Blood and Marrow Transplantation

OptumHealth Education Spotlight Conference
October 22, 2014

BAYLOR University Medical Center at Dallas

WELCOME

- Structure of Baylor Sammons Blood and Marrow Transplant Program
- BMT Team
- BMT Accreditation/Program Facts
- Some BMT Basics
- National and International Trends
- Our Trends

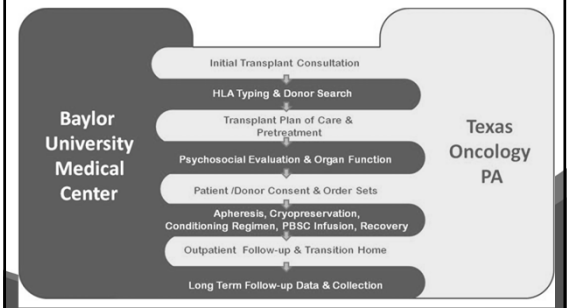
Program Facts

- Program initiated in 1983
- Is a partnership between Baylor University Medical Center and Texas Oncology PA
- Performs Autologous and Allogeneic (Related and Unrelated) Transplantation
- Performed 5000th Transplant in 2013
- Annually performs second most BMT in Texas

Program Overview

BUMC & TxO Coordination

BAYLOR Charles A. Sammons Cancer Center at Dallas — TEXAS ONCOLOGY More breakthroughs. More victories.



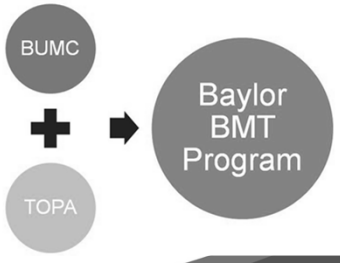
Program Overview

BUMC & TxO Coordination

BAYLOR Charles A. Sammons Cancer Center at Dallas — TEXAS ONCOLOGY More breakthroughs. More victories.

BUMC Responsibilities
Apheresis Collection Center
Inpatient Clinical
NMDP Transplant Center
Processing Facility
Program Administration
Quality Management & Compliance

TOPA Responsibilities
Outpatient Clinical
Professional Services (Physicians)
Quality Compliance



Program Physicians
Over 150 Years of Collective Transplant Experience

Carolina Escobar, MD
Attending physician

Edward Agura, MD
Program Director

Alan Miller, PhD MD
Chief of Oncology

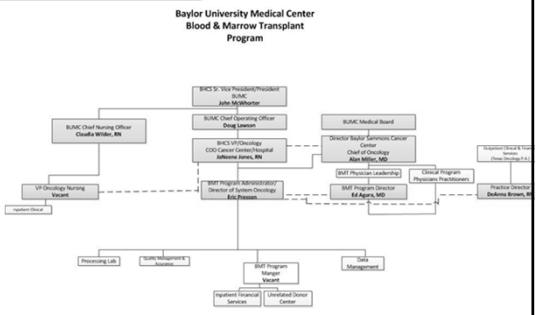
R. Brian Berryman, MD
Medical Director Outreach

Joseph Fay, MD
Attending physician

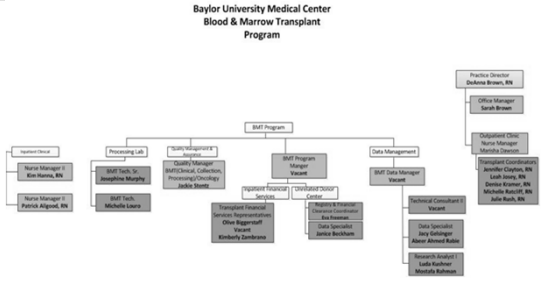
Luis Pinero, MD
Associate Program Director

Estil Vance, MD
Attending physician

Organizational Structure



Transplant Team



Foundation for the Accreditation of Cellular Therapy (FACT)

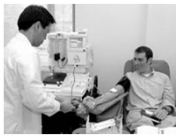
- Founded in 1996, FACT establishes standards for high quality medical and laboratory practice in cellular therapies. FACT is a non-profit corporation co-founded by the International Society for Cellular Therapy (ISCT) and the American Society of Blood and Marrow Transplantation (ASBMT) for the purposes of voluntary inspection and accreditation in the field of cellular therapy.
  - Components include:
    - Clinical Program
    - Apheresis Collection
    - Marrow Collection
    - Processing Laboratory
- The program at Baylor University Medical Center has been continually accredited since 1998. Most recent reaccreditation in 2014.

BMT Landmarks

- 1957 - Thomas
  - Safe Infusion of marrow into humans
- 1958 – Dausset
  - First HLA antigen described
- 1963 – Mathe
  - First succesful complete engraftment and survival over 1 year
  - Description of acute and chronic GVHD
- 1977 – Thomas
  - First 100 transplants for refractory acute leukemia reported from Seattle.
  - 13 long term survivors; 70% relapse

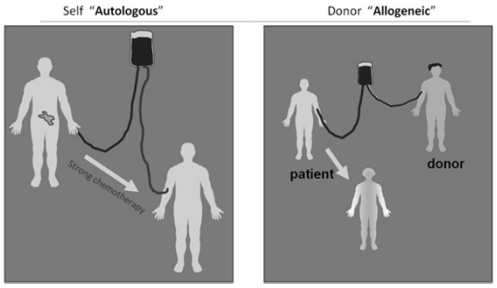
Blood and Marrow Transplantation

Types of Transplants



- Autologous
  - Uses patients own cells, stored prior to high dose therapy.
- Allogeneic Related
  - Family donor, usually sibling.
- Allogeneic Matched Unrelated
  - National Marrow Donor Program currently over 10.5 million volunteer donors in registry.
- Cord Blood

Types of Collection



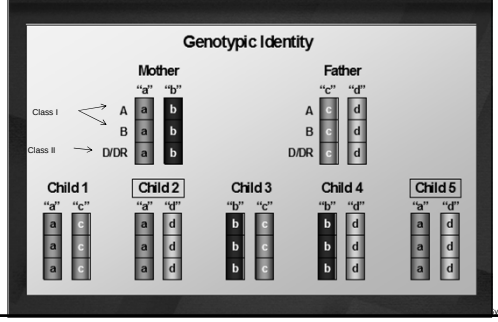
Allogeneic Blood and Marrow Transplantation

- Patient receives cells from a donor other than themselves.
  - Identical twin (syngeneic)
  - Matched sibling
  - Matched unrelated donor
  - Less than full match (family or unrelated)
    - Haplo-match
  - Cord blood
- Number of transplants continues to rise.
- For several diseases it remains the only curative option.

How Do We Choose a Donor

- In the early days of BMT almost all patients with a donor other than an identical twin had a severe and usually fatal complication called “secondary syndrome” marked by severe skin, gut and liver toxicity.
- It wasn’t until the mid to late 1960’s that an understanding of the Human Leukocyte Antigen (HLA) complex allowed us to select donors, and decrease the chances and severity of GVHD.

Allogeneic Bone Marrow Transplant (AlloBMT)
HLA-Matching

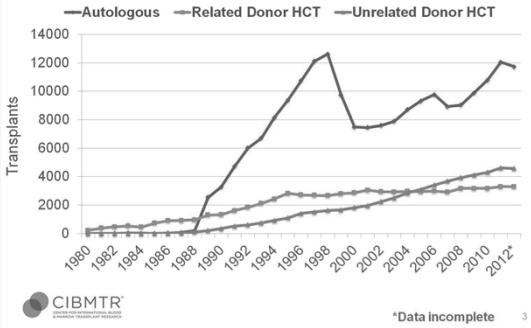


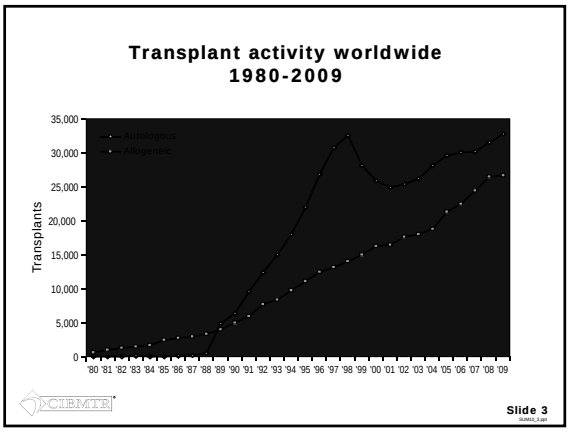
How Do We Type

- Classic – Through the mid-80’s typing was through serologic methods. Gave us “phenotype” information.
- Beginning in the mid-80’s we began to use more specific DNA based methods, giving us “genotype” information.
  - A phenotype such as HLA-A2 may comprise several genotypes, HLA-A*0201, *0205, *0213.
  - We have gone from the standard 6 antigen typing (2 each of HLA A,B and DR) to 10 antigen typing (HLA A, B, DR, DQ and C)
    - This has greatly improved results in unrelated transplants

NATIONAL AND INTERNATIONAL TRENDS AND OUTCOMES IN BLOOD AND MARROW TRANSPLANTATION

Transplant Activity in the US




Transplant activity worldwide
1980-2009
Transplants
35,000
30,000
25,000
20,000
15,000
10,000
5,000
0
'80 '81 '82 '83 '84 '85 '86 '87 '88 '89 '90 '91 '92 '93 '94 '95 '96 '97 '98 '99 '00 '01 '02 '03 '04 '05 '06 '07 '08 '09
CIBMTR
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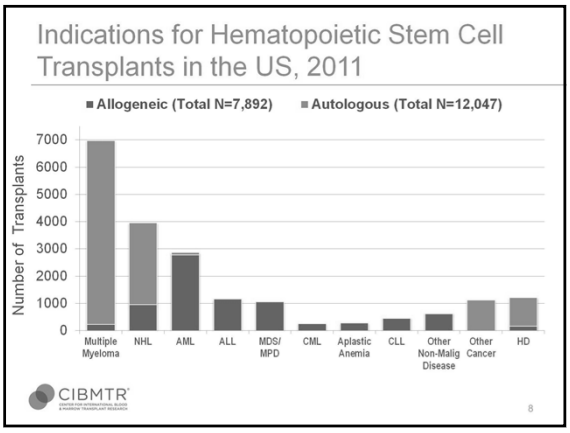
Indications for Hematopoietic Stem Cell Transplants in the US, 2011
Allogeneic (Total N=7,892)
Autologous (Total N=12,047)
Number of Transplants
7000
6000
5000
4000
3000
2000
1000
0
Multiple Myeloma
NHL
AML
ALL
MDS/ MPD
CML
Aplastic Anemia
CLL
Other Non-Malig Disease
Other Cancer
HD
CIBMTR
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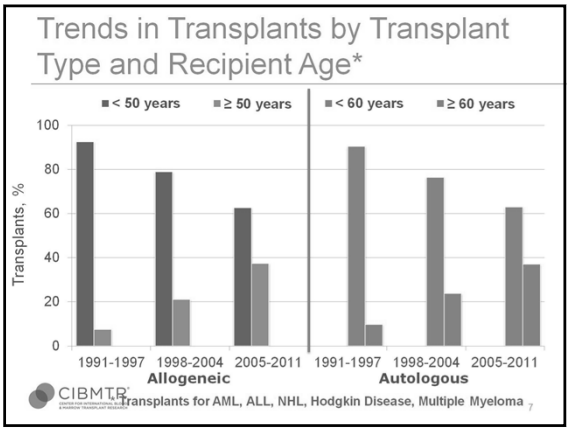
Trends in Transplants by Transplant Type and Recipient Age*
< 50 years
≥ 50 years
< 60 years
≥ 60 years
Transplants, %
100
80
60
40
20
0
1991-1997
1998-2004
2005-2011
Allogeneic
Autologous
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Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma
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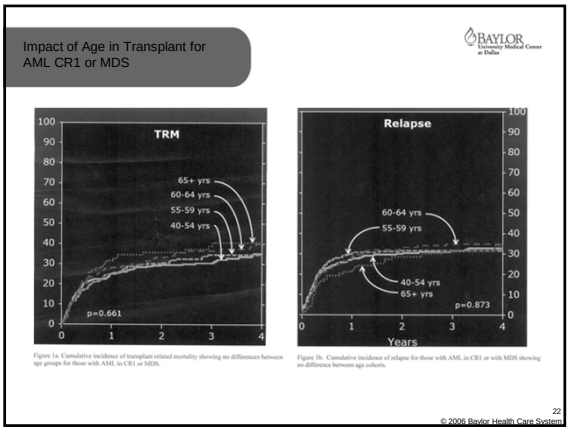
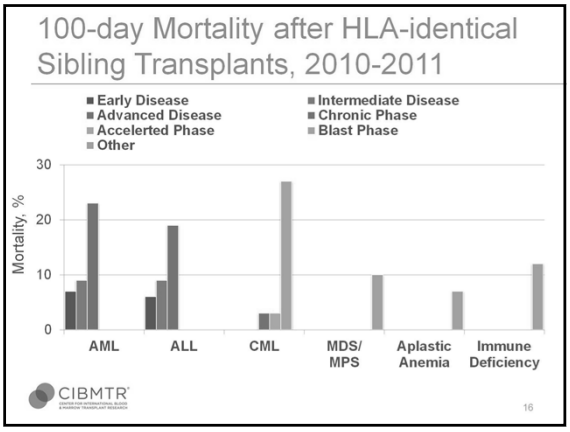

Impact of Age in Transplant for AML CR1 or MDS
BAYLOR
TRM
65+ yrs
60-64 yrs
55-59 yrs
40-54 yrs
p=0.661
Relapse
60-64 yrs
55-59 yrs
40-54 yrs
65+ yrs
p=0.873
Years
22
© 2006 Baylor Health Care System


100-day Mortality after HLA-identical Sibling Transplants, 2010-2011
Early Disease
Advanced Disease
Accelerted Phase
Other
Intermediate Disease
Chronic Phase
Blast Phase
Mortality, %
30
20
10
0
AML
ALL
CML
MDS/ MPS
Aplastic Anemia
Immune Deficiency
CIBMTR
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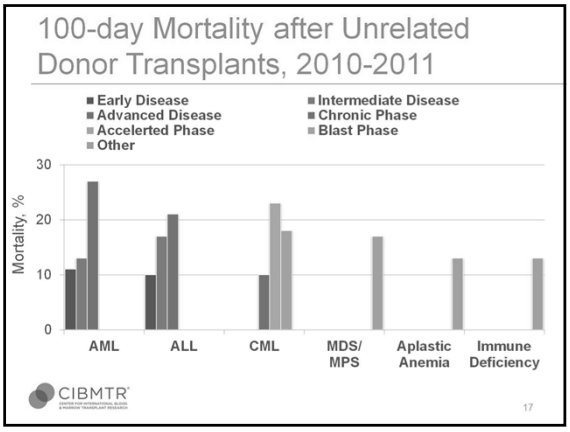
100-day Mortality after Unrelated Donor Transplants, 2010-2011
Early Disease
Advanced Disease
Accelerted Phase
Other
Intermediate Disease
Chronic Phase
Blast Phase
Mortality, %
30
20
10
0
AML
ALL
CML
MDS/ MPS
Aplastic Anemia
Immune Deficiency
CIBMTR
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Rationale for Non-myeloablative Transplantation

- Graft v. Malignancy plays a major role in the curative benefits of allogeneic transplant.
- The combined toxicity of the preparative regimen and GVHD contribute to the overall morbidity and mortality of allogeneic transplantation.
- Attempts to decrease toxicity by decreasing GVHD have resulted in increased relapse.
- Less intense preparative regimens may decrease overall toxicity while allowing engraftment.

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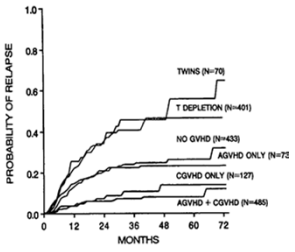
Probability of Leukemic Relapse



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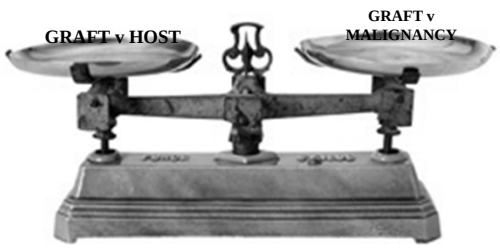

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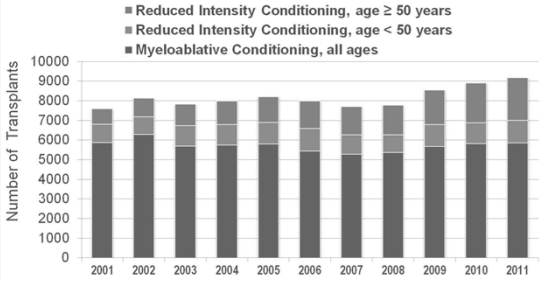
Allogeneic Transplants Registered with the CIBMTR



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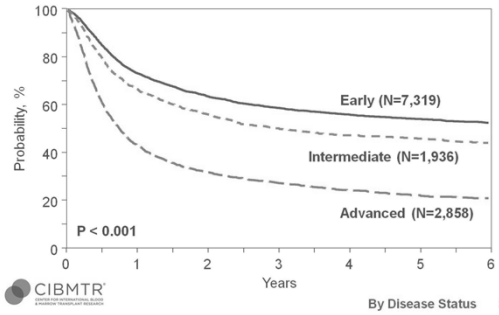
by Conditioning Regimen Intensity & Age 21

Survival after HLA-identical Sibling Donor Transplants for AML, 2001-2011



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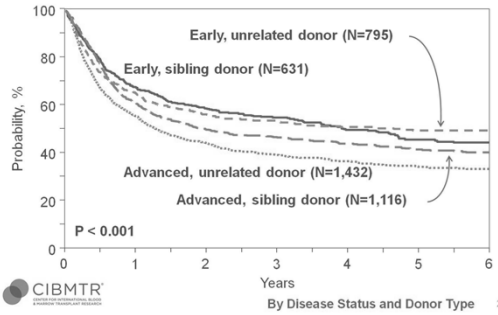
By Disease Status 24

Survival after Allogeneic Transplants for MDS, 2001-2011



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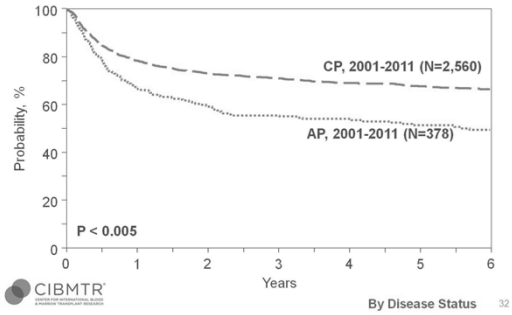
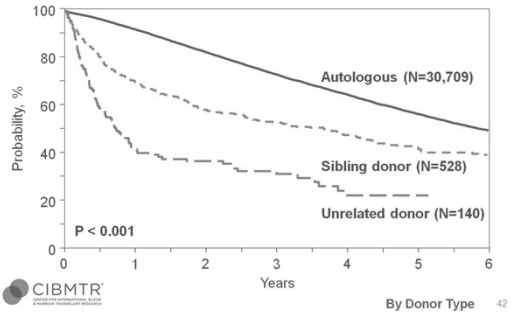
By Disease Status and Donor Type 27

Survival after HLA-identical Sibling Donor Transplants for CML, 2001-2011



By Disease Status 32

Survival after Transplants for Multiple Myeloma, 2001-2011



By Donor Type 42

Challenges in Long Term Survivors

- In general 50% of all patients receiving allogeneic bone marrow transplants will survive 5 years or more and be at risk for long term complications including:
  - Chronic Graft-vs-Host Disease (cGVHD)
  - Second Malignancies
  - Infections
  - Endocrine Deficiencies (Thyroid, Adrenal, Gonadal)
  - Skeletal (Aseptic Necrosis, Osteopenia)
  - Pulmonary (Bronchiolitis obliterans, interstitial fibrosis)
  - Renal (Nephropathy)
  - Ophthalmologic (Cataracts)
  - Growth (Impaired in children undergoing BMT)

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PROGRAM TRENDS

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Recent Volume Trends

- Changing oncology treatment practices contributed to recent declining volumes
  - New chemotherapy products and protocols (more options available to primary oncologist
  - Reduced and delayed referrals by oncologists for transplant
- Increased referrals and transplant volumes in FY14
  - Streamlined clinic intake process
  - Increased focus on program growth (via outreach clinics, referring physician education)

Inpatient & Outpatient Transplants

By Fiscal Year	2011	2012	2013	2014
Auto	128	119	114	82
Allo-related	46	37	28	46
Allo-MUD	76	78	56	93
Totals	250	234	198	221
Referral Totals	541	476	452	557

Source: Baylor BMT Data Team
FY14: July 2013 – January 2014 Annualized

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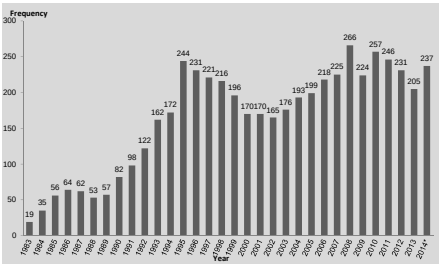
Transplants by Year

NUMBER OF BMT (AUTO & ALLO) TRANSPLANTS by CALENDAR YEAR (2014 annualized.



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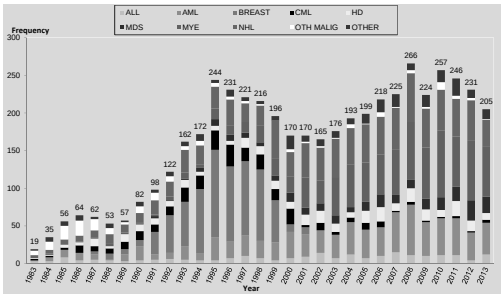
Transplant Volume by Diagnosis



Transplants by Cell Source