Immune Deficiency Foundation

Patient & Family Handbook
For Primary Immunodeficiency Diseases

6th Edition

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Clinical trials, also known as protocols or clinical research studies, are experiments that use a scientific approach to explore whether a new medication, treatment, or device is safe and effective for human use. This process is the final drug development step before a new drug or treatment is approved by the Food and Drug Administration (FDA) and made available to people. Clinical trials are key in advancing new medical knowledge and patient care.

Overview

Human testing is necessary to develop safe and effective treatments with acceptable side effects, while providing the greatest therapeutic benefit. Before any new medications or treatments are studied in humans, they are studied in laboratory animals to determine whether they are safe enough to test in humans. Animal studies must be evaluated to determine if they are safe. They must also show some positive outcomes before human testing begins.

To make sure that a new product being tested will work for different groups of people, it is important that the participants in the clinical trials are from different ages, genders, and disease groups. This is the best way to test potential treatments to see whether they should be approved for a larger group. However, clinical studies of new treatments are often first studied in adults prior to enrolling children, unless the condition for treatment predominantly affects children. A treatment could be a drug, medical device, or a biologic (made from living organisms or containing components of living organisms), such as a vaccine, blood product, or gene therapy.

Types of Clinical Trials

There are several types of clinical trials or studies. Some involve treatments or interventions, and some are observational that collect data or information only.

Treatment or Interventional: Involve a medical treatment or intervention such as medications, psychotherapy, new devices or new approaches to surgery, or radiation therapy. Example: new type of intravenous immunoglobulin (IVIG) replacement therapy.

Prevention: Look for better ways to prevent disorders from developing or returning. Different kinds of prevention research may study medicines, vitamins, vaccines, or lifestyle changes. Example: low salt diet to prevent high blood pressure.

Diagnostic: Look at better ways of identifying or diagnosing a particular disorder or condition. Screening studies are also a type of diagnostic research designed to learn better ways of detecting disorders. Example: newborn screening for Severe Combined Immunodeficiency (SCID).

Natural History: Study the evolution of a disorder (often present since birth) over the lifetime of an individual, to see the possible complications or changes in the disorder, and learn about recognizing and managing these problems to reduce their severity. Example: natural history study of Common Variable Immune Deficiency (CVID).
unsafe during this prolonged development process. The process is done in a step-by-step approach called Phase(s). Each phase of the process must be safely completed before moving on to the next.

**Phase I Trials**
These trials test a drug or a treatment in a small group of people usually the first time in humans. This may be done in a group of healthy individuals depending on the treatment or condition being studied. The purpose is primarily to determine a safe dose of the medication and determine possible side effects.

**Phase II Trials**
The drug or treatment is given to a larger group of people affected by the medical condition being treated to get initial efficacy data and determine the best dose(s) for safety and efficacy.

**Phase III Trials**
The study drug or treatment is given to an even larger group of individuals with the medical condition to prove effectiveness and monitor for side effects. Depending on the disease entity there is placebo group (subjects who do not get the investigational drug and may receive a similar looking pill or liquid or IV that does not contain any type of medication) for comparison to the investigational drug. The study of new immunoglobulin (Ig) products for replacement therapy does not include a placebo group of subjects since it would be unethical to exclude individuals with PI from getting Ig replacement therapy. This study often compares the new treatment to the currently used treatment to determine safety and efficacy. Phase III studies are typically the final step before the FDA considers whether to approve a medication or treatment.

**Phase IV Trials**
These trials are for study drugs or treatments that have been approved by the FDA. Phase IV studies are designed to get additional long-term safety information on a treatment as it is used when prescribed to individuals.

**Participating in Clinical Research**
Deciding to take part in clinical trials is something only you can decide once you have information about the study from the study doctor (investigator) and team. There are possible benefits as well as risks so you should discuss these and understand any concerns fully before making your decision.

Participation in clinical trials may allow you the benefit of a treatment option that is not otherwise available. Your participation allows you an active role in a decision that affects your life or the life of your child so careful consideration and discussion with your care team is necessary.

**Informed Consent**
Prior to enrolling into a clinical trial, you will be asked to sign an informed consent form. This is a document that describes, in detail, what the trial is about, what is expected of you if you participate, the potential risks, possible benefits, and any financial compensation offered. All subjects participating in a clinical trial will need to sign an informed consent document. As a subject you have rights, the most important of which is that you have the right to withdraw your consent from participating in the study at any time without it affecting your care. Informed consent is an ongoing process and you should be updated to any changes in the study or new findings that may affect your willingness to participate.

**Unknown Side Effects and Risks**
There is always a chance the treatment or medicine will not work. Known side effects will be described in the Informed Consent document but there may be other side effects that are not known by the study team at the time you start the study.

**Randomization**
This is a process used in some trials to prevent favoritism with one treatment versus another. One group receives the actual study treatment or medication, while the other will receive the most widely accepted treatment (standard approved treatment). Comparing the results from these two groups often shows which treatment is more effective and/or has fewer side effects. Before you decide to participate, you should understand your chance of being randomized into either group is about equal, like the flip of a coin. The doctor does not decide on what treatment or drug you get, it is usually done randomly by a study statistician or pharmacist.

**Placebo**
Placebos, which are inactive ‘look-alike’ drugs, are rarely used in primary immunodeficiency drug studies. However, in a placebo study there is the possibility that you may not be selected to be in the group receiving the actual drug being tested and will not know this until later in the trial.

Blinding
This is a term used in clinical trials which means that neither you or your doctor will know if you are getting the experimental treatment or standard treatment. This is done to reduce bias.

Protections and Safeguards
To assure patient safety and ethical practices, all clinical research is reviewed by an institutional ethics or review board. This panel reviews the proposed study to make sure it is ethical, that the risks do not outweigh the possible benefits and that concerns related to special populations such as children or pregnant women are addressed. There are also federal government agencies: The Office of Human Research Protection and The Food and Drug Administration (FDA) that have oversight over all clinical research conducted in the U.S.

You also have the right to privacy if you choose to participate in a clinical trial. You will be assured that the research staff will not share your health information with anyone without your consent.

Resources
- ClinicalTrials.gov: www.clinicaltrials.gov/ct2/about-studies/learn
- FDA: www.fda.gov/patients/clinical-trials-what-patients-need-know
- National Institutes of Health: www.nih.gov/health-information/nih-clinical-research-trials-you