Phases of Clinical Trials

This section has been reviewed and approved by the Cancer.Net Editorial Board [1], November / 2013

Watch theCancer.Net Video: Phases of a Cancer Clinical Trial, with Nicholas Petrelli, MD[2], adapted from this content

Key Messages:

- The term ?phase? is used to describe the goals of a clinical trial.
- Phase I clinical trials are used to show that a new treatment is safe for a small group of people and to find the best dose and schedule for future research of the drug or drug combination.
- Phase II clinical trials provide more information about the safety of the new treatment and how well it works to treat a specific type of cancer.
- Phase III clinical trials compare a new treatment or treatments with the standard treatment in a large group of people.

Clinical trials are done in phases. Each phase describes the general information about a new treatment that is being collected in a clinical trial, such as the dose, safety, and how well it works. The phases are called I, II, and III.

Preclinical research

Before a new treatment can be given to patients, the underlying research hypothesis (the explanation for how the new treatment works) must be proven in a laboratory. This stage is called preclinical research, and it often takes years to turn this knowledge into a new treatment.

If the laboratory research suggests that the treatment might be an effective cancer treatment, the sponsor of the clinical trial files an Investigational New Drug (IND) application with the U.S. Food and Drug Administration (FDA) asking permission to study the treatment in people. If the IND application is approved, researchers can move on to the next step of research, which includes studies to find out more about the treatment.

Phase I clinical trials

The goal of a phase I clinical trial is to show that a new drug or treatment, which has proven to be safe for use in animals, may also be given safely to people. Doctors collect data on the dose, timing, and safety of the treatment. People who participate in phase I clinical trials are often the first to receive a new therapy or a new combination of therapies.

In phase I clinical trials, the dose of the drug being studied is gradually increased to find the dose that works best without causing severe side effects. This process is called dose escalation. The first participants are given a small dose of the drug. If there are no or few side effects, the next participants are given higher amounts of the drug until the doctors find the highest dose with the fewest side effects. Sometimes, the doctors need to find out the best way to give the new treatment, such as by mouth or through a vein. In addition, the doctors collect data on how the drug is absorbed, processed, and spread throughout the body.

Phase I clinical trials generally last several months to a year and most often involve a small number of people, usually no more than 10 to 20. People whose cancers are no longer responding to standard treatments are often offered treatment in phase I clinical trials. Although phase I clinical trials are not primarily designed to test how well a treatment or combination of treatments work, an investigational treatment in this phase may help to slow or stop the growth of a person?s cancer. All currently available treatments were first tested for use in people in phase I trials.

Phase II clinical trials

Phase II clinical trials provide more detailed information about the safety of the treatment, in addition to evaluating how well it works. These clinical trials focus on finding out whether the new treatment works for a specific cancer, which may be measured by a decrease in tumor size or through blood tests. Phase II clinical trials take about two years to complete and usually involve about 20 to 40 people. Sometimes phase II clinical trials will assign patients to several possible treatments. This is known as a randomized phase II trial and may include up to several hundred patients. The new treatment needs to show it is likely to work and is safe when compared to the standard treatment for it to be tested in phase III clinical trials.

Phase III clinical trials

The goal of phase III clinical trials is to take a new treatment that has shown promising results when used for a small number of patients with a particular disease and compare it with the current standard of care for that specific disease. In this phase, data are gathered from large numbers of patients to find out whether the new treatment is better and possibly has fewer side effects than the current standard treatment. Phase III clinical trials are usually randomized, meaning that patients receive either the investigational treatment or the standard treatment in a non-ordered way. In phase III studies at least two (and often more than two treatment options) are compared. Although phase III clinical trials focus on patients with a

specific disease, they typically include patients of various ages, ethnicities, and both genders so that the results may be applicable to a large number of people. The number of people enrolled in a phase III clinical trial can range from the hundreds to the thousands, and these clinical trials take many years to complete.

Once a drug has been shown to work well to treat a specific cancer in a phase III clinical trial, the researchers can submit an application for FDA approval. If data from the clinical trials meet the FDA's standards, the treatment is approved for a specific use. However, doctors sometimes prescribe a drug for a use not specified by the FDA, but rather based on studies published in peer-reviewed journals showing that the treatment works for other diseases, conditions, or symptoms; this is called "off-label" use. Learn more about the drug development and approval process [3].

More Information

Finding a Clinical Trial [4]

Clinical Trials [5]

Additional Resource

Clinicaltrials.gov [6]

Links:
[1] http://www.cancer.net/about-us
[2] http://www.cancer.net/node/27091
[3] http://www.cancer.net/node/24505
[4] http://www.cancer.net/node/24878
[5] http://www.cancer.net/node/24863
[6] http://clinicaltrials.gov/