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Foundation**
Beauty. Strength. Transformation.

UNDERSTANDING CLINICAL TRIALS

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UNDERSTANDING CLINICAL TRIALS

WHAT ARE CLINICAL TRIALS?

A clinical trial is a type of medical research study that determines whether an intervention – a new drug, medical device or diagnostic tool – is safe and/or effective. The investigators leading a clinical trial develop a protocol – a detailed document that describes how the study will be performed. A clinical trial recruits volunteer study participants to test the intervention. Clinical trials are conducted by government agencies, universities, hospitals, and drug companies.

It takes an average of seven years for a promising intervention to progress through the steps of clinical testing. First, the protocol must be approved by the institutional review board (IRB), and by the Food and Drug Administration (FDA). Following this initial approval, the intervention progresses through a rigorous series of clinical studies. Some interventions that are being tested never complete the testing series. Others complete all of the testing, but they are not approved because they are either not safe or because they are not effective, or both.





WHAT ARE THE DIFFERENT TYPES OF CLINICAL TRIALS?

Clinical trials are categorized into four phases or steps.

- **Phase I trials:** Phase I clinical trials are the first time the drug is used by people. For these clinical trials, a small group of healthy volunteers are given the drug to determine the dose range that is tolerated for a single dose or for multiple doses. These studies are also performed to learn if the drug has any side effects.

- **Phase II trials:** If the phase I studies have demonstrated that the new drug is safe, phase II clinical trials are conducted on patients with the disease or condition to be treated, diagnosed or prevented. Phase II studies are performed to determine if the new drug is safe and effective at treating the disease. Phase II trials may also be performed to determine if drugs that are already on the market can be used for another purpose.

- **Phase III trials:** Phase III clinical trials are done as a final step to gain

CLINICAL TRIALS ALSO HELP US LEARN MORE ABOUT DISEASES AND OTHER HEALTH CONDITIONS.

regulatory approval to market the drug. In phase III trials, the drug is given to a large group of patients with the disease. For comparison, some of the study participants are given standard treatment, placebo or both.

- **Phase IV trials:** Phase IV trials, sometimes referred to as post-marketing surveillance, are performed after the drug is available and in use to the general public to provide additional details about the drug's safety. This may include side effects not observed in the earlier clinical trials. Evaluations may include different formulations, dosages, durations of treatment, and interactions of different medicines. Evaluations may also include new age groups, races and other types of patients. If new side effects are identified that are serious, the use of the drug may be limited or restricted. In some cases, the intervention may be removed from the market.

You may also hear clinical trials being described in the following ways:

- **Randomized trials:** In randomized clinical trials, the treatment options in breast cancer trials are assigned to the study participants by a computer. This gives you an equal chance of being assigned to any of the treatment groups. The different types of treatment groups may be called "arms". In some cases, the arms may differ by treatment type or by treatment length. By contrast, in non-randomized trials, the doctor chooses your treatment based on your health needs and other factors.

- **Blinded trials:** In blinded clinical

trials, you and/or the research team do not know what treatment you are receiving. If it is a single-blinded study, you do not know what treatment you are receiving. If it is a double-blinded study, neither you nor the research team knows what treatment you are receiving. By contrast, if the study is non-blinded, both you and the research team know which treatment you are receiving.

- **Basket trials:** This is a new type of clinical trial. Unlike most clinical trials which focus on the organ where the cancer is located, basket trials test cancers that share a specific molecular characteristic – regardless of where the cancer is found. For example, a basket trial may consist of patients with breast cancer, lung cancer and pancreatic cancer, if these cancers all behave the same way.

- **Umbrella trials:** In this type of clinical trial, the researchers focus on specific subtypes of a cancer. For example, an umbrella trial for breast cancer may group and treat study subjects with luminal A breast cancer vs HER2 breast cancer. Umbrella trials make it easier to look for common molecular characteristics among the study subjects.

WHY ARE CLINICAL TRIALS IMPORTANT?

Today, people are living longer in part because of the results of clinical trials. Imagine for a minute –medications and medical devices did not go through clinical trials before they were approved for public use. Clinical trials





also help us learn more about diseases and other health conditions. This includes learning how the condition develops, if there are certain characteristics that make us more likely to get a disease, and which treatment would be better for treating us.

WHO SHOULD PARTICIPATE IN A CLINICAL TRIAL?

For each clinical trial, the accompanying study protocol describes who can and cannot join the study. These enrollment characteristics may include age, gender, medical history, previous treatment, current health status, and the particular type or stage of cancer.

After you have signed an informed consent form, which indicates that you have agreed to participate in the clinical trial, a doctor or nurse will assess your medical history, perform a

physical exam and perform laboratory tests to determine whether you meet the eligibility criteria. Do not feel discouraged if you cannot join a specific clinical trial. The research team's top priority is to ensure that the study is right and safe for all of the patients. So if you are not selected, you can try to join another clinical trial.

HOW ARE CLINICAL TRIALS CONDUCTED?

Clinical trials follow the set of rules that are described in the protocol. After the protocol has been approved by the IRB and the FDA, the research team begins recruiting study subjects. Upon receipt of the signed informed consent from each study subject, these individuals are then treated and cared for as detailed in the protocol.

WHO CONDUCTS CLINICAL TRIALS?

Clinical trials are led by a principal investigator, who is usually a medical doctor. The clinical trial team may include doctors, nurses, study coordinators, social workers and other health care professionals.

WHO SPONSORS CLINICAL TRIALS?

The money to perform clinical trials is commonly provided by pharmaceutical companies who have produced a drug or medical device. Academic medical centers, federal agencies, and hospitals may also provide funds for clinical trials.

HOW LONG ARE CLINICAL TRIALS?

It takes an average of seven years from the beginning of clinical testing of the investigational drug to market approval. The average length of time for each phase is as follows: 21.6 months for phase I, 25.7 months for phase II and 30.5 months for phase III.

Sometimes, the general public has faster access to investigational drugs through one of following four FDA programs:

- **Fast track:** If the investigational drug is one of a few available medicines or if it is the only available option to treat a serious medical condition or if it proves to be superior to existing treatment, the FDA may place the

investigational drug on the fast track. This means that the research team will update the FDA more frequently about the progress of the study. Then, if the FDA thinks that the investigational drug is safe and effective, they will process it quicker for release to the general public.

- **Priority review:** Generally, when a research team submits an application for the FDA to approve the drug for



sale, the FDA begins their review within 10 months of the application submission. If a drug has shown much promise for treating a condition, the FDA may grant priority review to the medicine, and they will begin their review at 6 months after the application submission.

- **Accelerated approval:** Instead of waiting until the investigation drug has completed all three phases before reviewing the drug for approval, the FDA may complete their review much earlier. Typically the drugs that had priority review are the ones that receive accelerated approval.

WHERE ARE CLINICAL TRIALS CONDUCTED?

Clinical trials can take place in various locations such as hospitals, universities and community clinics.

WHAT ARE THE BENEFITS OF PARTICIPATING IN A CLINICAL TRIAL?

Less than 5% of all cancer patients are currently enrolled in a clinical trial. Further, even though cancer mortality is higher among minorities, less than 10% of racial and ethnical minorities are enrolled in clinical trials – with minorities being 60% as likely to enroll in a clinical trial compared to whites. The under-representation of minorities in clinical trials means that there are few studies that analyze and report safety and efficacy by race or ethnicity. Therefore, it is difficult to know if minority patients tend to have a specific

type or subtype of cancer and if they process certain drugs differently.

As a minority, participating in a clinical trial allows the researchers to conduct a study that is more representative of the general population and to gather racial and ethnic data on the disease and treatments that they are studying. Participating in a clinical trial also allows you to have access to the newest treatments and care that are hopefully more effective than the current standard care. As a clinical trial subject, your participation in the study could help you, as well as others who are affected by breast cancer. In some cases, participants are even compensated.

WHAT SHOULD I KNOW BEFORE I DECIDE TO BE PART OF A CLINICAL TRIAL?

When you express interest in learning more about a clinical trial, you will be provided with an informed consent form, which describes the clinical trial. If there is something on the form that you do not understand, the study doctors and nurses are available to answer your questions. Before you decide to be part of a clinical trial, make sure that you understand:

THE UNDERREPRESENTATION OF MINORITIES IN CLINICAL TRIALS MEANS THAT THERE ARE FEW STUDIES THAT ANALYZE AND REPORT SAFETY AND EFFICACY BY RACE OR ETHNICITY.



- the purpose of the study
- the tests and procedures that will be used
- the risks and benefits
- the length of the study
- how often you will meet with the clinical trial team
- how much of your time is expected
- what are your responsibilities
- what procedures are in place to keep you safe
- how to contact someone if you have an adverse effect
- what procedures are in place to keep your information confidential.

As a clinical trial subject, there are a few additional items to consider:

- You are not guaranteed to receive the new treatment being tested. Instead, you may receive the older treatment or you may receive the placebo.
- Depending on the type of treat-

ment being studied and your individual health, you may experience unpleasant, and sometimes serious, side effects. Often these side effects are temporary and end when the treatment stops. The researchers will warn participants of all known side effects, but unanticipated problems may arise.

- The experimental treatment may not work as well as intended, and in some cases, it may not work as well as standard treatment.
- You may be required to devote more of your time and make changes to your daily schedule. For example, you may spend more time traveling to the study site and you may spend time in the hospital. You may also spend more time taking treatments.



WHAT IS EXPECTED OF ME WHEN I PARTICIPATE IN A CLINICAL TRIAL?

As a research participant, you are an important part of the research study. It is important that you understand your role and how it impacts your safety and welfare. Some of your

research team

- telling the research team about what worries you about the study
- following directions for proper use, dosing, and storage of self-administered study medications

THE INSTITUTIONAL REVIEW BOARD ALSO HELPS TO PROTECT THE RIGHTS AND WELFARE OF RESEARCH SUBJECTS.

responsibilities include:

- reading the entire informed consent form and asking questions about what you don't understand about the study
- following all instructions from the

- telling the research team if you have any side effects, hospitalizations, missed doses, and pregnancy
- keeping scheduled appointments or if unable to do so, informing the research team as soon as possible

- notifying the research team when your contact information changes (for example, phone number, address)
- informing the research team if you choose to withdraw from the study

IS IT SAFE FOR ME TO PARTICIPATE IN A CLINICAL TRIAL?

The Food and Drug Administration helps to protect the rights and welfare of research subjects by performing in-

Review Board approves a proposed clinical trial if:

- informed consent will be obtained
- there are minimal risks to research subjects
- the risks to research subjects are reasonable when compared to the anticipated benefits of the study
- there is a clear plan for monitoring research subjects' data and safety
- there is a clear plan for maintaining

AT THE END OF EACH PHASE OF A CLINICAL TRIAL, THE RESULTS ARE COLLECTED AND ANALYZED TO DETERMINE IF THE EXPERIMENTAL DRUG IS EFFECTIVE AND SAFE, AND IF THERE ARE ANY SIDE EFFECTS.

spections of clinical trial study sites and the research team to ensure that the study is being performed properly, and by verifying the quality and integrity of data from the clinical trial.

The Institutional Review Board also helps to protect the rights and welfare of research subjects by ensuring that the proposed clinical trial follows ethical principles and meets federal regulations for the protection of research participants. The Institutional Review Board protects the rights and welfare of research subjects, by balancing the individual rights of research subjects with increased knowledge gained by society as a whole. The Institutional

research subjects' privacy and confidentiality

- there is a clear plan for applying safeguards for vulnerable research subjects

As the study progresses, the research team submits annual progress reports to the Institutional Review Board and alerts them of adverse effects experienced by the research subjects. Thus, the Institutional Review Board is continuously reviewing risk-benefit of the clinical trial and deciding if the study should continue.





HOW DO I ENROLL IN A CLINICAL TRIAL?

You can enroll in a clinical trial by signing an informed consent form. During the informed consent process, the research team will explain to you that your participation is voluntary, and that you can stop participating at any time. The researcher will also explain the study to you and answer any questions that you have. You can take the informed consent form home to think further about whether you would like to participate in the study. If you do decide to participate in the clinical trial, you must sign the informed consent form.

By signing the informed consent form, you are acknowledging that the researcher has provided you with all of the appropriate information so that you are “informed” (educated) about your rights and about all aspects about the study, and that you “consent” (agree) to voluntarily participate as a research subject. A typical informed consent form will include:

- the clinical trial’s purpose, procedures, treatment, length of research subject participation, approximate number of enrolled research subjects
- your right to voluntarily decide if you would like to participate in the study
- foreseeable discomforts to research subjects
- benefits to research subjects
- alternative treatments or procedures that might be advantageous to

research subjects

- plan for maintaining research subjects’ confidentiality and privacy
- contact information for the research team
- possible compensation



WHAT HAPPENS AFTER A CLINICAL TRIAL IS COMPLETE?

At the end of each phase of a clinical trial, the results are collected and analyzed to determine if the experimental drug is effective and safe, and if there are any side effects. The results will determine if testing should be stopped or if it is OK to move on to the next phase of the clinical trial. The results are submitted to the Institu-

tional Review Board and the Food and Drug Administration. The researchers may submit the results to science journals for peer-review and publication. The highlights from these studies are sometimes re-written in non-technical language for the general public to easily understand.

If the experimental drug completes all phases of the clinical trial and is shown to be safe and effective, the experimental drug could become the standard treatment.

TALKING WITH YOUR HEALTH CARE PROVIDER AND CLINICAL TRIAL STAFF

Clinical trials are led by a principal investigator, who is usually a medical doctor. The team may include doctors, nurses, study coordinators, social workers and other health care professionals. The clinical trial team is available to speak with you about the study and answer your questions. Below are some suggested questions that you can ask your research team:

- What is the purpose of the study?
- Who is going to be in the study?
- Where is the study site?
- How will I know that the treatment is working?
- Who will be in charge of my care?
- Why do researchers believe the new treatment being tested may be effective?

- Has the experimental drug been tested before?
- What kinds of tests and treatments are involved?
- How do the possible risks, side effects, and benefits in the study compare with my current treatment?
- How might this clinical trial affect my daily life?
- How long will the clinical trial last?
- Will hospitalization be required?
- Who will pay for my treatment?
- Will I be reimbursed for other expenses?
- What type of longterm follow up care is part of this study?
- Will I have access to the clinical trial results?

WHERE CAN I FIND A CLINICAL TRIAL?

If you would like to join a clinical trial, the best place to start is to ask your doctor or someone else on your medical team. Your doctor may know of a clinical trial that could be a good option for you and provide you with the relevant information. In other cases, your doctor may search for a clinical trial for you. If you decide to look for clinical trials on your own, a few sites are listed below. Be sure to bookmark the website for easy reference and print out the study protocol for the studies that interest you. You can



look at these websites on your own computer or on computers that are accessible to the general public – such as in public libraries. It is important that you remember to be your own advocate when looking up clinical trials to find the best breast cancer treatment. If your doctor does not support your interest in clinical trials or if they are unable to answer your questions, feel free to get a second opinion from another doctor.

- **ClinicalTrial.gov** has almost 8,000 breast cancer clinical trials.
- **EmergingMed.com** has over 1,000 breast cancer clinical trials.
- **BreastCancerTrials.org** has over 600 breast cancer clinical trials. There are almost 90 trials for early stage breast cancer and over 200 trials for advanced breast cancer.
- **CenterWatch** has over 700 breast cancer clinical trials. They are all currently recruiting study subjects.

WHERE CAN I FIND CLINICAL TRIAL RESULTS?

The clinical research team will inform you of where to find the results of the clinical trial. The results from clinical trials are usually published in scientific or medical journals. Some journals require a subscription to access articles.

HOW TO INTERPRET A CLINICAL TRIAL STUDY?

- **Baseline Characteristics:** Baseline characteristics are data collected at the beginning of a clinical trial. These include age, gender, weight, blood pressure, and current medications.
- **Investigation Drug/Experimental Drug:** This is the drug that is being tested in the clinical trial.
- **Sample Size:** The sample size refers to the number of research subjects in the clinical trial. When the study protocol is being developed, investigators perform mathematical predictions to determine how many study patients are needed to strengthen the validity of the results. This mathematical calculation is important because even though results from a research study may suggest that the experimental drug is effective, it could be a coincidence. When the same result is observed in many people, it is less likely to be due to coincidence.
- **Control Group:** The control group refers to the group of research subjects who receive either a dummy treatment, an older treatment or no treatment at all. With the control group, investigators are able to specifically determine how likely it is for patients receiving the treatment to get better on their own or on a different treatment.
- **Study Duration:** The study duration refers to the length of time of the research study. It is important that investigations treat “treatment group” patients and “control group” patients

during the same time period and observe the two groups of patients side-by-side. In the past, investigators used results of a “control group” that were monitored at an earlier time, perhaps when medical advances were not as good. This made the study non-ideal because it used an unfair comparison. Today, research studies are done on all treatment groups at the same time.

- **Study Sample:** The study sample refers to the group of research participants. The study sample represents a subset of the population who match the eligibility criteria of the study. Investigators often recruit a diverse group of study subjects so that they are representative of the general population.

- **Trial End Points:** Trial end points are the primary results or outcomes that the researchers are measuring. Some examples of trial end points include response rate – how well the cancer shrinks in response to treatment, duration of response – how long before the cancer starts to grow again, disease progression – does the cancer grow despite the treatment, and survival rate – how long do the patients live.

- **Response:** If the cancer completely disappears during treatment, this is a complete response – this is the best case scenario. If it shrinks incompletely, this is a partial response. If the treatment has no effect on the cancer, then the disease is stable. If the cancer disappears and then begins to grow again, this is called a relapse.

- **Disease Progression:** During treatment, if the cancer size increases by

20% or if a secondary cancer develops, this is called disease progression.

- **Survival:** At the end of a clinical trial, the research team continues to follow the research subject results so that they can present 5-year survival or 10-year survival data. These data refer to the percent of research subjects who are alive for 5 or 10 years, respectively, after treatment. Disease-free survival refers to the percent of research subjects who are alive and cancer-free after a specific number of years. Overall survival is the number of research subjects who are alive with or without cancer. Median survival is the length of time when half of the study subjects are still alive.

- **Adverse Events:** An adverse event refers to a change in a research subject’s health status during the clinical trial, and it is an unfavorable or unintended sign, symptom or disease. Some examples of adverse events include convulsions, nausea, hair loss, development of drug dependency or drug abuse, and death.

- **Statistical Significance:** This refers to whether an event or difference occurred by chance alone. In clinical trials, the level of statistical significance depends on the sample size, observations documented in the study, and the size of the differences or number of events that occurred.

GLOSSARY OF TERMS

A

Adverse Events: An adverse event refers to a change in a research subject's health status during the clinical trial, and it is an unfavorable or unintended sign, symptom or disease.

Arm: This refers to the treatment group of a clinical trial.

C

Clinical Trial: With the approval of the Food and Drug Administration (FDA) and the institutional review board (IRB), scientists conduct research studies to test new drugs, treatments or devices in volunteer research subjects.

Confidentiality: This is the assurance that a research subject's information will be kept in secret and that access to the information will be restricted to only authorized personnel.

Control Group: This is a group of patients who are similar in demographics as the experimental group of patients. The control

group may be healthy individuals who are receiving a placebo or they may be receiving standard therapy.

D

Data: Data are a series of observations, measurements and facts about the research subjects that are recorded during the study.

Disease Progression: If during treatment, the cancer size increases by 20% or if a secondary cancer develops, this is called disease progression.

Dosage Regimen: The dosage regimen refers to timing for each dose of the medication eg. twice per day, or the quantity of the medication that is given a specific time of dosing 2 tablets every 6 hours.

Double Blind: This refers to studies where neither the patients nor the physicians know which treatment the patient is receiving.

E

Efficacy: Efficacy is the

ability of the drug to produce beneficial effects on the duration or course of the disease.

Exclusion Criteria: Exclusion criteria refer to the factors that determine which individuals cannot participate in a research study. These criteria include age, gender, type and stage of the disease, treatment history and medication conditions.

Experimental Group: This is a group of patients who are receiving the intervention that is being tested.

F

FDA: The Food and Drug Administration (FDA) is an agency that controls and supervises food and drug safety.

H

HIPAA: The Health Insurance Portability and Accountability Act of 1996 provides guidelines to safeguard medical information.

I

Inclusion Criteria: Inclusion criteria refer to the factors that determine which individuals can participate in a research study. These criteria include age, gender, type and stage of the disease, treatment history and medication conditions.

Informed Consent: This describes the process by which the researchers provide information about a study to potential study volunteers. If you decide that you would like to be part of a study, you will sign a form to consent or agree to voluntarily participate in the study.

IRB: An institutional review board (IRB) is an independent committee that ensures that the research study is ethical and that it has minimal risks to the research subjects.

Investigator: This is a researcher in a clinical study. The principal investigator is the researcher who is responsible for the scientific and technical direction of the clinical trial.

P

Pathology report: A pathology report is a document that contains information on your cancer. This information is what the research team has learned about what the cancer cells and tissues looked like.

Peer-review: This is evaluation by experts in the field.

Phase: This is a step within clinical trial process: phase 1, 2, 3 and 4.

Placebo: This is a substance that has no therapeutic effect that is used as a control for testing new drugs. The placebo is physically indistinguishable from the experimental drug. If a study uses a placebo, the study is described as “placebo-controlled” and the study subjects who receive the placebo are called the “control group.”

Principal investigator: This is the researcher who is in charge of the study.

Protocol: A protocol is a map to a research study.

It includes details such as eligible characteristics of research subjects, methods, treatment, safety, and risk and benefits.

Prospective: When a study is described as prospective, it means that the researchers are providing the study subjects with a particular treatment and observing the study subjects over a period of time (usually months or years) to record results or outcomes. Outcomes could include side effects, and improved or worsened health conditions.

R

Randomized: In some types of studies, the study patients are randomly assigned by a computer to one of the treatment groups.

Research: This is a careful and systematic study to answer a question. In science, we perform research to better understand a disease and improve treatments.

Research costs: Research costs refer to the costs of the investigational drug as well as tests or office visits

that are needed for the clinical trial.

Research Subject: A research subject, study patient or human subject refers to a person who is being observed by researchers to determine the effect and safety of a treatment.

Response: Response refers to the effect of the treatment on cancer.

Risk: This is a measure of likelihood of harm to human health or the severity of harm that may occur.

Risk-Benefit Ratio: This is a comparison of individual subject risk and potential benefits to the individual and to society at large.

Routine care: Routine care refers to the doctor visits and other aspects of the medical care that you would have as part of your standard treatment.

S

Sequence: This is the order in which something occurs, such as the order in which you will receive the medication.

Single-Blind: This refers to studies where the patients do not know whether they are receiving the experimental drug or another drug.

Sponsor: The sponsor is the organization or person who oversees the clinical trial and is responsible for analyzing the data.

Statistically Significant: To determine if the outcomes between the various treatment groups did not differ simply because of chance, researchers do a test on the results to see if a p value of 0.05 or less was achieved. If a p value of 0.05 or less was achieved, then the results are statistically significant.

Study Sample: This refers to the group of research participants who are a "sample" of the general population or a "sample" of the group affected by a particular disease or condition.

Study Duration: The study duration refers to the length of the research study.

Survival: An important data outcome of a clinical

trial is the percent of research subjects who are alive 5 years and 10 years after treatment. Disease-free survival refers to the percent of research subjects who are alive and cancer-free after a specific number of years. Overall survival is the number of research subjects who are alive with or without cancer. Median survival is the length of time when half of the study subjects are still alive.



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