneic BMT
Levels of Data Collection

Start small but plan for growth: What are the most important questions to answer in the next 3-5 years? 5-10 years? 10-15 years?

- Simple Activity Data
- Basic Outcome Data
- TED/MED-A level data
- Comprehensive Data (CRF/MED B)
Thank You

If you want to go fast, go alone; if you want to go far, go with others.