

Clinical Trials

Asif Alavi MD

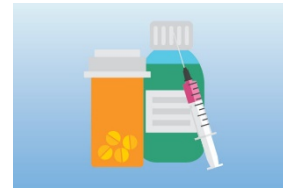
Assistant Professor

Karmanos Cancer Center/

Wayne State University

Clinical Research

- Medical research involving people
- Two types
 1. Observational Studies
 1. Clinical Trials



Observational Study

- Assesses health outcomes in groups of participants without assigning to particular intervention
- Example: Assess whether risk factor “R” predicts outcome after stem cell transplant

- Evaluates a medical, surgical, or behavioral intervention
 - Can be single arm (treatment only) or controlled (compared to SOC or placebo)
 - Goal is to assess safety and efficacy
- Example: Is new treatment “T” better than SOC at treating acute myeloid leukemia

Phases of Drug Development

	Phase 1	Phase 2	Phase 3	Phase 4
No. of Participants	15-30	<100	100 to thousands	Several hundreds to several thousands
Purpose	First in humans Find safe dose	Determine efficacy	Compare new agent with standard treatment	Post –market Long-term safety and efficacy

Common aspects of trial design

- **Controlled**
 - Early phase studies are single arm (not controlled)
 - Controlled study needed to determine efficacy of treatment
 - May involve placebo
- **Randomized**
- **Blinded**

Key Players

- Investigators
 - Principal Investigator
 - Co-Investigators
- Research Nurse
- Research Coordinator
- Regulatory personnel



Are Clinical Trials Safe?

- **Highly Regulated**
 - Must follow established protocols and standards
 - International Conference on Harmonization Good Clinical Practice (GCP)
- **Multiple Layers of Protection**
 - Investigators/Site research Staff
 - Site Scientific Review
 - Institutional Review Board
 - Sponsor
 - Data Safety Monitoring Committee
 - FDA/EMA
- **Strict Adherence to Study Protocol**
- **Careful Monitoring and Reporting of Adverse Effects**

Why participate?

- No other reasonable treatment option
- Potential for better treatment
 - Efficacy and Side effects
- Contribute to knowledge of disease and advancement of care
- Access to therapy

What should you ask?

- What is standard of care?
- How does clinical trial differ from this?
- What are risks and benefits?
- Financial considerations
- Review consent form

Consent form - do's and don'ts

Sign without reading consent



Read consent, get scared by side effects and decide not to participate



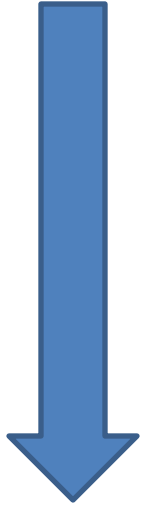
Review the consent AND ask clarifying questions



What should you NOT ask?

- Is this clinical trial better than standard care?
- Should I enroll in this clinical trial?
- Would you recommend this for your mom, dad, etc?

What happens after I sign consent?



- Screening
- Enrollment
- Assign to treatment
- Begin treatment

What happens while on treatment

- Trials may involve a one-time treatment or treatment over a period of time
- Regular visits
 - Assess for side effects
 - Assess response to treatment

When does study end?

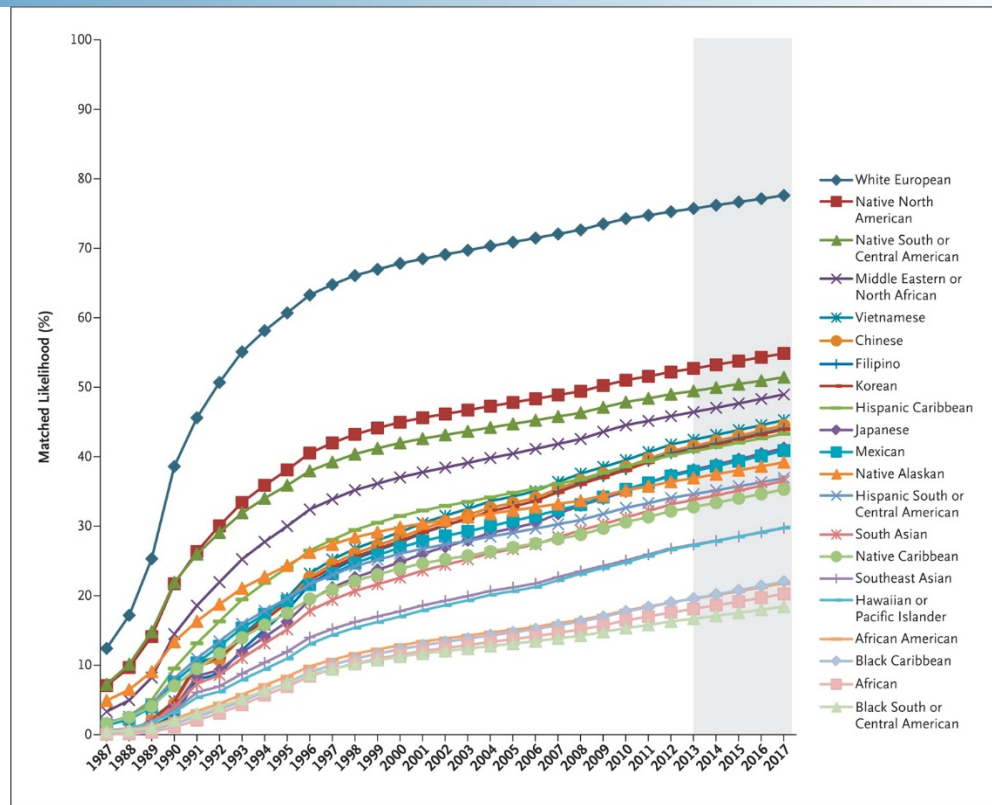
- **Treatment length**
 - One time treatment
 - Time-limited treatment
- **Treatment extensions**
 - Open label
 - Crossover
- **Follow-up**

Participant Responsibilities

- Know when the study begins and ends.
- Show up at scheduled appointments on time
- Follow directions for proper use, dosing and storage of self-administered study medications
- Follow directions for providing samples, and preparing for tests, procedures or examinations.
- Follow directions regarding other medications and procedures.
- Inform if other medical care is needed
- Truthful answers to questions
- Inform the staff if there are questions you would rather not answer.
- Keep study confidential
- Inform of contact information changes.
- Follow withdrawal procedures

Example

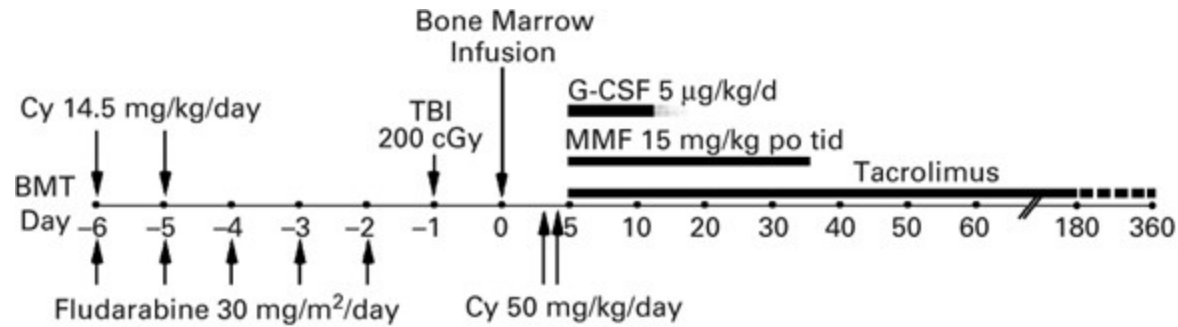
Problem: Lack of HLA matched donor limits availability of allogeneic (donor) stem cell transplant



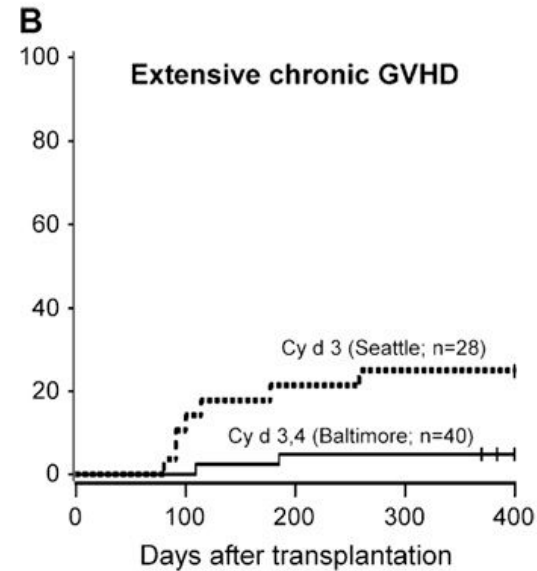
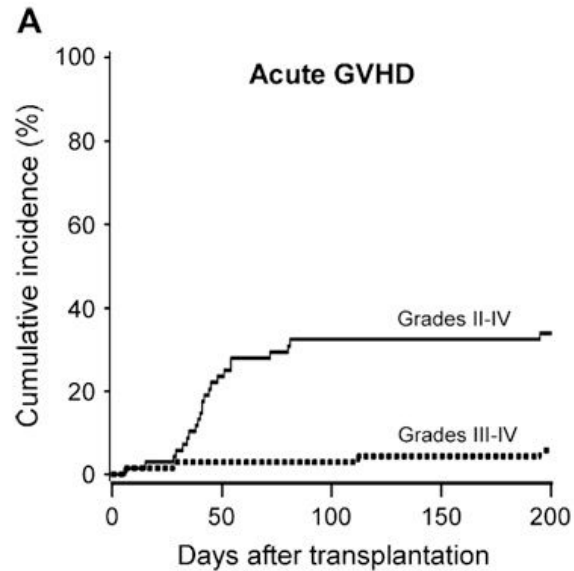
- Potential Solution: Use half-matched related donors
 - Parents, siblings, children
- Problem: Rejection, Graft v. Host Disease

Pre-clinical experiments

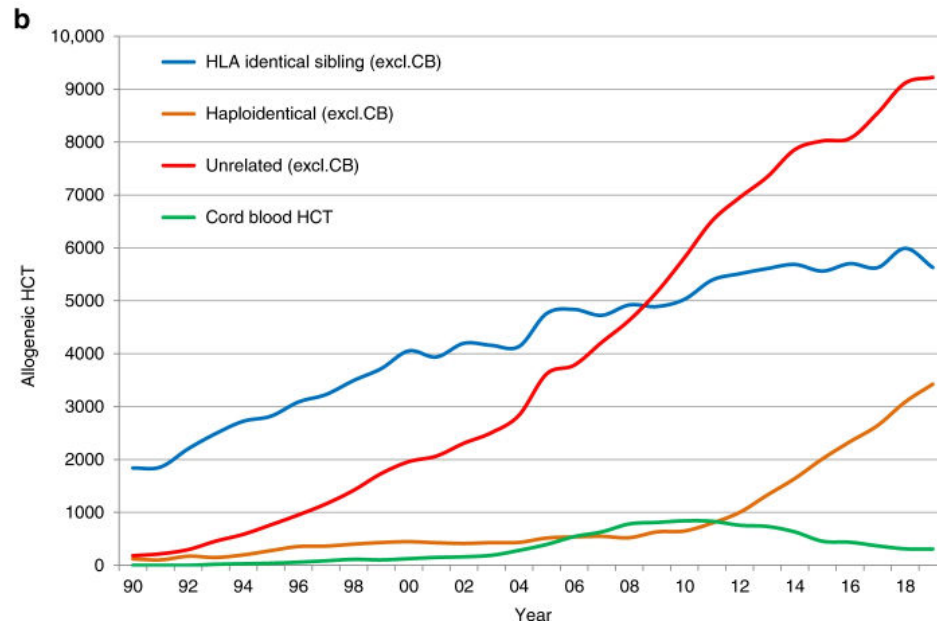
- Cyclophosphamide given after transplant can allow grafts to take
 - Need high dose
 - Timing matters
 - Stem cells are resistant to it



Luznik, et al. BBMT 2008



Luznik, et al. BBMT 2008



Passweg JR et al BMT 2021

Unmanipulated haploidentical in comparison



BARBARA ANN

CANCER INSTITUTE
Wayne State University

Check for updates



WILEY

RESEARCH ARTICLE

Comparable composite endpoints after

REGULAR ARTICLE



blood advances®

Check for updates

Regular Article

TRANSPLANTATION

HLA-matched

TRANSPLANTATION

HLA-haploidentical vs matched unrelated donor transplants with posttransplant cyclophosphamide-based prophylaxis

Mahasweta Gooptu,^{1,*} Rizwan Romee,^{1,*} Andrew St. Martin,² Mukta Arora,³ Monzr Al Malki,⁴ Joseph H. Antin,¹ Christopher N. Bredeson,^{5,6} Claudio G. Brunstein,⁷ Saurabh Chhabra,^{2,8} Ephraim J. Fuchs,⁹ Nilanjan Ghosh,¹⁰ Michael R. Grunwald,¹⁰ Christopher G. Kanakry,¹¹ Natasha Kekre,^{5,6} Joseph P. McGuirk,¹² Ian K. McNiece,¹³ Rohtesh S. Mehta,¹⁴ Marco Mielcarek,¹⁵ Filippo Milano,¹⁵ Dipenkumar Modi,¹⁶ Ran Reshef,^{17,18} Scott R. Solomon,¹⁹ Mark A. Schroeder,²⁰ Edmund K. Waller,²¹ Yoshiro Inamoto,¹⁵ Robert J. Soiffer,¹ and Mary Eapen²

V
ti
o
a
A
N
An
Be

H
ac
cc
By
Sel
Jae
Sel
Jor

Sh
Bo
He
Wi
Pri
Le
Jor
:Sii
Me
Jof
Scl

M
A
Y
S

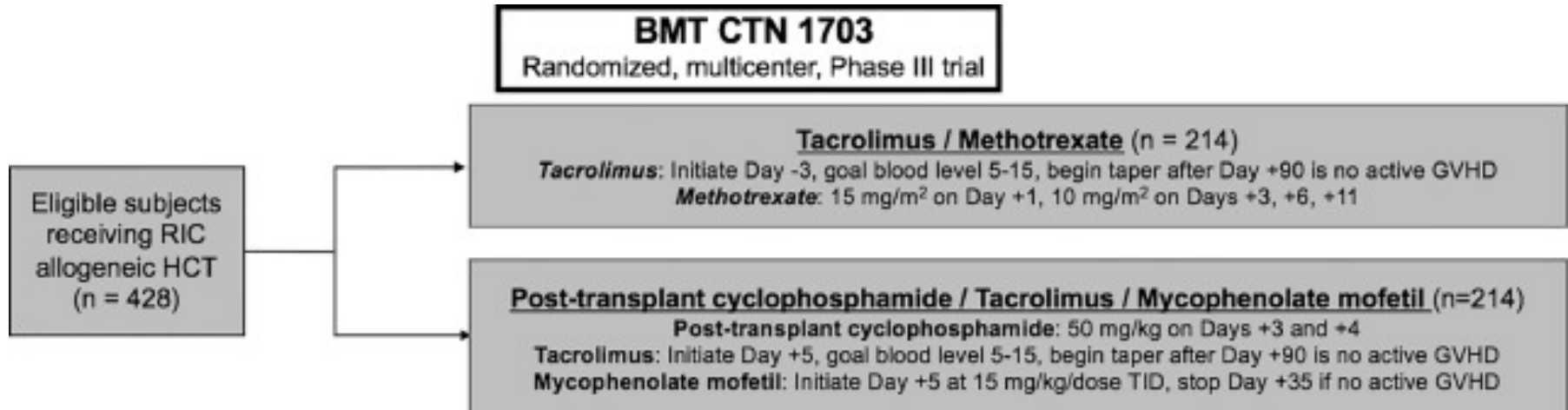
Ste
Phi
Ryc
Olk
Ept



original reports

National Marrow Donor Program–Sponsored Multicenter, Phase II Trial of HLA-Mismatched Unrelated Donor Bone Marrow Transplantation Using Post-Transplant Cyclophosphamide

Bronwen E. Shaw, MD, PhD¹; Antonio Martin Jimenez-Jimenez, MD, MS²; Linda J. Burns, MD¹; Brent R. Logan, PhD¹;
 Farhad Khimani, MD³; Brian C. Shaffer, MD⁴; Nirav N. Shah, MD⁵; Alisha Mussetter, BS⁶; Xiao-Ying Tang, MPH¹; John M. McCarty, MD⁷;
 Asif Alavi, MD⁸; Nosha Farhadfar, MD⁹; Katarzyna Jamieson, MD¹⁰; Nancy M. Hardy, MD¹¹; Hannah Choe, MD¹²;
 Richard F. Ambinder, MD, PhD¹³; Claudio Anasetti, MD³; Miguel-Angel Perales, MD⁴; Stephen R. Spellman, MBS⁶; Alan Howard, PhD⁶;
 Krishna V. Komanduri, MD²; Leo Luznik, MD¹³; Maxim Norkin, MD, PhD¹⁴; Joseph A. Pidala, MD, PhD³; Voravit Ratanatharathorn, MD⁸;
 Dennis L. Confer, MD⁶; Steven M. Devine, MD⁶; Mary M. Horowitz, MD, MS¹; and Javier Bolaños-Meade, MD¹³



The Journey of Post-transplant Cyclophosphamide

Lab Research

Early Phase study in
small population
(Addressed Health
Care Disparity)

Efficacy Confirmed in
Observational
Studies

Potential for use in all
types of donor stem
cell transplants

The Journey of Post-transplant Cyclophosphamide

DISCLAIMER

Lab Research

Early Phase study in
small population
(Addressed Health
Care Disparity)

Efficacy Confirmed in
Observational
Studies

Potential for use in all
types of donor stem
cell transplants

Summary

- Clinical Research is highly regulated
- Both observational research and interventional studies offer valuable information
- May offer new or better treatment options
- Advances the knowledge and treatment of disease which leads to better medical care