The Four Phases of Clinical Trials

Before new medical treatments like pharmaceutical drugs or medical devices can be approved for widespread patient use, they must go through extensive clinical trial testing in people. Clinical trials are research studies conducted with volunteer participants to evaluate the safety and efficacy of experimental treatments. Most experimental treatments must pass through four main phases of clinical trials before they can be submitted for approval. Each successive phase involves more participants and helps answer critical questions that allow researchers to determine if the experimental treatment is ready to be submitted to a government regulatory agency or agencies for review. Based on the information, these agencies decide if an experimental treatment can be approved for use in patients. The four main phases of clinical trials, which will be explained further below, are: Phase 1 - Assessing initial safety and dosage Phase 2 - Evaluating effectiveness and side effects Phase 3 - Confirming efficacy compared to standard treatments Phase 4 - Ongoing study of long-term effects after approval Understanding how an experimental treatment moves through these phases provides helpful context into the careful testing needed before a treatment is deemed ready for widespread therapeutic use. The pathway through clinical trials is lengthy but vital to ensuring an experimental treatment works and is safe for people with a specific condition or illness.

Phase 1 clinical trials: Is the treatment safe?

Phase 1 trials usually include a small number of people. This number varies from one trial to the next, but there are usually fewer than 100 participants in a Phase 1 trial. The participants may be people with a specific disease or condition or healthy volunteers. Researchers conduct Phase 1 trials to learn more about how a treatment behaves in the human body, to learn about any side effects that might happen when someone takes a treatment, or to find the right dose of a treatment to use in Phase II. In some Phase I trials, such as cancer trials, researchers will also look at how each participant's disease responds to treatment. In a Phase 1 trial, a dosage range of the experimental treatment is determined by testing increasingly larger doses with one or more groups of participants. The goal of this research is to learn the maximum tolerated dose with acceptable side effects. Researchers start with very low doses and gradually increase the dosage while closely monitoring for harmful side effects. Safety is carefully checked at each dose before approving further increases. Vital signs, blood tests, ECGs, and other medical tests are done frequently to detect any adverse events. Researchers also learn how the experimental treatment is taken up, moves through, is broken down, and exits the body in a Phase 1 trial. These Phase 1 trials are called Pharmacokinetic studies. Any interactions with food or other medications taken together with the experimental treatment are also studied in Phase 1. All of this information is crucial for designing safe protocols for the next testing phases. The ultimate goal of a Phase 1 trial is to determine a safe dosage range that can then be used in Phase 2 to start assessing efficacy. The safety of participants is the main goal in Phase 1, so any concerns observed can halt a trial.

Phase 2 clinical trials: Does the treatment work?

Phase 2 trials usually include more participants, up to several hundred people. While researchers continue to study a treatment's safety in Phase 2 trials, they also begin to collect data about if and how well a treatment works in people who have the disease or condition that it is being developed to treat. In a Phase 2 trial, participants who have a specific disease or condition get the study treatment at the dosage levels found to be safe in Phase 1. Then the research team monitors

participant health and disease symptoms to get an initial gauge of efficacy. For example, tumor size may be measured in cancer drug trials or viral load for antiviral medication trials. Clinical lab tests also analyze specific genes, proteins, or other substances (called biomarkers) that can indicate the experimental treatment's effect. In Phase 2 clinical trials, researchers refine the methods to set standards, goals, and optimal procedures for larger Phase 3 trials. Phase 2 clinical trials tell researchers more about how safe the experimental treatment is and how well it works before advancing to Phase 3.

Phase 3 clinical trials: Is it better than what's already available?

Phase 3 trials usually include large numbers of participants. Some Phase 3 trials are conducted in multiple countries and may include thousands of people. Phase 3 trials are used to collect more information about how safe a drug is and how well it works. Phase 3 trials will often compare an experimental treatment with the current standard of care to see if it works as well or better, or has fewer side effects, than what is already available to patients. To do this, researchers will assign participants to different treatment groups – participants in one treatment group will receive the new treatment, while participants in another group will receive standard-of-care therapy. Alternatively, participants in one group might receive the new drug plus standard therapy, while participants in another treatment group might receive standard therapy alone. Phase 3 trials can take many years to complete. Researchers might study the experimental treatment in different doses or with other treatments. Often, Phase 3 studies check how well the experimental treatment works over a longer period of time. They might include different people than earlier phase clinical trials did. For example, they might study how well the experimental treatment works in younger or older people. Depending on the intended patient population, these trials must include men and women, as well as people of different ages and racial and ethnic groups, if possible. Participants in these trials should represent the patients who are intended to use and benefit from the treatment if it is approved.

Phase 4 clinical trials: What else do we need to know?

Phase 4 trials may be done after a treatment or device has been approved for use. Phase 4 trials are done to study how safe a drug is and how well it works in large, diverse populations over long periods of time. Phase 4 trials might identify side effects that were not seen in smaller, shorter trials. While pre-approval trials gather data on safety and efficacy, many questions remain unanswered, especially those related to long-term exposure over years or decades. Phase 4 trials also monitor larger patient populations with broader demographic diversity regarding age, gender, ethnicity, and health status. These trials also examine the treatment in real-world conditions. Phase 4 trials may also evaluate efficacy for additional medical indications, different dosage regimens, or new combination therapies. Although expanding the therapeutic scope may be a goal, Phase 4 still prioritizes safety monitoring above all else. The four phases of clinical trials represent a systematic progression of research to evaluate a potential new medical treatment thoroughly. Phase 1 trials begin small, prioritizing safety in dozens of volunteers. Phase 2 expands to refine the methodology and get an initial readout on efficacy. Phase 3 trials are large-scale, often international, studies compared to standard-of-care. They provide robust data to determine risks versus benefits. Finally, Phase 4 trials continue safety vigilance while expanding real-world evidence on long-term impacts.

Each phase builds on the last, making sure populations are protected while bringing innovative therapies from laboratory promise to clinical availability.