C. W. Bill Young Cell Transplantation Program

STEM CELL THERAPEUTIC OUTCOMES DATABASE

CIBMTR CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

BUSOS_1.ppt

Stem Cell Therapeutic and Research Act of 2005 (P.L. 109-129)

- Authorizing law, preceded by efforts to:
  - Enact authorizing legislation for collection and distribution of cord blood units (CBU)
  - Re-authorize the National Bone Marrow Donor Registry (managed by NMDP)
- Appropriations for a National Cord Blood Stem Cell Bank Program, FY 2004-2006
  - 2004 Conference Report required an Institute of Medicine (IOM) study; report issued April 14, 2005
  - Appropriations totaled nearly $24 million ($1 million specified for IOM study)

CIBMTR

Stem Cell Therapeutic and Research Act of 2005 (P.L. 109-129)

- Signed December 20, 2005
- Aims are to increase:
  - Number of unrelated donor transplants
  - Public inventory of high quality CBU from diverse populations
  - Number of CBU available for research
- Opportunity to help more patients obtain transplants, other therapy

CIBMTR

CW Bill Young Cell Transplantation Program

- Established by legislation passed in 2005
- Successor to National Bone Marrow Donor Registry (contract held by NMDP since 1987)
- 5 components:
  - Bone Marrow Coordinating Center
  - Cord Blood Coordinating Center
  - Single Point of Access/Office of Patient Advocacy
  - Cord Blood Banks
  - Stem Cell Therapeutic Outcomes Database

CIBMTR

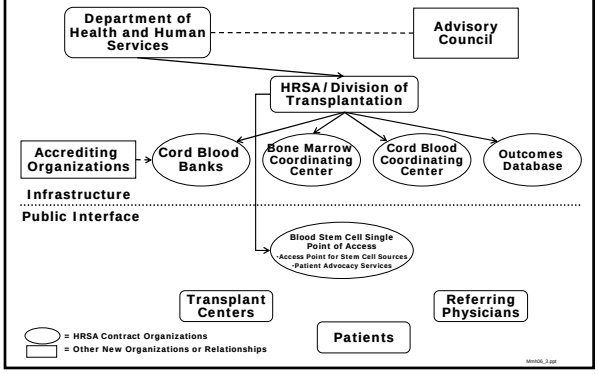
NAMD4_8.ppt

HRSA's Implementation Approach

- Guided by three principles:
  - Single Point of Access for patients and physicians to all sources of blood stem cells
  - Collection of high-quality diverse CBU, expeditiously
  - Complete data on clinical outcomes of transplants

CIBMTR

Stem Cell Therapeutic and Research Act of 2005: C. W. Bill Young Program Structure



MAN06_3.ppt

Coordinating Centers

- Provide access to adult donors and cord blood units
  - Recruitment/HLA typing
  - Inventory management
  - Patient-specific searches
  - Facilitate graft collection, transport
- Some operational research

CIBMTR

NAMD4_8.ppt

SPA/OPA

- Allow patients to identify potentially suitable adult donors and cord blood units through a single search
- Support patients and families through the search and transplantation process

CIBMTR

NAMD4_8.ppt

Cord Blood Banks

- Collect, store and distribute cord blood for transplantation
- Relationships with hospitals/obstetricians

CIBMTR

NAMD4_8.ppt

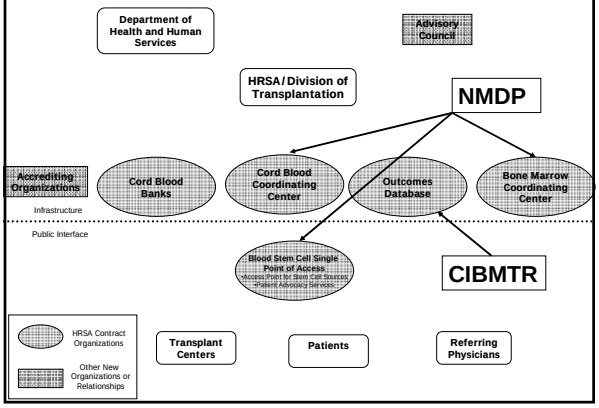
SCTOD

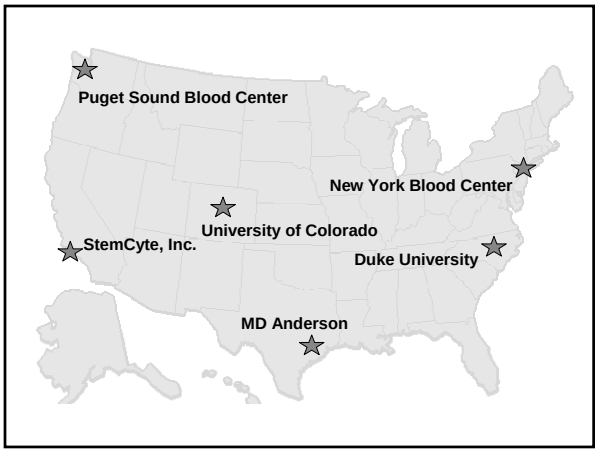
- Collect data on outcomes of all *allogeneic* hematopoietic stem cell transplants in the US
- Collect data on outcomes of all transplants facilitated by the CW Bill Young Program – even if transplant done outside the US
- Include alternative uses of hematopoietic stem cells
- Core set of data – sufficient to allow center-specific survival and other analyses
  - Subset of Report Form data
- Establish related donor-reicpient specimen repository

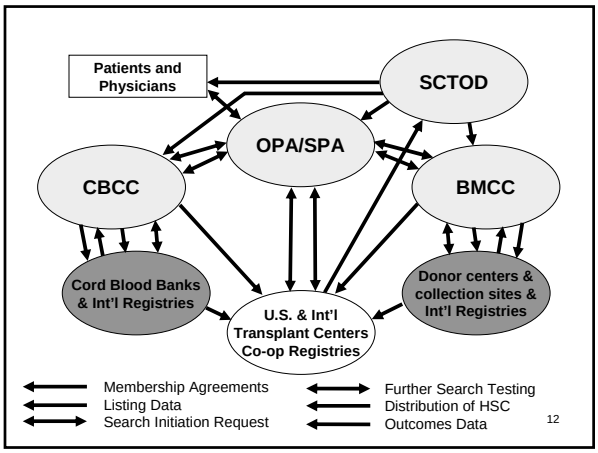
CIBMTR

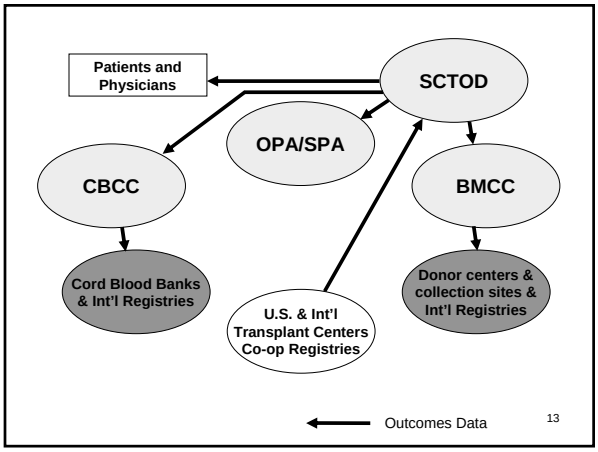
NAMD4_8.ppt

C.W. Bill Young Cell Transplantation Program: *Contracting Structure*









Under the Contract, the CIBMTR, operating as the SCTOD, will-

- **Collect data on *ALL* allogeneic hematopoietic cell transplants with a recipient or donor in the U.S.**
- **Collect data on other cellular therapies, too**
- **Establish related donor-recipient repository**
- **Establish electronic data capture systems**
- **Disseminate data within the Program**
- **Make data publicly available**
- **Perform and publish center-specific outcomes for U.S. transplant centers**
- **Perform analyses of optimal size for the adult donor registry and cord blood unit inventory**
- **Conduct and support other research using the data collected under the contract**

CIBMTR

HOW DOES THIS RELATE TO WHAT WE ARE ALREADY DOING?

CIBMTR

CENTER FOR INTERNATIONAL BLOOD AND MARROW TRANSPLANT RESEARCH

- Established July 2004
- A research affiliation between the IBMTR and the NMDP to support clinical research in BMT & related fields
- Clinical Research includes
  - Observational Studies (including immunobiologic correlates)
  - Clinical Trials
  - Health Services Research
  - Statistical Methodology

CIBMTR

IBMTR

- Established in 1972 to monitor and study outcomes of bone marrow transplants
- Maintains a database of clinical information on recipients of autologous and allogeneic hematopoietic stem cell transplants in ~450 centers in 47 countries
- Collates basis data set on all patients in member centers (registration) and comprehensive data (research) on a subset
- Provides scientific and statistical support for analyzing those data

CIBMTR

NMDP

- 1986 – U.S. government appropriated funds to establish the National Bone Marrow Donor Registry (Donor Panel)
- 1988 – U.S. Organ Transplant Amendments Act – mandated collecting outcome data (Recipient Registry); also collects donor outcomes
- ~150 transplant centers and 90 donor centers
- Collects comprehensive data on all transplants it facilitates in member centers
- Repository with matched recipient/donor blood samples

CIBMTR

DBV06_04.ppt

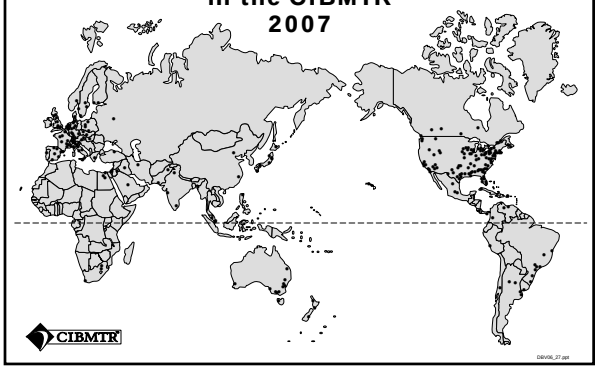
CIBMTR – 2 Campuses

- Milwaukee – Medical College of Wisconsin
  - 5 MDs; 5 PhDs and 6 MS statisticians; 37 additional research and administrative staff
- Minneapolis – NMDP Coordinating Center
  - 3 MDs; 4 MS statisticians; 9 additional research and administrative staff
- Close relationship with NMDP Operations staff who provide support in multiple areas – increasing interaction with new contract

CIBMTR

NAMD4_8.ppt

Location of Centers Participating in the CIBMTR 2007



CIBMTR

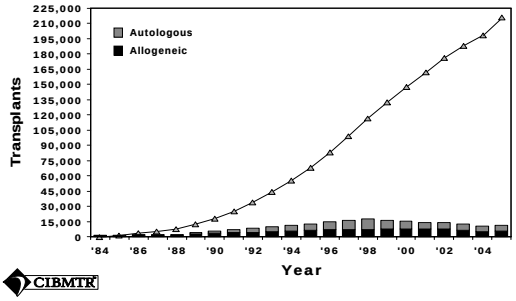
DBV06_07.ppt

CIBMTR DATA COLLECTION

- Basic ("essential") data
  - All patients
  - Transplant Essential Data (TED) / EBMT MED-A
- Comprehensive data
  - Subset of patients
  - CIBMTR: Report Form collected prospectively on patients identified at time of TED submission
  - NMDP:(Slightly different) Report Form collected on all patients receiving transplants facilitated by NMDP

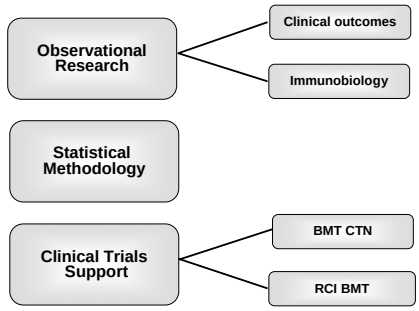
CIBMTR

CIBMTR
Number of Cases Registered, 1984-2005

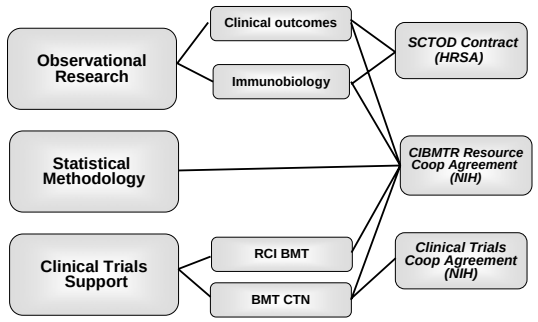


CIBMTR

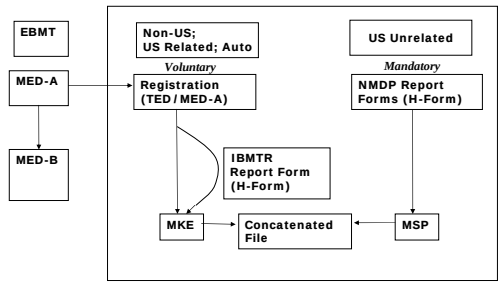
THREE MAIN AREAS OF SCIENTIFIC ACTIVITY



THREE MAIN AREAS OF SCIENTIFIC ACTIVITY FUNDED BY FEDERAL GRANTS/CONTRACTS

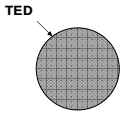


Current Data Flow



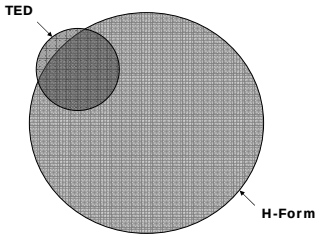
CIBMTR

CURRENT DATA COLLECTION



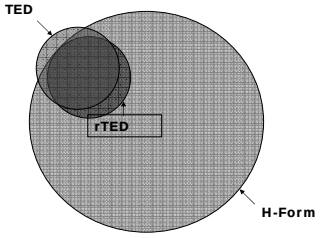
CIBMTR

CURRENT DATA COLLECTION



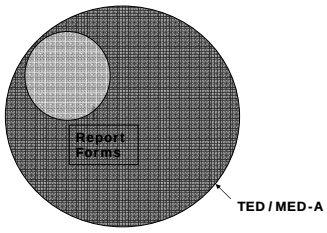
CIBMTR

CURRENT DATA COLLECTION



CIBMTR

CURRENT DATA COLLECTION – numbers of cases collected



CIBMTR

CHALLENGE

Accommodate the many demands for data in a way that meets the needs of SCTOD and all other users, ensures quality, is maximally efficient and minimizes demands on transplant centers

CIBMTR

TED / MED-A not sufficient to meet needs of the SCTOD

- Center-specific analyses mandated
  - Assess quality of transplant centers
  - Essential to have sufficient data to adjust for patient mix
    - Measures of clinical status and co-morbidities
- Product information essential for C.W. Bill Young Program to assess quality of operations (graft procurement, processing, storage, transport)

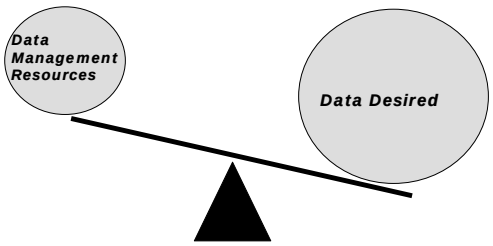
CIBMTR

CIBMTR REPORT FORM NOT APPROPRIATE FOR MANDATORY SCTOD REPORTING

- Detailed patient, disease, transplant outcomes
  - Up to 70 pages
  - 6-10 hours to complete
- SCTOD forms require approval from US Office of Management and Budget
  - Data collection burden must be justified

CIBMTR

Need to Balance….



CIBMTR

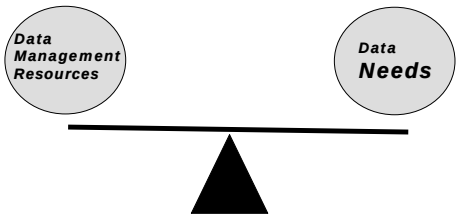
CHALLENGE

Accommodate the many demands for data in a way that meets the needs of all users, ensures quality, is maximally efficient and minimizes demands on transplant centers

- **Meet the needs of the SCTOD**
- **Have detailed data on a sufficient number of patients data for research**
- **Not drive people crazy (crazier)**

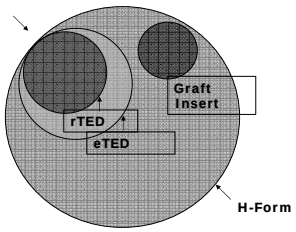
CIBMTR

Need to Balance….



CIBMTR

DATA COLLECTION FOR SCTOD AND FOR COMPREHENSIVE RESEARCH



CIBMTR

Data Needs for Cord Blood Banks

We must figure out the management of -

- Significant adverse events – Real time
- Other adverse events - Periodic
- "Real-time" data that're not significant AEs
- Periodic data reports
  - ?monthly, bimonthly, quarterly

CIBMTR

NAMD4_8.ppt

INTERNATIONAL PERSPECTIVE

- BMT as a therapy is unique in *requiring* a high level of international cooperation especially for unrelated donor transplants
- US government is not unique in its interest in collecting data on HCT
  - Several countries already have mandatory reporting
  - Variability in data collected and data used

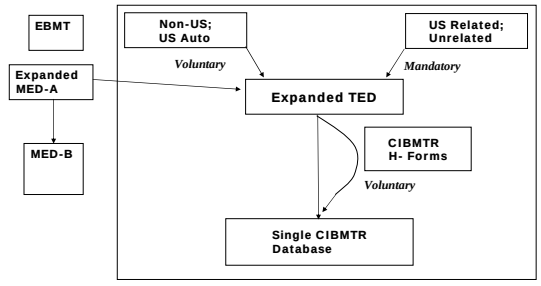
CIBMTR

INTERNATIONAL CONSENSUS ON COMMON DATA SET

- Facilitate collaboration
- Inform policy makers as to the appropriate level of data collection
- Minimize burden to transplant centers since data entered in one system could be transferred to another – enter once, use often

CIBMTR

Future Data Flow?



CIBMTR

Meeting the Challenge – Collecting Data on all Allografts

- Data Working Group – internal group with representatives from SCTOD, Coordinating Centers, SPA/OPA, CB Banks addressing Program needs, logistics
  - Meets at ~6 wk intervals
  - Subcommittees addressing specific aspects of the Program
- Data Advisory Group – broad participation of data users/suppliers

CIBMTR

Data Advisory Group

- ASBMT
- BMT CTN
- EBMT
- APBMT
- PACT
- NIH
- HRSA
- FDA
- FACT
- Transplant Centers
  - Physicians
  - Data managers
- CB Banks
- Donor Centers
- Patients/families

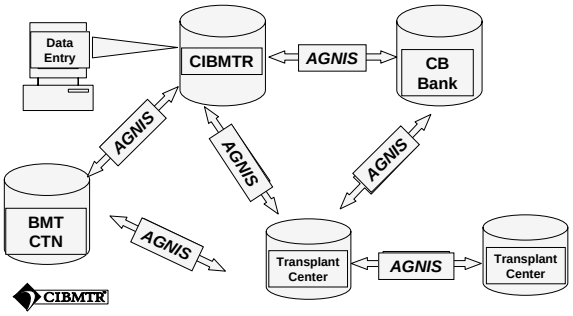
CIBMTR

Meeting the Challenge – Electronic Data Collection (EDC) Systems

- Goal: support systems that are already operating well; replace inefficient paper systems to enhance speed and accuracy
  - Continue to accept StemSoft data
  - Continue to accept EBMT eletronic TED data
- Short-term solution: FormsNet2.0, a web-based EDC, designed to capture TED and Report Forms – July 2007
- Long-term solution: AGNIS

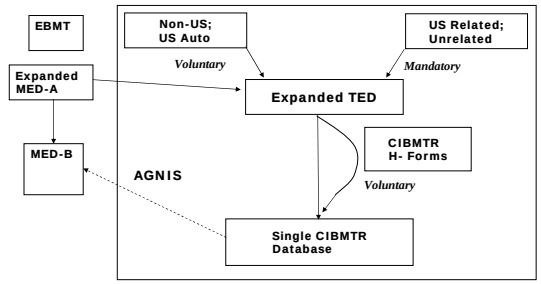
CIBMTR

AGNIS: A Growable Network Information System



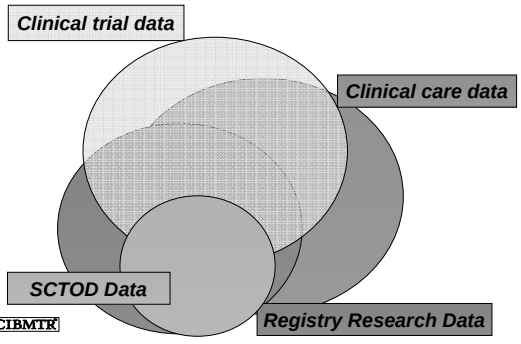
CIBMTR

Future Data Flow?



CIBMTR

MULTIPLE DATA USES –
Collect once, use often
From the Transplant Center Perspective



CIBMTR

Initiatives in Data Management: Common Data Elements and AGNIS

- AGNIS: A Growable Network Information System
  - Funded by NIH Roadmap
- BMT CTN – Children's Oncology Group Data Exchange
  - Simplifies access for Pediatric BMT Group
  - Funded by NIH Roadmap and NHLBI
- These projects leverage the resources of NCI's caBIG (Cancer Bioinformatics Grid)

CIBMTR

Meeting the Challenge – Ensuring Sufficient Data for Research

- Revise and harmonize IBMTR and NMDP forms – single form to be available in July
  - No duplicate reporting
  - Single audit/quality improvement program
- Re-examine selection algorithms for comprehensive data forms
  - May not need to submit full form for every unrelated donor transplant

CIBMTR

PGM02_2.ppt

Meeting the Challenge – Making Data available

- Websites – CIBMTR, NMDP, new C.W. Bill Young Program website
  - Increased emphasis on providing outcomes data
- Information services – access to more detailed data
- Working Committees – access to research data and statistical expertise

CIBMTR

PGM02_2.ppt

Meeting the Challenge: Related Donor-Recipient Specimen Repository

- Will build on experience with NMDP Unrelated Research Repository
- Implementation plan for collection of related pairs
  - Sample type
  - Center Participation
  - Data collection
  - Sample access and distribution
  - Timeline

CIBMTR

NMDP Research Repository

- Established in 1988
  - Pretransplant blood specimens from all unrelated stem cell transplants facilitated by NMDP (~215 recipients, ~230 donors per month)
  - Relocated from San Francisco, California to Minneapolis in Fall of 2006
- Protocol based on survey of investigators to establish sample collection and storage priorities in 2004
  - Repository receives 20ml of whole blood from Donors and Recipients; any source of DNA from infused CBUs

CIBMTR

NMDP Repository Inventory Summary

- Specimen Type Summary
  - Donor and Recipient pairs — N = 12,973
  - Unique Donors — N = 21,324
  - Unique Recipients — N = 18,540
  - Unique CBU — N = 198
- Sample Type Summary
  - PBMCs — N = 162,893 vials
  - Granulocytes — N = 63,775 vials
  - Whole Blood — N = 141,668 vials
  - Whole Blood in DMSO — N = 47,206 vials
  - Filter Cards — N = 67,653 cards
  - Serum — N = 38,260 vials
  - B-LCLs — N = 138,954 vials

CIBMTR

NMDP Repository Usage

- Support unrelated hematopoietic stem cell transplant research
  - Retrospective transplant outcome analysis
    - Comprehensive collection of clinical outcome data
    - Pair clinical data with stored sample testing
  - Example: NMDP Donor/Recipient Pair project
    - Allele level HLA testing at 11 loci
    - 9,000 transplant pairs tested, since 1996
  - Over 15 additional studies approved or in process
- Shipped over 9,500 samples in 2005

CIBMTR

Related Donor-Recipient Repository Specimen Collection Priorities

- Minimal burden to patient and donor
  - Reasonable volumes for pediatric and adult patients
- Specimen material suitable for current and future DNA based assay systems
- Storage procedures consistent with core competencies of NMDP Research Repository

CIBMTR

SCTOD Repository Steering Committee Recommendation

- 10 ml from each donor and recipient
  - Single blood tube
- Processing and storage
  - 1 filter paper card, 5 – 75ul spots
  - 5 – 1ml aliquots at -80ºC
  - 4 – 1ml aliquots in LN
    - 3 – 1ml aliquots at NMDP
    - 1 – 1ml aliquot stored off site in Master Repository
- Flexible processing and storage protocols to accommodate short draws

CIBMTR

Center Participation

- Centers will be recruited to generate a representative sample of related allogeneic transplant activity in the U.S.
  - Equivalent numbers as is currently collected for unrelated donor repository
- Collection limited to U.S. centers that currently participate in the NMDP Unrelated Research Sample Repository
- Center selection analysis in progress
  - QOL and Long Term Follow-up

CIBMTR

Performance and Reimbursement

- Performance monitoring
  - Modeled on NMDP CPI program
    - All NMDP centers must achieve 75% submission
- Reimbursed $35/sample and $10/valid excuse
    - Excuses: Refuse to participate or medical deferral

CIBMTR

Case Selection

- Collect all consecutive related allogeneic transplant cases from select centers
  - Standard collection protocol
- Paired pre-transplant samples only

CIBMTR

Data Collection

- Collect SCTOD Transplant Essential Data (TED) form and Product Insert (from harmonized Form)
- Ensure data on SCTOD TED is sufficient for studies utilizing research samples

CIBMTR

Sample Access and Distribution

- Samples released for studies through the CIBMTR Working Committee process
- Inventory summaries and query tool to be available on program .gov Web site

CIBMTR

Timeline

- February 2007: Submit final project plan to HRSA for approval.
- March 2007 (pending HRSA approval): Submit protocol and consent changes to NMDP/MCW IRBs
- April 2007: Release protocol and consents for approval at local IRBs
- Summer 2007: Implement specimen collection at approved sites

CIBMTR

Under the Contract, the CIBMTR, operating as the SCTOD, will-

- Collect data on *ALL* allogeneic hematopoietic cell transplants with a recipient or donor in the U.S.
- Collect data on other cellular therapies, too
- Establish related donor-recipient repository
- Establish electronic data capture systems
- Disseminate data within the Program
- Make data publicly available
- Perform and publish center-specific outcomes for U.S. transplant centers
- Perform analyses of optimal size for the adult donor registry and cord blood unit inventory
- Conduct and support other research using the data collected under the contract

CIBMTR

CIBMTR PRODUCTIVITY

- >400 Centers registered >14,000 transplants in 2005
- 17 Working Committees
  - 196 Approved Studies (19 involving specimens from repository)
- American Society of Hematology
  - 2005: 9 studies presented
  - 2006: 12 studies presented
- Publications:
  - 2006: 20 studies published
  - 2007 to date: 10 in press; 17 under review
- >1600 patients enrolled on clinical trials

EN704_16.ppt

Some Key Findings

- HLA-mismatched cord blood transplants acceptable alternative for adults unable to find a matched unrelated adult donor
- Cord blood may be preferable graft type for unrelated donor transplants in children
- Consolidation therapy beneficial prior to autotransplantation for AML
- Survival similar with PB and BM transplants but more CGVHD with PB
- Access to BMT and BMT outcomes influenced by race
- QOL of long-term survivors – and their spouses – affected by BMT

BUS06_23.ppt

These studies are possible because of the commitment of individuals in many centers to work together and share data.

BUS06_23.ppt

DATA DOESN'T JUST HAPPEN

- Providing the data needed to do good clinical research is hard work

CIBMTR Centers 2006