Clinical Trials From A to Z: Understanding the Basics

Barbara Weinstein, RN, BSN, CCRP
NHLBI Office of the Clinical Director
National Institutes of Health

Disclosure

• Nothing to disclose

AND

• “This presentation does not represent an official statement of the NHLBI”

My Goals

• Define and describe clinical trials.
• Demonstrate how to find a clinical trial.
• Describe how patients are protected while participating clinical trials.
• Discuss important things to consider before participating in a clinical trial.
• Discuss what happens when a clinical trial ends.

What is a Clinical Trial?

Medical Practice

The science or practice of the diagnosis, treatment and prevention of disease.

Source: Oxford Dictionary of Nursing, Oxford University Press 2014

What is a Clinical Trial?

Clinical Trial

“Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s) and/or to identify any adverse reactions to investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigations product(s) with the object of ascertaining its safety and/or efficacy.”

From the ICH Guideline for Good Clinical Practice
What is a Clinical Trial?

RESEARCH involving PEOPLE

Types of Clinical Trials

• Treatment
• Prevention
• Diagnostic
• Screening
• Quality of Life
• Genetic

Types of Clinical Trials

Treatment

Treatment research generally involves an intervention such as medication, psychotherapy, new devices, or new approaches to surgery or radiation therapy.

Prevention

Prevention research looks for better ways to prevent disorders from developing or returning. Different kinds of prevention research may study medicines, vitamins, vaccines, minerals, or lifestyle changes.

Diagnostic

This refers to the practice of looking for better ways to identify a particular disorder or condition.

Screening

Screening research aims to find the best ways to detect certain disorders or health conditions.
Quality of Life

Also known as "supportive care," this research explores ways to improve comfort and the quality of life for individuals with a chronic illness.

Types of Clinical Trials

Genetic

Genetic studies aim to improve the prediction of disorders by identifying and understanding how genes and illnesses may be related. Research in this area may explore ways in which a person's genes make him or her more or less likely to develop a disorder. This may lead to development of tailor-made treatments based on a patient's genetic make-up.

Types of Clinical Trials

Randomized: The element of chance is used to assign trial subjects to different treatment or control groups*. VS.

Non-Randomized: All subjects receive the same treatment.

* If you are in a randomized study, you cannot choose your group

Clinical Trial Design

Single Blind: The subject is unaware of the treatment assignment

Double Blind: The subject, the investigator, the monitor, and sometimes the data analysts are unaware of the treatment assignment

Blinding: One or more parties to the trial are unaware of the treatment assignment

Single blind vs. Double Blind
Phases of Clinical Trials

Clinical trials are categorized by four different “phases” that differ in their purpose. 

**Phase I**
Phase I trials include the initial introduction of an investigational drug into humans.
- Closely monitored
- Conducted in patients or in normal volunteer subjects
- Designed to determine:
  - metabolism and pharmacologic actions of the drug in humans
  - side effects associated with increasing doses
  - if possible, obtain early evidence on effectiveness
Total number of subjects is generally 20-80.

**Phase II**
Phase II trials are controlled clinical studies:
- Conducted in patients with the disease or condition under study
- Designed to determine:
  - the effectiveness of the drug for a particular indication or indications
  - the common short-term side effects and risks associated with the drug.
Phase II studies usually involve no more than several hundred subjects.

**Phase III**
Phase III trials are expanded trials...
- Conducted after preliminary evidence suggesting effectiveness of a drug has been obtained.
- Designed to gather the additional information about effectiveness and safety needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling.
Phase III studies usually include from several hundred to several thousand subjects.

**Phase IV**
Phase IV studies are post-marketing studies.
- delineate additional information about the drug’s risks, benefits, and optimal use.

Which Phase Is It?
Who’s Who in Clinical Trials

Principal Investigator (PI) – Ultimately responsible for all aspects of the trial.

Associate Investigators -
- Physicians
- Research Nurse
- Data Manager
- Protocol Navigator
- Statistician

Other Healthcare Staff -
- Floor Nurses
- Laboratory Staff
- Social Workers, Interpreters, etc.
- Radiology, EKG, etc.

How Study Participants are Protected

- Ethical guidelines
- Federal regulations and regulatory bodies
- Institutional review boards (IRBs)
- Consent
- Eligibility

It’s gonna get a little dry now....

Nuremberg Code

- 10 ethical principles related to human research.
- Developed as a result of the Nuremberg trials.

Website: http://www.hhs.gov/ohrp/archive/nurcode.html

Declaration of Helsinki

- First declaration in 1964; most recent update in 2013.
- The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.
- Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects to adopt these principles.

Website: http://www.wma.net/en/30publications/10policies/b3/

Belmont Report

- Describes the ethical principles and guidelines for the protection of human subjects.
- Created in April 1979.
- Applies three ethical principles:
  - Respect for person
  - Beneficence
  - Justice

Belmont report can be found: http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html#
Federal Regulations

• The codes of federal regulations are rules by which research must be conducted.
• These rules define how research subjects must be protected.


The FDA

• The Food and Drug Administration started as the Division of Chemistry in 1862.
• Passage of the Federal Food and Drugs Act of 1906 added regulatory functions to the agency.
• July 1930: Name changed to FDA.

Source: http://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm124403.htm

How Study Participants are Protected

The FDA

• The FDA is responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, our nation’s food supply, cosmetics, and products that emit radiation.

Source: http://www.fda.gov/AboutFDA/WhatWeDo/

Institutional Review Board

IRB Membership

• Composed of 5 diverse members
• At least one scientific
• At least one non-scientific
• One not affiliated with the institution conducting the research or an immediate family member of someone working for the institution
• Diverse in terms of race, gender, cultural background, and community attitudes.

Source: 45 CFR Part 46, section 46.107

IRB Roles

• Reviewing proposed research.
• Reviewing current research.
• Suspending research.
• Terminating research
• Accountable for adhering to the CFRs.

Source: 45 CFR Part 46, section 46.107
Informed Consent

• What is informed consent?
• What you should look for in a consent?

What is Informed Consent?

Informed consent is a process...
• Adequate information to allow for an informed decision about participation in the clinical investigation.
• Facilitating the potential participant's understanding of the information.
• An appropriate amount of time to ask questions and to discuss with family and friends the research protocol and whether you should participate.

What to Look For in a Consent

• Research is involved
• Purpose of research
• Voluntary
• Expected duration of participation
• Description of procedures to be followed
• Description of what is experimental
• Description of risks or discomfort
• Description of benefits

Eligibility

Eligibility for a clinical trial is determined/assessed by very specific inclusion/exclusion criteria.

Some examples of inclusion/exclusion criteria:
• Ability to understand and give informed consent
• Ability to perform activities of daily living
• Specific laboratory values
• Disease history
• Prior therapies
• Age
How Study Participants are Protected

Eligibility

Why do we have eligibility criteria?
- to identify appropriate subjects
- to ensure that they are protected

How Do I Find a Clinical Trial?

- ClinicalTrials.gov
- Considerations in deciding whether or not to participate.
INCLUSION CRITERIA:
You MUST have these to participate

EXCLUSION CRITERIA:
You MUST NOT have these to participate

• Access to leading experts.
• May receive investigational drug that performs better than what is currently on the market or where none presently exists.
• Help others.

Why Participate in a Clinical Trial?

• Access to leading experts.
• May receive investigational drug that performs better than what is currently on the market or where none presently exists.
• Help others.
Why You Might Decide Not to Participate

- Investigational new drug trial: The study drug may not work as well as standard therapy.
- Investigational new drug trial: The study drug may cause serious side effects.
- You may be required to see your doctor more frequently, or have more frequent lab visits.

Top 10 Questions

patients ask me when they are deciding whether to participate in a clinical trial

- Why You Might Decide Not to Participate
- Top 10 Questions
- How Much Will it Cost Me?
- Additional Questions to Ask

How Much Will it Cost Me?

- Patients need to ask for a detailed description of what costs are covered and what costs are not covered. When asking about costs, distinguish between the pre-trial or evaluative period and during the trial.
- Lodging (short term vs. long term)
- Travel
- Subsistence
- Non-trial related medical costs

- Will the results of the study be provided to me?
- How will my research team and my medical team communicate while I am participating in the trial?
- If I benefit, will I be allowed to continue after the trial ends?

What Does the Research Team Expect of Participants?

- Compliance
- Communication

Additional Questions to Ask

- Will the results of the study be provided to me?
- How will my research team and my medical team communicate while I am participating in the trial?
- If I benefit, will I be allowed to continue after the trial ends?
Resources

Clinical Trials Information
• http://clinicaltrials.gov - Comprehensive registry of federally and privately supported clinical trials conducted in the United States and around the world.

Patient Support Organizations
• http://www.aamds.org - The Aplastic Anemia & Myelodysplastic Syndromes International Foundation
• http://www.mds-foundation.org - The Myelodysplastic Syndromes Foundation
• http://www.pnhfoundation.org - The Paroxysmal Nocturnal Hemoglobinuria Research and Support Foundation
• http://rarediseasesnetwork.epi.usf.edu/bmfdc/index.htm - The Bone Marrow Failure Disease Consortium

Contact Information

Barbara Weinstein, RN, BSN, CCRP
NHLBI Office of the Clinical Director
National Institutes of Health

Phone: 301-594-4180
Fax: 301-402-3088
Email: weinsbar@nhlbi.nih.gov

QUESTIONS?