CLL SOCIETY
Resource Library

CLINICAL TRIALS

A clinical trial for those living with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) is a carefully controlled research study that is conducted by clinician-scientists to improve the overall care and treatment of those living with the disease. Advances in treatment for blood cancers depend on clinical trials. New medications are studied as well as new combinations of medications, and sometimes already approved medications are being investigated for a different indication or disease. Clinical trials save lives, yet only 5% of adults with cancer participate. Participation in clinical trials can be a valuable part of disease management because they can provide early access to cutting-edge therapies that would not otherwise be available.

HOW SAFE ARE CLINICAL TRIALS?

Clinical trials are designed with strict ethical guidelines and safety measures to protect participants. Those who choose to participate are required to attest to understanding the potential risks and benefits before joining a trial and they are free to leave the trial at any point. While it's impossible to eliminate all risks, researchers and government agencies require multiple things to take place before the clinical trial design is ever approved to minimize risk and ensure patient safety. Here are a few of those steps:

- **Researchers perform pre-clinical trials in a laboratory setting** – Before investigational drugs are approved for testing in human clinical trials, they must first be thoroughly studied in a laboratory setting with strict federal and medical oversight to ensure safety. During this step, researchers assess how the drug interacts with biological tissue samples. This may include cells, tissues, and animal models. The pre-clinical trial setting is utilized to evaluate the effectiveness of the drug (or drugs) being studied and to determine the appropriate safe dosage levels that will be used during the human clinical trial.
- **Researchers develop the proposed clinical trial design** When researchers feel they have enough data to move forward with developing an application to perform a clinical trial, they must first put together a detailed research proposal that outlines the study's objectives, eligibility criteria, treatment plan, and data collection methods. The protocols and clinical trial design must ensure consistency and safety throughout the trial.
- **An application for "initial drug approval" is submitted to the FDA** – The data that is obtained during the pre-clinical trial is meticulously reviewed by the FDA to assess how safe the drug will be and to help determine how well the drug might work. After reviewing the pre-clinical trial information and the proposed study design, a decision is then made on whether the researchers can proceed to human clinical trials. During this phase, the FDA also must review and ultimately approve the proposed clinical trial design and associated protocols of the study.
- **The drug is reviewed by an Institutional Review Board (IRB)** – After the initial drug approval application is accepted by the FDA, an expert medical Institutional Review Board (also known as an independent ethics committee) plays a crucial role in ensuring the ethical conduct of research involving human subjects is carried out. The IRB is a committee established within an institution (such as a university, hospital, or research organization) whose primary purpose is to protect the rights and safety of individuals who participate in research studies. They are responsible for reviewing research proposals to ensure that they adhere to ethical guidelines and legal requirements. When researchers plan a study involving human subjects, they submit their research protocols and related materials (such as informed consent documents) to the IRB who conduct a thorough review of the study design, plan for participant recruitment, informed consent procedures, and potential risks and benefits. Based on their assessment, the IRB can approve the clinical trial design, require modifications, or disapprove of the research project altogether.

WHAT DO THE DIFFERENT PHASES OF A CLINICAL TRIAL MEAN?

For a drug to be approved by the FDA, it must undergo three distinct phases of a trial. Then a fourth phase occurs after drug approval to ensure that data is still being collected long-term. Here are the phases of clinical trials with brief explanations:

- **Phase I Trial – Is the drug safe, and what's the best dose?** These early clinical trials involve small groups of healthy individuals who initially receive a very low dose. They are closely monitored and if no significant problems are observed, another group of participants are given gradually increasing dosages until an optimal level is found. These Phase I trials aim to ensure safety and efficacy, but they carry the most risk due to limited knowledge of the drug's effects on humans. They also usually require the most frequent visit schedule for laboratory and clinical safety monitoring.
- **Phase II Trial – Does the drug work?** Phase II trials involve a larger group of individuals who all receive the drug to evaluate the effectiveness and closely monitor for side effects. Phase II trials are usually mid-sized, and the goal is to measure patient response and survival outcomes.
- **Phase III Trial – Is the new drug better than the current standard of care?** Phase III trials last longer and involve more participants. They are large-scale studies that are conducted to compare the standard treatment being used to treat the disease against the new drug being tested. Placebos may be used during this phase, so it is important for anyone who is considering a clinical trial to ask whether they may not get the drug being tested.
- **Phase IV Trial – What else can be learned about the already approved drug?** Phase IV trials, also known as post-marketing surveillance trials or post-approval studies, monitor the real-world outcomes of a drug and evaluate the long-term safety and effectiveness in larger and more diverse populations.

CLINICAL TRIALS (continued)

WHAT HAPPENS ONCE THE HUMAN CLINICAL TRIAL HAS BEEN APPROVED TO TAKE PLACE?

After the FDA approves the application for initial drug approval, the trial design and protocols have been established, and the study has received IRB approval, the researchers can then take steps to begin recruiting for the clinical trial. This is the time when interested individuals go through a rigorous screening process to ensure they are eligible to participate in the clinical trial. Participants will receive detailed information about the study and will be required to sign an Informed Consent. This form explains the study, procedures, benefits, requirements, risks involved, and other relevant details of the study. During the clinical trial, the principal investigator is continually monitoring to ensure safety protocols are being followed and they are responsible for reporting findings to the IRB and the trial sponsor.

WHAT KIND OF RISKS ARE ASSOCIATED WITH PARTICIPATING IN A CLINICAL TRIAL?

Participating in clinical trials can be beneficial, but it is important to be aware of potential risks. Phase I trials tend to carry more risk since less is known about the drug at that point and it has only thus far been tested in laboratory settings.

- As clinical trials progress and study populations become larger and more diverse, unexpected side effects and health risks may occur.
- Participants are randomly assigned to either treatment or control groups and blinded to ensure reliable and accurate study findings. Blinding (single-blind or double-blind) prevents bias by keeping participants and researchers unaware of who is receiving what treatment. Also, participants are not guaranteed that they will receive the drug being tested (although, this is rare when cancer drugs are being studied due to ethical requirements).
- Clinical trials can be somewhat inconvenient because they require more time than standard care, including travel to study sites for medical appointments, detailed tests, multiple blood draws, and many follow-up visits.
- Many clinical trials cover study-specific medications and testing, but participants may still incur expenses for travel, co-payments, or lost wages due to time away from work.
- There is a possibility that the medication being received may not be effective.

WHAT ARE THE BENEFITS OF PARTICIPATING IN A CLINICAL TRIAL?

- One of the biggest benefits of participating in a clinical trial is gaining early access to cutting-edge therapies that may even be more effective than other available treatments. And in some cases, there is no cost to receive these cutting-edge therapies.
- You are making a contribution to medical research, which helps gather valuable data for the development of better therapies for future patients.
- There is close monitoring and care throughout the study period, including regular medical assessments, laboratory tests, and follow-up visits.
- Participants gain access to experts at leading medical institutions.
- Participation in a clinical trial can provide a sense of empowerment and hope from taking an active role in managing one's health.
- Individuals who enroll in clinical trials are free to leave at any time, for any reason, without penalty.

WHAT QUESTIONS SHOULD I ASK WHEN I'M CONSIDERING A CLINICAL TRIAL?

- What is the purpose of the study?
- What is the clinical trial phase, and does the study involve randomization and placebo arms?
- What are the possible short and long-term risks, side effects, and benefits?
- What treatments, medical tests and procedures does the study require?
- How often is the treatment administered?
- What is the anticipated length of the study?
- Are medications provided for the study and will insurance cover any costs?
- Where will my treatment take place?
- How will I know if the treatment is working?

DOES INSURANCE USUALLY COVER CLINICAL TRIALS?

When considering a clinical trial, it is important to understand which charges are covered by the clinical trial sponsor, and which are covered by the insurance company. The trial sponsor or funder usually pays for investigational medications and research-related tests. However, some tests and treatments that are considered a part of the participants usual standard of care may be billed to insurance. It is important to note that out-of-network care may not be covered. General cost information should be provided by those conducting the study before individuals sign the consent to participate. However, keep in mind costs covered may not reflect each participant's individual costs. It is recommended that individuals contact their insurance companies to fully understand coverage and any additional costs that may be incurred before agreeing to participate in a clinical trial.

HOW CAN I FIND OUT IF THERE IS A CLINICAL TRIAL FOR ME?

Finding a clinical trial can be overwhelming. Individuals are often left to search on their own through www.ClinicalTrials.gov, leaving them with more questions than answers. The Leukemia and Lymphoma Society's Nurse Navigator Program can provide some assistance. But the best place to start is to have a conversation with your healthcare provider. Many offices that participate in clinical trials have a Nurse Navigator who will be able to connect you with a clinical trial and help guide you through the process.