Leveraging Resources to Design, Conduct and Analyze Hematopoietic Stem Cell Transplant Clinical Trials: The Ongoing Collaboration between the Center for International Blood and Marrow Transplant Research and the Blood and Marrow Transplant Clinical Trials Network

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BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK

CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

NIH National Heart, Lung, and Blood Institute

National Cancer Institute at the National Institutes of Health

Conflict of Interest

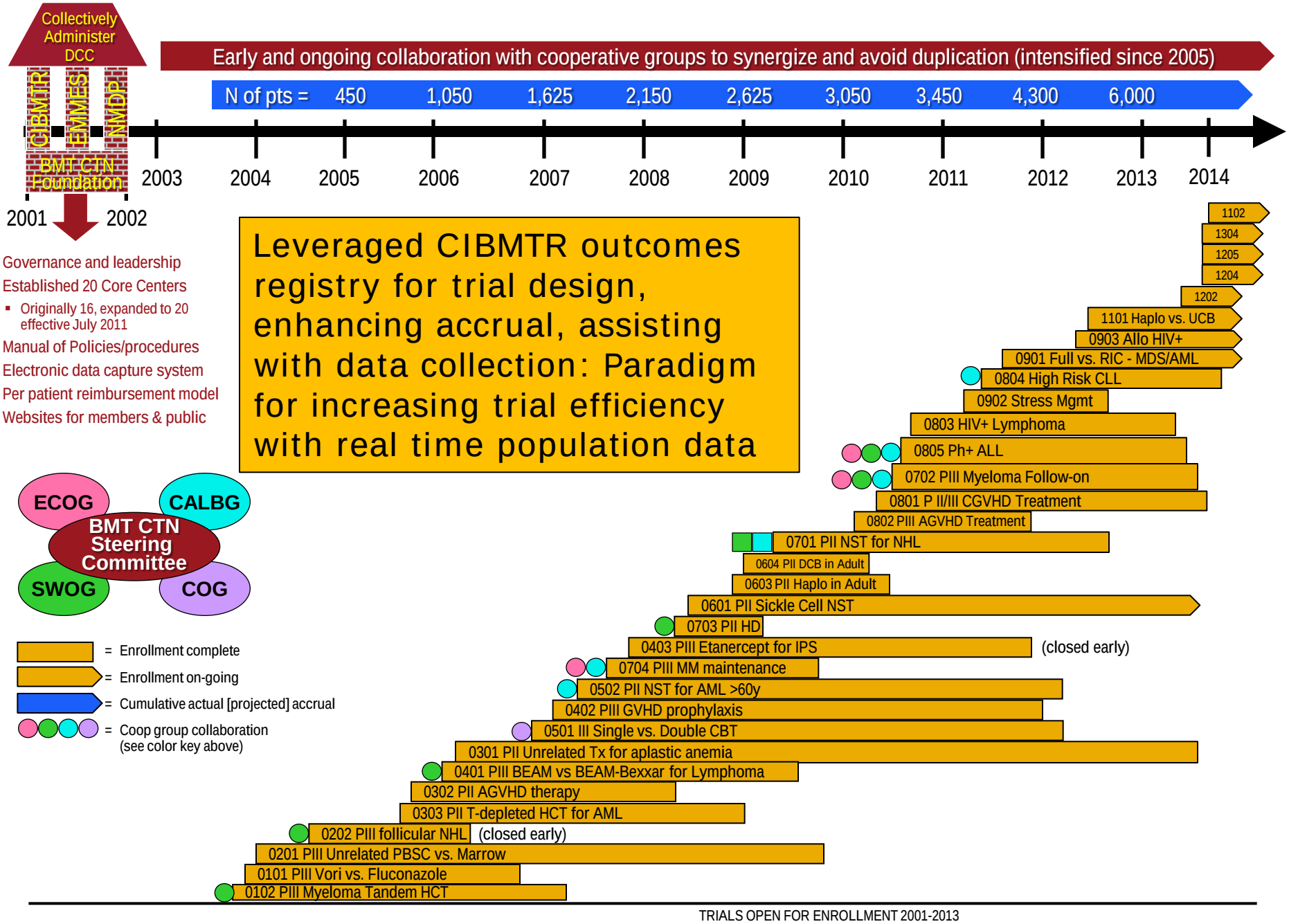
- No relevant conflict of interest to disclose

Introduction

- Hematopoietic Stem Cell Transplantation (HCT) uses blood stem cell sources to treat blood and marrow disorders
- Clinical trials in HCT are particularly challenging due to:
  - Heterogeneous diseases
  - Limited patient populations
  - Multiple competing risks
  - Lack of resources to conduct national studies

BLOOD AND MARROW
TRANSPLANT
CLINICAL TRIALS NETWORK

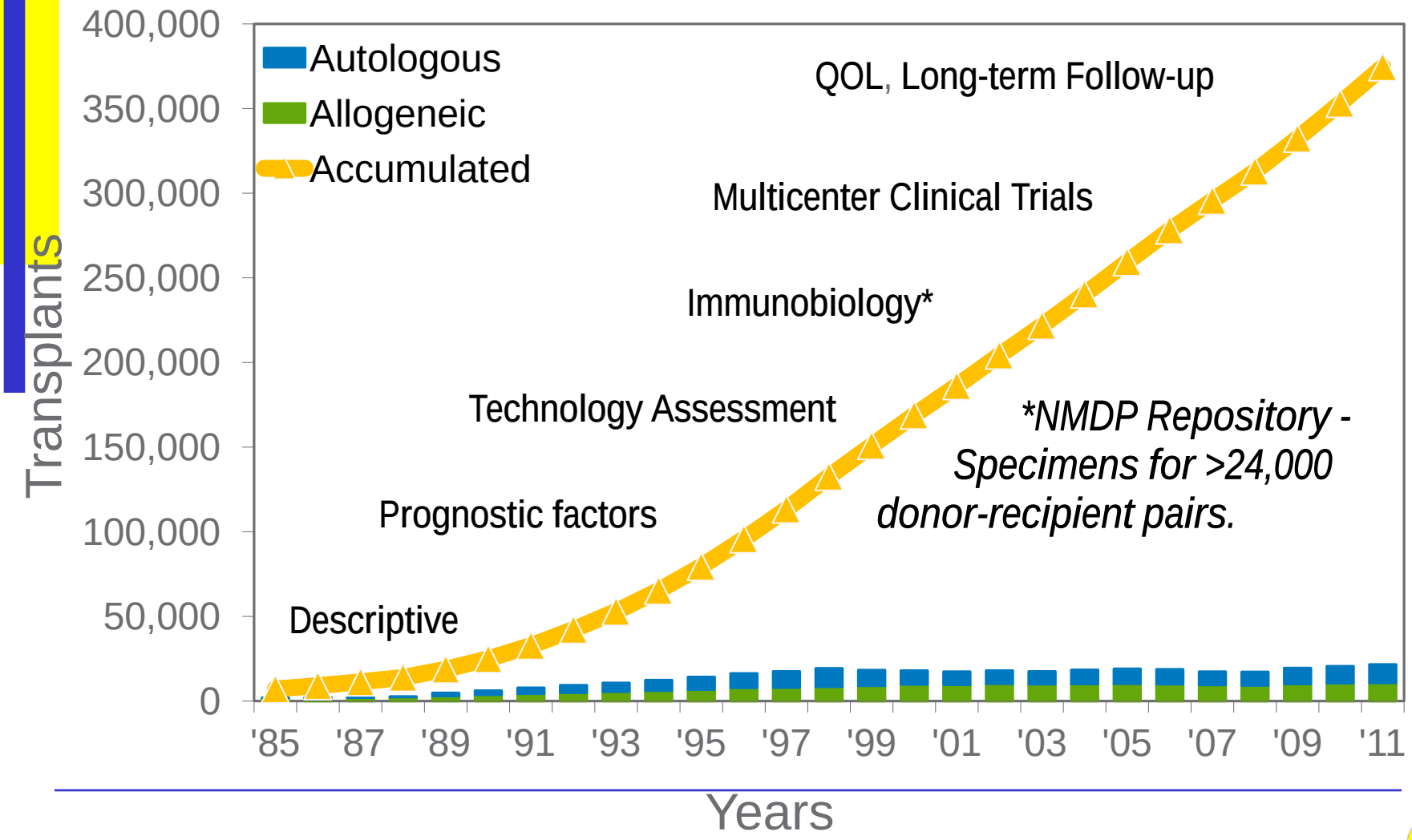
- Blood and Marrow Transplant Clinical Trials Network (BMT CTN)
- Funded in 2001 by NHLBI/NCI
- Conduct large multi-institutional HCT clinical trials
- Goal is to understand the best treatment approaches
- 20 core and 80+ affiliate centers


Collectively Administer DCC
CIBMTR
EMMES
NMDP
BMT CTN Foundation
2001
2002
Early and ongoing collaboration with cooperative groups to synergize and avoid duplication (intensified since 2005)
N of pts = 450 1,050 1,625 2,150 2,625 3,050 3,450 4,300 6,000
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
Governance and leadership
Established 20 Core Centers
Originally 16, expanded to 20 effective July 2011
Manual of Policies/procedures
Electronic data capture system
Per patient reimbursement model
Websites for members & public
Leveraged CIBMTR outcomes registry for trial design, enhancing accrual, assisting with data collection: Paradigm for increasing trial efficiency with real time population data
ECOG
CALBG
BMT CTN Steering Committee
SWOG
COG
= Enrollment complete
= Enrollment on-going
= Cumulative actual [projected] accrual
= Coop group collaboration (see color key above)
1102
1304
1205
1204
1202
1101 Haplo vs. UCB
0903 Allo HIV+
0901 Full vs. RIC - MDS/AML
0804 High Risk CLL
0902 Stress Mgmt
0803 HIV+ Lymphoma
0805 Ph+ ALL
0702 PIII Myeloma Follow-on
0801 P II/III CGVHD Treatment
0802 PIII AGVHD Treatment
0701 PII NST for NHL
0604 PII DCB in Adult
0603 PII Haplo in Adult
0601 PII Sickle Cell NST
0703 PII HD
0403 PIII Etanercept for IPS
(closed early)
0704 PIII MM maintenance
0502 PII NST for AML >60y
0402 PIII GVHD prophylaxis
0501 III Single vs. Double CBT
0301 PII Unrelated Tx for aplastic anemia
0401 PIII BEAM vs BEAM-Bexxar for Lymphoma
0302 PII AGVHD therapy
0303 PII T-depleted HCT for AML
0202 PIII follicular NHL
(closed early)
0201 PIII Unrelated PBSC vs. Marrow
0101 PIII Vori vs. Fluconazole
0102 PIII Myeloma Tandem HCT
TRIALS OPEN FOR ENROLLMENT 2001-2013

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

- Mission is to advance HCT and cellular therapy research worldwide
- Collaboration between Medical College of Wisconsin and National Marrow Donor Program
- National leader in HCT research since 1968
- >350,000 transplants registered
  - >20,000 in 2013
- Funded by NIH, HRSA and other supplementary sources

Center for International Blood and Marrow Transplant Research – Collects data on most HCTs done in the US – and in ~100 international centers



Research Data Available

- **Baseline recipient data**:
  - Diagnosis, demographics, transplant procedure, clinical
- **Baseline donor data**:
  - Demographics, HLA typing, ID markers, laboratory
- **Follow-up recipient data**:
  - Transplant outcomes, GVHD prophylaxis, immune reconstitution, chimerism, infection, organ function, subsequent HCT, new malignancy, death

Design Considerations

- Protocol concept is presented and approved by the BMT CTN Steering Committee
- A team is formed which includes physicians/statisticians/coordinators
- Next step is to consult the CIBMTR physicians/statisticians about appropriate endpoints
- Design the protocol and go through the various approval bodies

Sample Size Estimation

- Well designed studies are built on solid estimates
- Query registry for estimates of effect size
- Incidence/Prevalence of outcomes
- Assess important stratification factors
- Feasibility…

Feasibility

- Target center participation
- Obtain projections
  - Adjust for reality-“Horowitz factor”
- Ongoing monitoring to identify accrual barriers
  - All studies!!!
  - BMT CTN #1102: assess patient referral
  - BMT CTN #1101: monitor transplants that are being performed

Clinical Trial + Population-based data

- = efficient use of resources
- BMT CTN #1102 Allogeneic transplant vs best available therapy for MDS
  - AdvEDC: Enrollment, quality of life and overall survival
  - CIBMTR: Standard CIBMTR follow-up
- BMT CTN #1202 biomarker outcomes
  - AdvEDC: Enrollment, specimen tracking, early outcomes that require closer monitoring
  - CIBMTR: Standard CIBMTR follow-up

Concurrent Controls

- BMT CTN #1203
- Phase II randomized three arm study of 3 GVHD prophylaxis strategies
  - 270 patients; 90/arm
- Comparison to concurrent control from CIBMTR
  - 270 controls from centers not participating in the randomized study
- Design data capture to ensure data are collected consistently.

Long Term Outcomes

- Complement clinical trial data with long term outcomes
  - Cost effective
  - Efficient use of resources
- BMT CTN #0102 Auto/Auto vs Auto/Allo for Myeloma
- BMT CTN #0201 PB vs BM
- BMT CTN #0603/0604 Haplo vs DUCB

Summary

- Efficient use of resources is paramount to the success of designing, conducting and analyzing HCT clinical trials
- Ongoing collaboration between BMT CTN and CIBMTR leverages resources to make HCT clinical trials feasible
- Complementing clinical trial data with population based data
- Serves as a good model for efficient use of resources

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- **NCI:**
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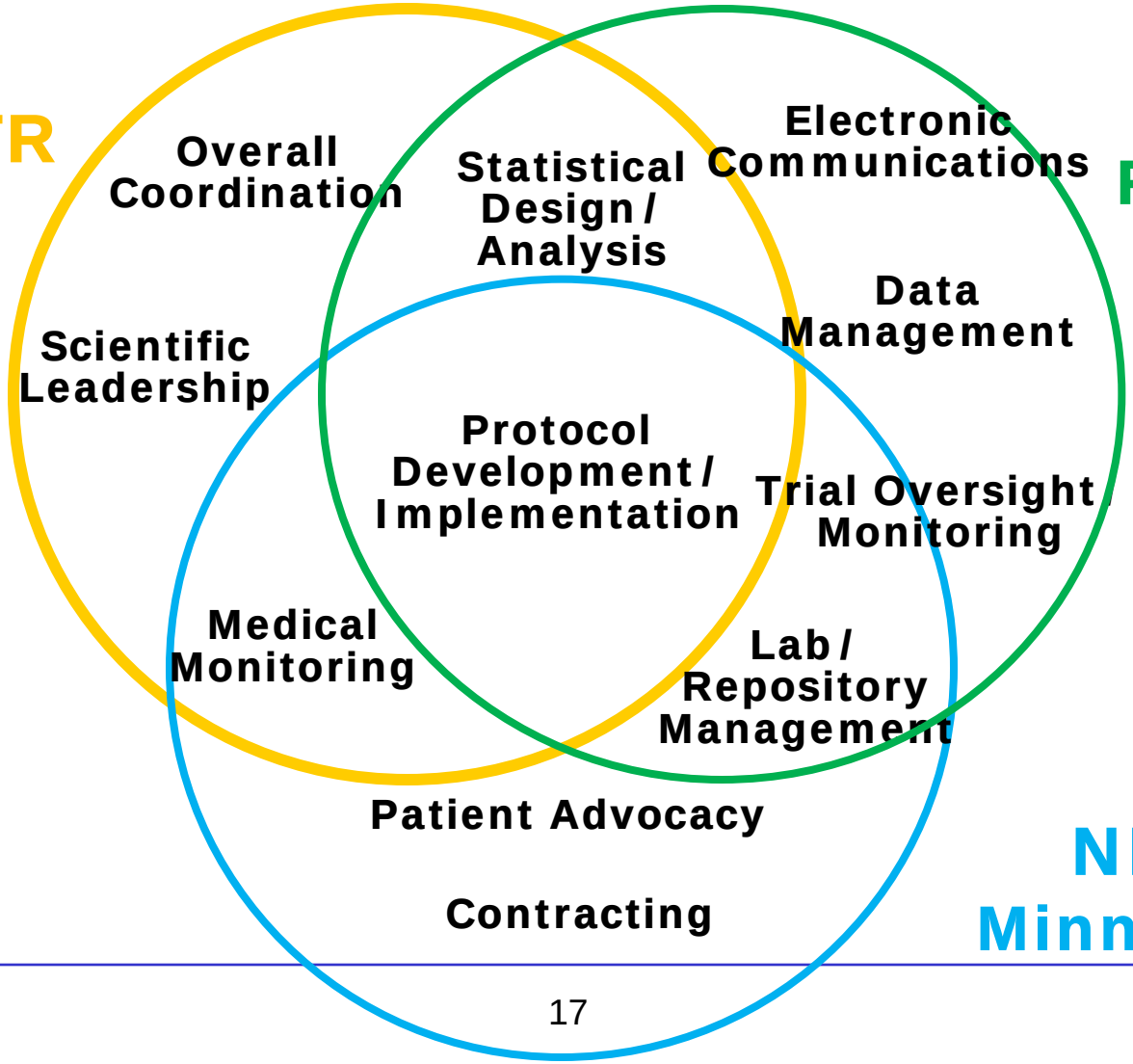
  - Roy Wu, PhD
- **Patients and their families**

Questions?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