Clinical Trials: What You Need to Know

Clinical trials are studies in which people volunteer to test new drugs or devices. Doctors use clinical trials to learn whether a new treatment works and is safe for people. These kinds of studies are needed to develop new treatments for serious diseases such as cancer.

Deciding to take part in a clinical trial can be hard if you have cancer. But it is your choice to make, if there is a clinical trial for which you qualify. A lot has changed over the past few decades, and many people want to know as much as possible about all of their options before they make up their minds.

There is always uncertainty when you're thinking about a clinical trial. Part of it is that the doctors in charge of a clinical trial don't know ahead of time how things will turn out. If they did, there would be no need for the study in the first place. So there's no simple answer to the question, "Should I take part?"

Most people don't pay much attention to clinical trials until they have a serious illness like cancer. Medical breakthroughs (the results of clinical trials) often make the news, but you usually don't hear about clinical trials themselves unless something has gone wrong in one of them. For instance, the media is quick to report an instance when a volunteer in a study is harmed. Although it is very rare, people have been harmed or even died while taking part in clinical trials. Reports of these tragic outcomes are important, because they help to expose problems in the system. These problems can then be handled so that they don't happen again. Because of bad things that happened in the past, there are now laws, requirements, and procedures in place to protect the rights and the health of human volunteers.

What you usually don't hear about in the news are the thousands of people who are helped each year because they decided to take part in a clinical trial. You also aren't likely to hear about the millions who benefit from others' participation in clinical trials.

There is no right or wrong choice when it comes time to decide on taking part in a clinical trial. The decision is a very personal one and depends on many factors, including the benefits and risks of the study and what you hope to achieve by taking part. It also depends on your own values, preferences, and priorities.

Knowing all you can about clinical trials in general -- as well as the ones you are thinking about taking part in -- can help you feel better about your decision. If you do decide to take part, knowing what to look for and what to expect ahead of time can be helpful, too.

This guide will address many basic questions and concerns so that you will be better prepared to discuss clinical trials with your doctor and your family. It should help you decide which questions you need to ask and what the answers may mean for you. But in the end, only you can decide if taking part in a clinical trial is right for you.

One last note: this guide focuses on clinical trials for people who are being treated for cancer. But most of the information here applies to other types of clinical trials, too.

Why do we need clinical trials?

Clinical trials show us what works (and what doesn't) in medicine. They are the best way doctors have found to learn what works best in treating diseases like cancer. Clinical trials are designed to answer 2 important questions:

- Does the new treatment work in humans? If it does, doctors are also looking for how well it works. Is it better than what's now being used to treat a certain disease? If it's not better, is it at least as good, perhaps while causing fewer side effects? Or does it work in some people who aren't helped by current treatments? In other words, is it a step forward? A treatment that doesn't offer anything new probably isn't worth studying.

- Is the new treatment safe? This must be answered while realizing that no treatment or procedure -- even one already in common use -- is entirely without risk. But do the benefits of the new treatment outweigh the possible risks?

Answering these questions, while exposing as few people as possible to an unknown treatment, often requires several different clinical trials. They are usually grouped into "phases." Clinical trials in each phase are designed to answer certain questions, while trying to make sure the people taking part are kept as safe as possible. Every new treatment is tested in several phases of clinical trials before being considered reasonably safe and effective. These phases are discussed in the section, "What are the phases of clinical trials?"

How long have clinical trials been used?

Some doctors and scientists conducted what would now be thought of as clinical trials as far back as the late 1700s, but clinical trials were not used widely until the middle of the 20th century. Up until that time, doctors relied on their own experience in similar cases and on the teachings of those who came before them. Progress was slow, and very few medicines could even be tested.

With the discovery of the first antibiotics and other drugs, doctors needed a reliable way to tell what worked from what didn't. They also needed ways to find out which of the countless remedies available at that time were safe for people to use. So they came up

with ways to test and compare treatments in certain groups of people. The results of these early clinical trials proved to be more useful than relying on whether or not something worked for one person or a few people.

In the United States, the Food and Drug Administration (FDA) began overseeing the safety of new treatments in the late 1930s, but didn't require proof that they actually worked until the early 1960s. Today, new drugs and medical devices must go through several phases of clinical trials (discussed later) before they can be approved for use. The FDA must approve new drugs and medical devices (but not dietary supplements) before they can be advertised or sold to the public.

Based on what we have learned about cancer in recent years, researchers can now develop new treatments in a more logical way and much faster than in the past. But it's still a hard process that takes a long time.

New treatments have to pass many tests before they get to you.

Clinical trials are only a small part of the research that goes into developing a new treatment. Drugs of the future, for example, first have to be discovered or created, purified, described, and tested in labs (in cell and animal studies) before ever reaching human clinical trials. About 1,000 potential drugs are tested before just one reaches the point of being tested in a clinical trial.

On average, a new cancer drug has at least 6 years of research behind it before it even makes it to clinical trials. But the major holdup in making new cancer drugs available is how long it takes to complete clinical trials themselves. It takes an average of about 8 years from the time a cancer drug enters clinical trials until it is approved.

Why so long? To be sure it is safe and effective, researchers look at each new treatment in several different studies. Only certain people are eligible to take part in each clinical trial. And cancer clinical trials take years to complete. It takes months, if not years, to see if a cancer treatment works in any one person. And figuring out if a drug really improves survival can take a very long time.

The biggest barrier to completing clinical trials is that not enough people take part in them. Fewer than 5% of adults (less than 1 in 20) with cancer will take part in a clinical trial. According to the Pharmaceutical Research and Manufacturers of America (PhRMA), more than 800 cancer medicines were being tested in clinical trials in 2009 (the most recent year numbers were published). Not all of these drugs will prove to be useful, but those that are may be delayed in getting approved because so few adults volunteer.

The main reason people give for not taking part in a clinical trial is that they didn't know the studies were an option for them. But there are many other reasons. Some people may want to take part but aren't eligible. Some people are uncomfortable with the idea of being a volunteer in a study. Others worry that they won't be treated fairly or could be

harmed by an unproven treatment. All of these are valid concerns. We have addressed them in more detail in the section, "Should I think about taking part in a clinical trial?"

What happens before clinical trials?

One of the most important points that must be decided before a clinical trial can be done is whether it is ethical to ask patients to volunteer for the experimental treatment. Has the study been designed, as much as possible, to make sure the people involved will be safe? Will the volunteers get a treatment that is at least as good as, and maybe even better than, what they would get if they did not volunteer for the study? Scientific panels are set up to review and approve all clinical trials to make sure questions like these are answered before the researchers are allowed to sign up patients. Certain types of information are needed before these questions can be answered.

Pre-clinical (or laboratory) studies

Clinical trials are medical research studies involving people. But they are done only after *pre-clinical* studies suggest that the proposed treatment is likely to be safe and will work in people.

Pre-clinical studies, also called *laboratory studies*, include:

> **Cell studies:** These are often the first tests done on a new treatment. To see if it might work, researchers look for effects of the new treatment on cancer cells that are grown in a lab dish or a test tube. These studies may be done on human cells or animal cells.
>
> **Animal studies:** Treatments that look promising in cell studies are next tested on cancers in live animals. This gives researchers an idea of how safe the new treatment is in a living creature.

Pre-clinical studies give a lot of useful information, but they don’t give all the answers that are needed. After all, humans and mice can be very different in the way they absorb, process, and get rid of substances. A treatment that works against cancer in a mouse may or may not work in people. And there may be side effects and other problems that did not show up when the treatment was studied in mice.

Cell studies and animal studies can be confusing when the news media reports them without making it clear that the studies were not done on people. Some reporters may not know how many more tests the treatment must go through before it can be used in humans. And rarely does anyone mention how many of the treatments being studied will fail one or more of these tests.

If the pre-clinical studies are completed and the treatment still seems promising, the FDA must give permission to test it in humans.

The investigational new drug (IND) application

Before a clinical trial can be started, the research must be approved. An *investigational new drug (IND) application* or *request* must be filed with the FDA when researchers want to study a drug in humans. The IND application must contain certain information, as described below. The FDA reviews this information before human clinical trials start. Here is some of the required information on an IND request:

Pre-clinical studies: Results from studies, including those on animals, allow the FDA to decide whether the product is reasonably safe for early testing in humans. This part may also include any experience with the drug in humans (if the drug has been used or studied in another country, for example).

Manufacturing information: This explains how the drug is made, who makes it, what is in it, how stable it is, and more about the physical qualities of the drug. The FDA uses this information to decide whether the company can make batches of the drug that will always be exactly the same.

Clinical protocols and investigator information: Detailed outlines for the planned clinical studies are looked at to see if the study might expose subjects to unnecessary risks (see "The study protocol" in the section "How do I figure out which study is for me?"). Information on the clinical investigators who will supervise the study is reviewed to find out if they are qualified to run clinical trials. Finally, the research sponsor must commit to getting informed consent from the research subjects, having the study reviewed by an institutional review board (IRB), and following all the rules required for studying investigational new drugs (see "Safeguards in institutions" in the section "What protects the study participants?").

Some facts about clinical trials: Important points to keep in mind

Clinical trials are vital in studying all aspects of medicine, not just cancer. The stakes may seem higher when researching medicines to treat cancer, but all new treatments (drugs and medical devices) must go through clinical trials before being approved by the FDA.

Fact: All clinical trials are voluntary.

You always have the right to choose whether or not you will take part in a clinical trial for which you meet the criteria. The level of care you get should not be affected by your decision. And you have the right to leave a clinical trial at any time, for any reason. If you decide to leave the study, talk to your doctor first. You will want to know how quitting the study might affect your health and what other treatment options you have. You should also tell the research group that you are quitting and why. Your health care team may ask that you agree to continue to be watched for a certain length of time to look for any long-term effects of treatment. We discuss these issues further in "What would

taking part in a clinical trial involve?" in the section "What protects the study participants?"

Fact: Not all clinical trials study treatments.

Even though we talk about research studies as if they are all about treatments, many clinical trials look at new ways to detect, diagnose, or learn the extent of disease. Some even look at ways to prevent the disease from happening in the first place.

Fact: Even among clinical trials that do study treatments, not all of them study drugs.

Many clinical trials test other forms of treatment, such as new surgery or radiation therapy techniques, or even complementary or alternative medicines or techniques.

Fact: When clinical trials do look at drugs, not all of them study new ones.

Even after a drug has been approved for use against a type of cancer, doctors sometimes find it works better when given a certain way or when combined with other treatments. It may even work on a different cancer. Clinical trials are needed to study these possibilities as well.

Fact: Very few cancer clinical trials involve a placebo.

A placebo is a fake treatment, inactive ingredient, or sham pill used in some types of clinical trials to help make sure results are unbiased. A placebo is sometimes called a "sugar pill." Over the years, doctors have observed that some people begin to feel better even if they just think they're being treated. Although this effect tends to be brief, and does not really affect a cancer, it can make a new treatment seem to help. The possibility of getting a placebo keeps people from knowing if they are getting the treatment being studied or not, which makes the results more likely to be valid.

Placebos are rarely used alone in cancer research unless no known effective treatments exist. It's certainly not ethical to have someone take a placebo if an effective standard treatment is already available. When cancer clinical trials compare treatments, they compare the new treatment against the current standard treatment. At times, a study may be designed so that patients may not be told which one they are getting, but they know they are at the very least getting treatment that meets the current standard of care.

In some clinical trials, the doctors want to learn if adding a new drug to the standard therapy makes it work better. In these studies, some patients get the standard drug(s) and the new one being tested, while other patients get the standard drug(s) and a placebo. But none of the patients would get only a placebo. Everyone gets standard treatment if there is a standard treatment available. (See the next section for an example of a phase III study

that uses a placebo.) For more information about placebos and how they are used in some studies, see our document called *Placebo Effect*.

What are the phases of clinical trials?

Clinical trials are usually conducted in distinct phases. Each phase is designed to answer certain questions. Knowing the phase of the clinical trial is important because it can give you some idea about how much is known about the treatment being studied. There are pros and cons to taking part in each phase of a clinical trial.

Although there are clinical trials for devices as well as other diseases and treatments, drugs for cancer patients are used in the examples of clinical trial phases described here.

Phase 0 clinical trials: Exploring if and how a new drug may work

Even though phase 0 studies are done in humans, this type of study is not much like the other phases of clinical trials. It is included here because some cancer patients may be asked to take part in these kinds of studies in the future.

Phase 0 studies are exploratory studies that often use only a few small doses of a new drug in each patient. They test to find out whether the drug reaches the tumor, how the drug acts in the human body, and how cancer cells respond to the drug. The patients in these studies must have extra biopsies, scans, and blood samples. The biggest difference between phase 0 and the later phases of clinical trials is that there is no chance the volunteer will be helped by taking part in a phase 0 trial. Because drug doses are low, there is also less risk to the patient in phase 0 studies compared with phase I studies.

Phase 0 studies help researchers find out which drugs do not do what they are expected to do. If there are problems with the way the drug is absorbed or acts in the body, this should become clear very quickly in a phase 0 trial. This process may help avoid the delay and expense of finding out years later in phase II or even phase III clinical trials that the drug doesn't act as it was expected to based on lab studies.

Phase 0 studies are not yet being used widely, and there are some drugs for which they would not be helpful. Phase 0 studies are very small, mostly with fewer than 20 people. They are not a required part of testing a new drug, but are part of an effort to speed up and streamline the process.

Here's how a phase 0 study might work:

Lucia has taken several courses of chemotherapy after her cancer spread. The chemo helped at first, but the cancer came back again. After talking with her doctor, Lucia does not think she wants any of the current options that are offered for standard treatment. She is interested in a clinical trial that might help her. She has found a phase III clinical trial of a new drug, but the study she wants doesn't start enrolling for nearly 4 weeks.

Then, her doctor tells her about a new substance that has been studied and tested in the lab, including animal studies. It looks like it might help her type of cancer. Phase I human studies have not started, but a phase 0 study of the new drug, called "EX-0," is available. This study will only take a few days and is not expected to have many side effects, because patients will be getting very small doses of the drug. Lucia learns that extra blood samples and biopsies will be needed to find out how quickly the drug goes into her blood and what it does with the tumor. She decides that, even though this will not help her personally right now, it might help someone else in the future. She knows that other members of her own family have had this type of cancer, and she wants them and others to have as many good options as possible.

When she meets with the research coordinator, he explains in detail how the study will work. He goes out of his way to make sure that Lucia understands that the study cannot help her at all. Any information gained from the study would help the drug maker know whether they should continue with human studies. Lucia makes sure that taking the Phase 0 study drug will not keep her from going into the phase III study next month. She also asks more questions about what is known about side effects that happened in animal studies, and what else she might expect. Lucia decides that she is willing to take these risks, so she signs the consent form and finds out which days she will need to be at the study center over the next 2 weeks. She answers some medical questions and signs release forms to get her medical records from her doctor and the hospital where she was treated. The staff draws some blood and they plan to start testing next week.

Phase I clinical trials: Is the treatment safe?

These studies are usually the first studies of a new drug that involve people. Although the treatment has been tested in lab and animal studies, the side effects in people can't always be predicted. For this reason, these studies usually include a small number of people (15 to 50) and may be reserved for those who do not have other good treatment options. Often, people with different types of cancer are eligible for the same study. These studies are usually done in major cancer centers.

The main reasons for doing phase I studies are to find out the highest dose of the new treatment that can be given safely without serious side effects. They also help to decide on the best way to give the new treatment. The first few people in the study often get a low dose of the treatment and are watched very closely. If there are only minor side effects, the next few patients may get a higher dose. This process continues until doctors find the dose that is most likely to work while having an acceptable level of side effects.

Safety is the main concern at this point because this is usually the first time the treatment has been used in people. Doctors keep a close eye on how the people in the study are doing. They watch for any serious side effects. Because of the small size of phase I studies, rare side effects may not be seen until later. Special tests, such as blood tests to measure levels of the drug in the body at certain time points, are often a part of these clinical trials. Some studies may require time in a hospital. Placebos (sham or inactive treatments) are not part of phase I trials.

These studies are not designed to find out if the new treatment works against cancer. Overall, phase I trials are the ones with the most potential risk. And only phase 0 has a smaller chance of helping you than phase I. But phase I studies do help some patients. For those with life-threatening illnesses, weighing the potential risks and benefits carefully is key.

Here's an example of how a typical phase I clinical trial might work:

Bruce was diagnosed with cancer 4 years ago. He was first treated with radiation therapy, but the cancer was later found to have spread to distant parts of his body. His doctor told him chemotherapy drugs A and B might help him. Bruce's cancer shrank for a short time while he was taking drug A, but then it began to grow again. Drug B did not work for him.

Because Bruce is still fairly young, his doctor suggests he might want to consider trying a new form of treatment, "EX-1," which is being studied in a phase I clinical trial at a nearby university hospital.

Bruce talks with the doctor conducting the study. The doctor explains that the drug being studied showed some promise in lab tests, but exactly how well it will work in people is still unknown. What's more, it may have side effects that haven't been seen yet. After getting all of his questions answered and weighing his options, Bruce decides to take part in the study.

Because 3 people have already enrolled in the study and have had no major side effects, Bruce will be the first person to get a higher dose of the treatment. He will need to stay in the hospital overnight on the first night. This is both to watch for any unexpected reactions and to take blood samples every few hours so that doctors can figure out how long the treatment stays in his body. He will get to go home the next day, but must return regularly over the next few weeks to be watched closely until it is time for the next treatment.

Phase II clinical trials: Does the treatment work?

If a new treatment is found to be reasonably safe in phase I clinical trials, the treatment can then be tested in a phase II clinical trial to see if it works the way researchers think it will.

Usually, a group of 25 to 100 patients with the same type of cancer gets the new treatment in a phase II study. They are treated using the dose and method found to be most safe and effective in phase I studies. In a typical phase II clinical trial, all the volunteers usually get the same dose, and no placebo is used.

But some phase II studies do randomly assign participants to 1 of 2 treatment groups, much like what is done in phase III trials (see below). These groups may get different doses or get the treatment in different ways to see which provides the best balance of safety and effectiveness. Phase II studies are often done at major cancer centers, but may also be done in community hospitals or even doctors' offices.

Doctors look for some evidence that the treatment works. The type of benefit or response they look for depends on the goals of the clinical trial. This may mean the cancer shrinks or disappears. Or it might mean there is an extended period of time where the cancer does not get any bigger, or there is a longer time before a cancer comes back. In some studies the benefit may be an improved quality of life. Many studies look to see if people getting the new treatment live longer than they would have been expected to without the treatment.

If a certain percentage of the patients benefit from the treatment, and the side effects aren't too bad, the treatment is allowed to go on to a phase III clinical trial. Along with watching for responses, the research team keeps looking for any side effects. Larger numbers of patients get the treatment in phase II studies, so there is a better chance that less common side effects may be seen.

An example of a phase II clinical trial:

Angela was diagnosed with cancer several months ago. Only one form of treatment, drug C, is known to work for people with her type of cancer, but it only works in about half of the people who try it. After several months of this treatment, Angela's doctor told her that it did not seem to be helping in her case.

After doing a little research online, Angela and her doctor decide her best bet may be to enroll in a clinical trial. They find a phase II study being done by a doctor nearby, who is testing a new type of medicine, called "EX-2." This medicine was already found to be safe in phase I studies. Although not many people have tried EX-2, a couple of people with Angela's type of cancer were helped by it.

Angela, like all of the other people in this study, will get EX-2 once a week as an outpatient at a local hospital. Before getting the drug each week, she will have a physical exam and blood tests to see how her body is responding to the medicine. She will also have scans done after several weeks to see if the drug is affecting the cancer. She had tests like this while getting drug C, but this time the tests and exams are done more often. All of the extra testing is paid for by the group running the study.

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

Treatments that have been shown to work in phase II studies usually must successfully go through one more stage of testing before they are approved for general use. Phase III clinical trials compare the safety and effectiveness of the new treatment against the current standard treatment.

Phase III clinical trials usually have a large number of patients, at least several hundred. These studies are often done in many places across the country (or even around the world) at the same time. They are more likely to be offered by community-based oncologists.

Because doctors do not yet know which treatment is better, patients are often chosen at random, (called *randomized*) to get either the standard treatment or the new treatment. When possible, neither the doctor nor the patient knows which of the treatments the patient is getting. This type of study is called a *double-blind study*. Randomization and blinding are discussed in more detail later on.

As with other studies, patients in phase III clinical trials are watched closely for side effects, and treatment is stopped if they are too bad. Placebos may be used in some phase III studies, but they are never used alone if there is already a treatment available that works.

An example of a phase III clinical trial that could involve a placebo:

Li has just been diagnosed with cancer. His surgeon was able to remove the tumor, but tells Li that this kind of cancer returns in about one-third of patients. For this reason, doctors usually recommend giving a short course of chemotherapy drug D. Although this is the best drug available for reducing the chance the cancer will come back, some cancers still return after drug D is used.

Li's doctor tells him that a new type of treatment, called "EX-3," is now being studied. EX-3 was designed to be given along with drug D. Earlier studies in animals and people have shown that the combination of drug D and EX-3 seems to be safe and effective. But it is not yet known if this combination will be better than the current standard of drug D alone in reducing the risk of the cancer coming back. So the doctors are testing it in a phase III clinical trial.

To do this, they've designed a study that assigns people with this cancer to 1 of 2 groups: one group will get drug D plus EX-3, while the other group will get drug D plus a placebo. The patients will not know whether they are getting EX-3 or the placebo. But all patients will be getting drug D, which is the accepted standard of care. The people who get EX-3 may do better than those who get the placebo. On the other hand, they may do worse because of things like unknown side effects. Or both groups may do about the same, in which case EX-3 would not be any better than the placebo. (If this happens, drug D alone would remain the standard care.)

Li, in deciding whether to take part in the clinical trial, needs to understand that he will be randomly assigned to 1 of the 2 treatment groups, and neither he nor his doctor will have control over this. He also needs to understand that while on this study, he will not know if his group is getting EX-3 or a placebo (he may find out after the study ends).

Submission for FDA approval: New drug application (NDA)

In the United States, when clinical trials show a new drug treatment is more effective and/or safer than the current standard treatment, a new drug application (NDA) is submitted to the Food and Drug Administration (FDA) for approval. The FDA then reviews the results from the clinical trials and other relevant information. If the FDA has questions, it may ask for more information or even require that more studies be done. This can extend the approval process to more than 5 years.

Based on its review, the FDA decides if the treatment is OK to be used in patients with the type of illness the drug was tested on. If it is, the new treatment often becomes the standard of care, and newer drugs must then be tested against it before being approved.

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

Even after testing a new medicine on thousands of people, the full effects of the treatment may not be known. Some questions often still need to be answered. For example, a drug may get FDA approval based on the fact that it was shown to reduce the risk of cancer recurrence. But does this mean that those who get it are more likely to live longer? Are there rare side effects that haven't been seen yet, or side effects that only show up after a person has taken the drug for a long time? These types of questions may take many years to answer fully, and may not be critical for getting a medicine to market. They are often addressed in what are known as phase IV clinical trials.

Phase IV studies look at drugs that have already been approved by the FDA. The drugs are already available for doctors to prescribe for patients, but these studies are still needed to answer important questions.

When thinking about taking part in a phase IV trial, you should know that the drug has already been approved for use. You do not need to enroll in the study to get the medicine. At the same time, the care you would get in these types of studies often is very much like what you could expect if you were to get the treatment outside of a clinical trial. You should be reassured that in taking part you would be getting a form of treatment that has already been studied a lot and that you would be doing a service to future patients.

Who sponsors and runs clinical trials?

The National Cancer Institute (NCI) sponsors (pays for) a good portion of the thousands of cancer clinical trials going on at any one time. The NCI is a part of the National Institutes of Health (NIH), which is funded by US tax dollars. These studies are often run by NCI-sponsored cancer cooperative groups, which are networks of doctors and institutions across the country who specialize in a certain aspect of cancer.

In the United States, there are currently 10 major cooperative groups conducting cancer studies:

American College of Radiology Imaging Network (ACRIN)

American College of Surgeons Oncology Group (ACOSOG)

Cancer and Leukemia Group B (CALGB)

Children's Oncology Group (COG)

Eastern Cooperative Oncology Group (ECOG)

Gynecologic Oncology Group (GOG)

National Surgical Adjuvant Breast and Bowel Project (NSABP)

North Central Cancer Treatment Group (NCCTG)

Radiation Therapy Oncology Group (RTOG)

Southwest Oncology Group (SWOG)

Other government agencies, including parts of the Department of Veterans Affairs and the Department of Defense, also sponsor cancer clinical trials.

The other main sponsors of clinical trials are pharmaceutical and biotechnology companies, which must prove their medicines are safe and effective before they can be marketed. Some non-profit organizations also sponsor clinical trials.

Researchers conduct clinical trials in many different settings. Major cancer centers are often the focal points of clinical trials research. Because they usually have the most advanced facilities and highly trained staffs, they can conduct all phases of clinical trials. But they are not the only places where these studies take place.

Community hospitals across the country also take part in clinical trials, although these are usually phase II or III studies. Many of these hospitals are part of the NCI's Community Clinical Oncology Program (CCOP). CCOP members conduct the same clinical trials across the country. Community hospitals may conduct privately sponsored and other types of studies, too.

Doctors in private practice can also be involved in clinical trials, either as members of cooperative groups or by being actively involved in privately sponsored research. But many doctors decide not to conduct clinical research, for a number of reasons.

What this may mean for you

At one time, clinical trials were done only at major medical centers. This often meant that patients had to travel long distances and were treated by doctors they did not know very well. This is sometimes still the case, especially with phase I and some phase II studies. Of course, this is not necessarily a bad thing. Many people prefer to be treated in major cancer centers because of their experience, reputation, and resources. Ultimately, the hassles of traveling must be weighed against the chance of being helped by the treatment.

Patients now have more options. This may include staying closer to home during a study or even staying with their own doctors. Your doctor may or may not be involved in clinical trials. If he or she is, you may be eligible for one of them. Whether this is the right study for you is, of course, a question worth asking. Keep in mind, each study also has its own requirements that a person must meet to take part. See "Eligibility (inclusion) criteria" in the section called "How do I figure out which study is for me?" to learn more about this.

Although clinical trials are now done in many different settings, this should not affect the quality of care you receive. No matter where a study is done, the same rules are in place to protect patients.

Having so many options can be a burden in and of itself. With the thousands of clinical trials under way across the country, how can you -- or even your doctor -- decide which one is best for you? At this time, there is no complete list of all the cancer clinical trials. But there are some good places to start looking if you're interested. We'll explore these in the section, "What's out there? Finding clinical trials."

Should I think about taking part in a clinical trial?

This is one of the toughest questions many people with cancer will face. The answer won't be the same for everyone. When trying to decide, first ask yourself some basic questions:

- Why do I want to take part in a clinical trial?
- What are my goals and expectations if I decide to take part? How realistic are these?
- How sure are my doctors about what my future holds if:
  - I decide to participate?
  - I decide not to participate?
- Have I considered:
  - The chance of benefit versus risk?
  - Other possible factors, such as time and money?
  - My other possible options?

Some of these questions may not have clear-cut answers, but they should help you start thinking about some important issues. Each person's situation is unique, and each person's reasons for wanting or not wanting to take part in a study may be different.

Risk versus benefit

Each clinical trial offers its own opportunities and risks, but most have some things in common. For the most part, clinical trials (other than phase 0) have some of the same potential benefits:

- You may help others who have the same condition in the future by helping to advance cancer research.
- You may have access to treatment that is not otherwise available, which might be safer or work better than current treatment options.
- You may increase the total number of treatment options available to you, even if you haven't yet had all of the standard treatments.

- You may feel you have more control over your situation and are taking a more active role in your health care.
- You will probably get more attention from your health care team and more careful monitoring of your condition and the possible side effects of treatment.
- Some study sponsors may pay for part or all of your medical care and other expenses during the study. (This is not true for all clinical trials. Be sure you know who is expected to pay for your care before you enroll in the study.)

Some of the possible downsides of being in a study can include:

- The new treatment may have unknown side effects or other risks, which may or may not be worse than those from existing treatments. This is especially true of early phase trials.
- As with other forms of therapy, the new treatment may not work for you even if it helps others.
- There may be inconveniences such as more frequent office visits and testing, as well as time and travel commitments.
- If you take part in a randomized clinical trial, you may not have a choice about which treatment you get. If the study is blinded, you (and maybe your doctor) will not know which one you are getting (although this information is available if needed for your safety). This will be explained to you before you decide to take part.
- Insurers may not cover all of the costs of taking part in a clinical trial, but they usually cover the costs of what would normally be standard care. Be sure to talk to your insurance provider and to someone involved with the study before you decide to take part, so you know what you may have to pay for.

Answers to some common questions about clinical trials

Most people have some concerns about taking part in a clinical trial, often because they're not really sure what it will mean for them. Taking time to get as much information as you need before you decide is the best way to be sure that you will make the choice that is right for you.

Will there be risks?

Yes, all clinical trials have risks. But any medical test, drug, or procedure has risks. The risk may be greater in a clinical trial because some aspects of any new treatment are unknown. This is especially true of phase I and II clinical trials, where the treatment has been studied in fewer people.

Perhaps a more important question is whether the risks are outweighed by the possible benefits. People with cancer are often willing to accept a certain amount of risk for a chance to be helped, but it is always important to be realistic about what this chance is. Ask your doctor to give you an idea of what the possible benefits are, and exactly what benefit is likely for you.

With this in mind, you can make a more informed decision. Some people may decide that any chance of being helped is worth the risk, while others may not. Others may be willing to take certain risks to help others.

Will I be a "guinea pig?"

There's no denying that the ultimate purpose of a clinical trial is to answer a medical question. People who take part in clinical trials may need to do certain things or have certain tests done to stay in the study.

But this does not mean that you will not get excellent, compassionate care while in the study. In fact, most people enrolled in clinical trials appreciate the extra attention they get from their health care team. In 2005, the Coalition of Cancer Cooperative Groups surveyed over 1,700 people with cancer on their awareness and attitudes about clinical trials. Only a few had taken part in clinical trials. But most of those who did were very satisfied: 96% said they were treated with dignity and respect, 92% said they had a positive experience, and 91% would recommend that family or friends take part in a clinical trial if faced with cancer.

Will I get a placebo?

Most cancer clinical trials do not use placebos unless they are given along with an active drug. It would be unethical to give someone an inactive medicine if it would deny the person a chance to get a drug that has already been shown to work.

Unfortunately with cancer, there are some situations for which there are no effective treatments. In rare cases, testing a new treatment against a placebo might be needed to prove that the treatment is better than nothing at all.

The very least you should expect from any clinical trial is to be offered the standard of care already being used. (See the section, "Phase III clinical trials: Is it better than what's already available?" for an example of a phase III study using a placebo.)

Can my doctor or I pick which group I'm in?

No. Most studies are *randomized*. This means that each person who takes part in the study gets assigned to either the treatment group or the control group. This is used in many phase III studies because it helps reduce the risk that one group will be different from the other when they go into the study, which could affect outcome. This is especially helpful to make sure that the groups contain people in similar states of health, so the results are not skewed in favor of one group. If people were allowed to choose which treatment they got, the study results might not be as accurate. For example, people

who were sicker might tend to choose one treatment over the other. If the new treatment was then found not to work as well, doctors couldn't be sure if this was because the treatment wasn't as good or because it was tested in sicker people.

Often people have a 50:50 chance of ending up in one group or the other. In some cases, the study may allow for a different ratio, such as 2 out of 3 people getting the new treatment and only 1 out of 3 getting the standard treatment.

Some people find the concept of randomized studies distressing, since neither the patient nor the doctor can choose which group the patient is in. This can be especially true if a study is looking at 2 totally different treatments and a person sees one as better than the other. But remember, doctors are doing the study because they really don't know which one is better. Unfortunately, taking part in such a study is sometimes the only way a person has a chance of getting a new form of treatment. But even then, that treatment may or may not be the best one for him or her.

Will I know which group I'm in? Will my doctor know?

Each study is different. In a *blinded* study, the patient doesn't know which treatment he or she is getting. In a *double-blinded study*, neither the patient nor the doctor knows which treatment is being used. Not knowing what you are getting can be hard. Your doctor can always find out which group you are in if there is an important medical reason (such as a possible drug reaction), but it may result in your being removed from the study. Blinding reduces the risk that the doctors will be biased in their evaluations of the patients' outcomes. These controls help make the study results more reliable.

The possibility of getting a placebo can also be upsetting to some people. But this very rarely means you would get no treatment, unless there was no effective standard treatment to compare with the new treatment. Again, in the example above, Li will definitely get drug D, but he will also get either EX-3 or a placebo.

Will my information be kept confidential?

As much as possible, all of your personal and medical information will be kept confidential. Of course, your health care team needs this information to give you with the best possible care, just as they would if you were not in a clinical trial.

Medical information that is important for the study, such as test results, is usually put on special forms and into computer databases. This is then given to the people who will analyze the study results. Your information is assigned a number or code -- your name is not on the forms or in the study database. Sometimes, members from the research team or from the Food and Drug Administration may need to look at your medical records to be sure the information they were given is correct. But your personal information is not given to them and is never used in any published study results.

Other questions you should ask your research team

Each clinical trial is unique, with its own potential benefits and risks. Before you decide to take part in a clinical trial, you may want answers to these questions. Some people take notes, record the discussion, or bring a friend with them to help recall the answers and think of other questions:

- Why is this study being done?
- What is likely to happen if I decide to take part or decide not to take part in the study?
- What are my other options (standard treatments, other studies)? What are their pros and cons?
- How much experience do you have with this particular treatment? With clinical trials in general?
- What were the results in earlier studies of this treatment? How likely are they to apply to me?
- What kinds of treatments and tests would I need to have in this study? How often are they done?
- Will this require extra time or travel on my part?
- How could the study affect my daily life?
- What side effects might I expect from the study? Are there other risks? (Keep in mind that there can also be side effects from standard treatments and from the disease itself.)
- Will I have to be in the hospital for any parts of the study? If so, how often, for how long, and who will pay for it?
- Will I still be seeing my regular doctor? Who will be in charge of my care during the study?
- Will I have any costs? Will any of the treatment be free? Will my insurance cover the rest?
- If I am harmed as a result of the research, what treatment will I be entitled to?
- How long will I be in the study?
- Are there reasons I would be removed from the study? Are there reasons the study might be stopped early?
- Is long-term follow-up care part of the study? What would it involve?

- If the treatment is working for me, can I keep getting it even after the study ends?
- Can I talk to other patients already taking part in the study?
- Will I be able to find out about the results of the study?

You might find it helpful to include trusted friends and family members in your decision making process. They may ask questions you hadn't thought of and can help make sure that you're making a decision that's right for you. Also, getting a second opinion from a doctor who is not involved with the study can give you a broader sense of whether this study is the best one for you.

What protects the study participants?

Several levels of safeguards are in place to help protect the people who take part in clinical trials. There are still risks involved with any study, but these safeguards try to reduce the risk as much as possible.

Three basic principles, as outlined in the Belmont Report from the late 1970s, provide the basis for research involving humans:

- **Respect for persons:** Recognizing that all people should be respected and have the right to choose what treatments they receive
- **Beneficence:** Protecting people from harm by maximizing benefits and minimizing risks
- **Justice:** Trying to ensure that all people share the benefits and burdens of research equally

These principles are upheld by individuals and groups at the sites conducting research, and also by government agencies charged with overseeing clinical trials. A very important part of patient protection is the informed consent process, which is described in detail in the section "What would taking part in a clinical trial involve?"

Safeguards in institutions

Centers conducting clinical trials have committees that review all potential and ongoing clinical trials to protect the safety of those in the study. These are required for all federally funded clinical trials, but even privately sponsored studies typically undergo such reviews.

Institutional review boards (IRBs)

Institutional review boards (IRBs) are groups of people responsible for protecting the welfare of the people who take part in the study and making sure that studies comply with federal laws. The boards are often made up of medical experts (such as doctors and nurses), other scientists, and non-medical people. All of the people on the IRB cannot come from only one of these groups. In other words, an IRB couldn't be a group of just

doctors. Many institutions have their own IRBs, but some smaller centers may use larger, "central" IRBs. The Federal Office of Human Research Protections (OHRP; see below) oversees the activities of IRBs.

Researchers who want to start a study must first submit the study protocol (the plan that describes the study in detail) to the IRB for review. The IRB must decide if the study would be acceptable on medical, ethical, and legal grounds. In other words, does the study address a worthwhile question, and is it doing so in a way that ensures the safety of those taking part as much as possible? One of the most important jobs of an IRB is to make sure the informed consent form that people entering the study must sign is accurate, complete, and easy to understand. Once a study begins, the IRB also follows its progress regularly to look for potential problems.

If you take part in a clinical trial, you can contact the study's IRB directly with any questions or concerns regarding safety.

Data safety monitoring boards (DSMBs)

Data safety monitoring boards (DSMBs) are used for phase III (and some earlier phase) studies. They are committees made up of doctors and other scientists not involved in the study. Their job is to look at study statistics. They monitor the results of the clinical trial at different time points and can stop a study early (before all of the intended participants have been enrolled or completed the study) if:

- It becomes clear that the new treatment is much more (or much less) effective, so as to allow all study participants to get the better treatment
- Safety concerns arise (such as risks of the new treatment clearly outweighing the benefits), so that no more people are exposed to possible harm

The clinical investigator

The clinical investigator is the person who is in charge of all aspects of a particular study. Most often the clinical investigator is a doctor; in some settings this person is called the *principal investigator*, or PI. Ultimately, the responsibility for patient safety in a clinical trial lies with the clinical investigator. Part of this responsibility is letting the study sponsor know right away when serious side effects occur.

Many clinical investigators have years of experience in running clinical trials. Their credentials are submitted to the FDA along with the investigational new drug application before the study is approved.

Government agencies

Several government agencies play roles in ensuring that all research is conducted with patient safety in mind. These include:

Office of Human Research Protections

The Office of Human Research Protections (OHRP) is the government's main guardian of people's safety and welfare in clinical trials. It was established in 2000 to coordinate efforts to protect all people involved in federally funded research. It enforces the rules regarding the informed consent process, institutional review boards (IRBs), and the participation of people with special needs in clinical trials, such as children and those with mental disabilities.

The OHRP has suspended research activities at several institutions in the past few years, including those in some major research centers, until system flaws were corrected.

The OHRP also educates research centers and individuals to help them comply with current clinical trials standards.

Food and Drug Administration

The Food and Drug Administration (FDA) has the final say about whether or not a new treatment can be given to patients. Once all phases of clinical trials on a new treatment are completed, the FDA reviews the information and decides if it is safe and effective enough to be approved.

But the FDA's role in many clinical trials begins long before this. Any sponsor seeking approval for a new treatment must submit all study protocols to the FDA before the clinical trials are allowed to begin. See "The investigational new drug (IND) application" in the section "What would taking part in a clinical trial involve?" for more.

The FDA also inspects (audits) sites conducting clinical trials, especially if there is reason to think they are not following proper procedures. If serious problems are found, the FDA can forbid a particular site or doctor from doing any further research.

But the authority of the FDA is not absolute. Clinical trials that study treatments that are already on the market are not subject to the same FDA regulations (although many are still done in much the same way). And substances considered to be "dietary supplements" do not need FDA approval to be sold in the first place. [Dietary supplement makers aren't required to prove that their products are safe or effective. So they usually do not bother to conduct clinical trials. A fairly small number of clinical trials are done to study the effects of dietary supplements. Most of these are funded by the National Institutes of Health (NIH).]

National Cancer Institute

The National Cancer Institute (NCI), part of the NIH, sponsors many of the cancer clinical trials going on at any one time, including those being conducted by cooperative groups. Proposals for such studies must be approved by the NCI before funding is granted. The NCI also audits each site involved in NCI-sponsored research at least once every 3 years.

What's out there? Finding clinical trials

People find out about clinical trials in different ways. Most people who enter clinical trials do so after hearing about them from their doctor. Many cancer patients actively look for clinical trials on the Internet or in other places, hoping to find more options for treatment. Some clinical trials are advertised directly to patients.

If you already have a particular clinical trial in mind, you may want to go to the section "How do I figure out which study is for me?" to learn what you should know about the study.

Sources of information about clinical trials

At this time there is no one source to find out about all of the cancer clinical trials now enrolling patients. But you should know about several resources. These resources can be divided into 2 main types: clinical trials lists and clinical trials matching services.

Clinical trial lists

These sources give you the names and descriptions of clinical trials of new treatments. If there is a study you are interested in, you will probably be able to find it in a list. The list will often include a description of the study, the criteria for patient eligibility, and a contact person. If you (or your health care providers) are willing and able to read through descriptions of all the studies listed for your cancer type, then a list may be all you need. Some organizations that provide lists can help you narrow the list a little, according to the kind of treatment you are looking for (chemotherapy, immunotherapy, radiation therapy, etc.) and the stage of your cancer.

Clinical trials matching services

Over the past few years, several organizations have developed computer-based systems to match patients with studies they may be eligible for. This service is often offered online.

Each may differ somewhat in how it works. Some of the services allow you to search for clinical trials without registering at the site. If you have to register, they usually assure you that your information will be kept confidential. Either way, you will probably have to enter certain details, such as the type of cancer, the stage of the disease, and any previous treatments you may have had. When given this information, these systems can find clinical trials for which you may be eligible, and save you the time and effort of reading descriptions of studies that are not relevant to you. Some groups also allow you to subscribe to mailing lists so that you are informed as new studies open up.

Although they are usually free to users, most clinical trial matching services get paid for listing studies or get a finder's fee from those running the studies when someone enrolls. Because of this, there may be some differences in the way they rank the studies, or the order in which they present the studies to you.

How to choose a clinical trials matching service: Because different services work differently, be sure you understand how the service you are looking at operates. Ask the following questions. (Note that the answers do not necessarily mean that the service is not worth using.)

- Is there a fee for using the service?
- Do I have to register to use the service?
- Does the service keep my information confidential?
- Where does the service get its list of clinical trials?
- Does the service rank the studies in any particular order? Is this based on fees they get?
- Can I contact the service through the Internet or by telephone?

The American Cancer Society Clinical Trials Matching Service: After reviewing the available matching services, the American Cancer Society now works with eviti, Inc. to provide a free, confidential, and reliable matching and referral service for patients looking for clinical trials.

The American Cancer Society helps patients find high quality care in clinical trials that best match their medical needs and personal preferences, while helping researchers study more effective treatments for future patients

The TrialCheck® database, maintained by eviti, Inc., is a comprehensive database that includes the National Cancer Institute, and industry trials. To our knowledge, this is the most complete matching database of cancer clinical trials available.

The clinical trials information provided by the American Cancer Society is not biased in any way. It is updated every day, as is the contact information that allows patients to get in touch with the doctors and nurses at cancer centers running each of the studies.

You can access the TrialCheck system through our Web site, www.cancer.org, or through a toll-free number, 1-800-303-5691.

Other clinical trials lists and matching services: The National Cancer Institute (NCI) sponsors most government-funded cancer clinical trials. The NCI has a list of active studies (those currently enrolling patients), as well as some privately funded studies. You can find the list on their Web site at www.cancer.gov/clinicaltrials or by calling 1-800-4-CANCER (1-800-422-6237). You can search the list by the type and stage of cancer, by the type of study (for example, treatment or prevention), or by zip code.

The National Institutes of Health (NIH) has an even larger database of clinical trials at www.clinicaltrials.gov, but not all of these are cancer studies.

EmergingMed provides a free and confidential matching and referral service for cancer patients looking for clinical trials at www.emergingmed.com, or you can call 1-877-601-8601.

CenterWatch[SM] (www.centerwatch.com) is a publishing and information services company that keeps a list of both industry-sponsored and government-funded clinical trials for cancer and other diseases.

Private companies, such as pharmaceutical or biotechnology firms, may list the studies they are sponsoring on their Web sites or offer toll-free numbers so you can call and ask about them. Some of these firms also offer matching systems for the studies they sponsor. This can be helpful if you are interested in research on a particular experimental treatment and know which company is developing it.

How do I figure out which study is for me?

Whether your doctor suggests a certain clinical trial or you use the available lists or matching services on the Web, how do you know which study makes the most sense for you?

You could be eligible for several studies at the same time. There may be obvious reasons for not choosing some, such as those that are being done too far away from where you live, but with others the choice may not be so clear. Understanding what each study involves can help you make your decision.

The study protocol

The study protocol is the written plan for how a clinical trial is to be conducted. It is what is submitted to the FDA and to an institutional review board (IRB) before a new treatment can be studied. A protocol contains the following information:

- Why the study is being done (including the goals of the study)
- Information about the treatment being tested, often including results of studies done before
- The phase of the study and how many people will be enrolled
- Who is eligible for the study
- How the treatment is to be given
- What tests will be done during the study and how often
- Other information that will be collected on participants

Actual study protocols can be as long as100 pages or more, and they can be very technical. Because they are not written with patients in mind, making sense of their language is not always easy.

The clinical trial lists available on the Web often include summaries of these protocols, just highlighting some key points. Research team members may also have protocol summaries or other information about the study they can share with you. Often, the most

important information for patients looking for studies is the eligibility criteria (see below) and any information available about the new treatment.

Eligibility, or inclusion and exclusion criteria

All clinical trials have guidelines about who can take part. Each person has to match those to be in the study. For instance, some studies are looking for volunteers with a certain type of illness, or a certain stage of disease, while others are looking for healthy volunteers. Some studies look for people who have been treated for their illness, and others look for people who have not. The factors that allow a person to sign up for a study are called *inclusion criteria*. In order to take part in the study, a person has to have all the factors on this checklist. These criteria are used to help be sure that the researchers will be able to answer the questions they plan to study.

There are also factors that can exclude a person from each study. For example, a study may be looking for people of a certain age, so people older and younger would not be able to take part. Having certain medical conditions may mean that you cannot take part in a study, as can taking certain drugs. Factors that disqualify people from taking part are called *exclusion criteria*. In order to take part in the study, a person cannot have any of the factors on this checklist. These criteria are often used to be sure that the people in the study can safely take part. They also help make sure that the researchers will be able to answer their questions.

For cancer clinical trials, the inclusion and exclusion criteria usually have to do with:

- The type of cancer a person has
- The stage (extent) of the cancer
- Previous treatments a person had
- The length of time since a person last received treatment
- Results of certain lab tests
- The medicines a person is taking
- Other medical conditions the person has
- Any previous history of another cancer
- A person's activity level (also known as performance status)

Other factors, such as a person's sex, may also be part of the criteria. There are usually other criteria for each study, as well.

Advertisements and clinical trial lists may not contain all of a study's eligibility criteria. If you've found a study you think you might qualify for, you can usually contact someone involved with the study to get a full list of the criteria.

I think I'm eligible. Now what?

Once you've found a study that you think you're eligible for, deciding if it's the right one for you can still be hard. There may even be more than one that looks promising. Again, it is important to learn as much as you can.

Talk with someone connected to the study. This could be the clinical investigator or principal investigator (PI) -- the person in charge of the study -- or a research coordinator. Research coordinators are usually nurses. One of their jobs is to check to see if people meet eligibility criteria before they get into a study. They also make sure that the study protocol is followed for each patient. They often serve as a link between study patients and their doctors.

Both PIs and research coordinators should be able to answer your questions about the study. See the section "Should I think about taking part in a clinical trial?" for a list of questions you might want to ask. They can give you answers about their particular clinical trial, but they are not likely to be helpful in discussing other studies you might be thinking about. What's more, they could be biased (even if they don't mean to be) toward their own study.

If you haven't done so already, talk to your doctor about clinical trials you are looking at. Bring in whatever information you can, so that your doctor can help you figure out what might be right for you. No doctor knows about every clinical trial being done, but your doctor knows your medical situation best and can probably tell you if the study is worth considering. This discussion can take some time, so you may need to make a special appointment to allow your doctor enough time to look over the information you provide.

You might also want to get a second opinion from a doctor not connected to the studies you are looking at. Doctors who are well known in their fields usually know about the latest experimental treatments, and they may be able to point to those that look more promising.

If you have access to the Internet, you can find some information on your own. Try to find out if the new treatment has been studied before or if it is being studied now in other diseases, as well as if any results are available. If this is hard for you, have someone close to you help or do it for you. People with a medical background may have an easier time sorting through such information.

Finally, talk to friends and family members you trust. Although the final decision is yours, their opinions may give you insight into things you had not thought about.

What about cost? Will my insurance cover it?

It is important to get these questions answered before deciding to take part in a clinical trial. Recent studies have shown that the overall costs of taking part in a clinical trial are

not much more than the costs of treatment outside of a study. Still, insurance coverage can vary widely.

When insurers do cover costs related to clinical trials, it is usually only for tests, treatments, or doctor's visits that would have been part of your treatment plan if you were not taking part in a study. In other words, they are not likely to pay for special tests or treatments you are getting just because you're in the study.

The study sponsor (whether it is the government or a pharmaceutical or biotechnology company) usually provides the new treatment at no cost and pays for special testing or extra doctor visits. Some sponsors may pay for more than this; for example, some may offer to pay you back for travel time and mileage. It is important to find out what will be paid for before entering the study.

Private insurers

In the past, insurers were sometimes reluctant to pay for any of the costs related to a clinical trial. Their concern was that they would be paying for treatments that had not been proven to work.

In recent years, many (but not all) major insurance providers have volunteered to cover some of the costs of clinical trials. Still, they may limit which types of trials they will cover. They are more likely to pay for costs from phase II or phase III clinical trials, but most of the time they look at each request on a case-by-case basis.

Medicare

Medicare normally covers any cancer care when it is part of either:

- A clinical trial for the diagnosis and treatment of cancer; or
- A clinical trial funded by the National Cancer Institute (NCI), NCI-Designated Cancer Centers, NCI-Sponsored Clinical Trials Cooperative Groups, or another federal agency that funds cancer research.

This care may include the following:

- Routine tests, procedures, and doctor visits
- Services or items that are part of the experimental treatment, such as costs to give the investigational drugs
- Health care needs linked to being in a clinical trial, such as a test or hospitalization because of a side effect or problem

What costs are not covered by insurance?

- Investigational drugs, items, or services that are being tested as part of the clinical trial
- Items or services used only to collect data for the clinical trial

- Anything that is provided for free by the sponsor of the clinical trial
- Any co-insurance and deductibles

Cancer prevention trials currently are not covered by Medicare. If you are not sure whether your trial meets all of the requirements, discuss these concerns with your doctor or call the Medicare information number (1-800-633-4227). Other trials may be covered, so be sure to ask about other clinical trials before you begin taking part in one that may not be covered.

Laws about insurance coverage of clinical trials

Recognizing the importance of clinical trials, many states have passed laws about insurance coverage for research studies. And more states are now looking at such laws. A few states have worked out voluntary agreements with insurance companies to cover clinical trials.

The types of studies and exact coverage required by these laws vary from state to state -- some cover all clinical trials, while others may cover only certain phases of clinical trials. For a list of state clinical trials insurance laws, see our document *Clinical Trials: State Laws Regarding Insurance Coverage*.

The federal government has become involved, too. One of the goals of the new Affordable Care Act is to make coverage available for cancer treatment that is done in clinical trials. This would allow more people to take part in them.

What you can do

If possible, find out what your insurer will cover before you get involved in a clinical trial.

Find out if your state has laws that require them to cover routine costs of clinical trials. Then gather as much information as you can about the study and contact your insurance provider to find out about coverage. Many providers may not be able to give you a simple yes or no answer, because they may review claims on a case-by-case basis. But you may be able to find out if they've covered costs for clinical trials like yours (or ones that studied the same treatment) in the past.

Have a summary of your study available, and, if possible, any results of previous studies of the treatment. You may need to ask your doctor or the study's research coordinator to help you get this information. If needed, your doctor may be able to give your insurer the reasons this study is a good match for you.

Study sponsors are often eager to recruit eligible patients for their clinical trials, and they may be willing to cover some costs your insurance does not. If needed, ask your doctor or the research coordinator to contact the study sponsor on your behalf.

What would it be like to take part in a clinical trial?

Having an idea of what you can expect from taking part in a study can help relieve some of your concerns and make things go more smoothly. The first thing you will need to do is give your informed consent to take part in the study.

Informed consent

The people running the study are required to get your written, informed consent before you take part in any way (often even before you have any needed tests to see if you are eligible for the study). In the informed consent process, the researchers (doctors or nurses) will explain the details of the study to you and answer your questions and concerns.

You will then be given a written consent form to sign. Consent forms are not all the same, but they should include the following:

- The reason for the study (what the researchers hope to find out)
- Who is eligible to take part in the study
- What is known about the new type of treatment
- The possible risks and benefits of the new treatment (based on what is known so far)
- Other treatments that may be an option for you
- The design of the study (whether it is randomized, double blinded, etc.)
- How many and what types of tests and doctor's visits are involved
- Who must pay for the costs of the clinical trial (tests, doctor's visits, etc.) and for the costs if you need additional care as a result of the clinical trial
- A statement about how your identity will be protected
- A statement about the voluntary nature of the study and your right to leave the study at any time without fear of affecting the care that you would normally get outside the study
- Contact information if you have further questions

Before you sign the consent form, ask questions. Be sure someone from the research team goes over the form with you in detail. Efforts are made for consent forms to be easy to understand, but there still may be words or ideas that are confusing to you. You may want to bring someone along with you to the meeting to help make sure all your concerns are addressed.

Be sure you understand what is involved and what is expected of you. Try to explain what you heard to your doctor or nurse to make sure you've got it right. Recent surveys have shown that although most people are satisfied with the informed consent process, more than half do not understand some of the main points on the consent form.

Finally, don't feel rushed into making a decision. Take the consent form home with you if you need to. Ask trusted family members and friends what they think. If possible, you may want to get a second opinion from another doctor, too.

Taking part in the study

Once you've signed the consent form, you will be ready to take part in the study. You will probably need to have blood tests or imaging tests done before you start treatment (if you haven't had them recently). A full medical history and physical exam are also usually done. The results are needed before you start the actual study to be sure that you meet the eligibility criteria and to help ensure your safety.

As mentioned earlier, some studies may require you to stay in a hospital for a day or 2 to get treatment. In other studies the participants are treated much the same way as other patients who aren't in a clinical trial.

You may have tests done more often to find out how well the treatment is going and to look at how you are doing. You will likely get more attention as a study participant than you would otherwise. The doctors and nurses may examine you more often and will want to know if you are having any side effects (called *adverse events*) while being treated.

Because the possible complications may not fully be known, it is very important to let the research team know about anything out of the ordinary. They can then decide if symptoms you are having are related to the study, and if they need to be treated or your treatment needs to be changed.

Your may quit taking part in the study for any number of reasons:

- You complete treatment on the study
- The treatment does not appear to be working for you
- You have serious side effects while in the study
- The study itself is stopped early because the treatment either has proven to work, has proven to not work as well as the standard treatment, or it's been found to be too harmful
- You decide to leave the study

Once you are out of the study, the researchers may still watch you for a time so they can continue to get an idea of how you are doing.

Some studies let you stay on the new treatment even after the study ends. This is known as *open label*, because you and your doctor know which treatment you are getting. This option varies among clinical trials, so be sure to ask about it before you begin.

What if I want to leave the study early?

You will be told many times before you enter the study that taking part in the study is always voluntary. This is an important point. You have the right to leave the study at any time, for any reason. Your doctor will still take care of you to the best of his or her ability.

No matter when or why you leave the study, you may be asked if the researchers can follow up with you from time to time to see how you are doing. This may give them with important information and can also help ensure your safety, even though you are no longer taking part in the study.

What if I'm not eligible for a clinical trial?

Although some people may be too ill or have other problems that do not allow them to take part in clinical trials, most people will probably be eligible for some type of study. This is true even if they've had many different treatments already. Of course, not all studies you are eligible for are a good fit for you. It's always important to understand the purpose of the study and to have a good idea of the possible risks and benefits for you.

Clinical trials offer the best access to experimental treatments. Study protocols, which are written based on the results of studies done before, are strictly followed and patients are watched carefully.

Some people may be interested in a certain treatment that is only available in clinical trials, but may not meet the eligibility criteria outlined for the studies. In some of these cases, a person's doctor may ask the study sponsor if they can get an eligibility waiver or special exception to allow the person into the study, even though they do not strictly meet all of the criteria. This decision is usually made by the study's clinical investigator, who sometimes consults with others involved in the study about the request. If entered in the study, the person is treated according to the study protocol (the same tests, doctor's visits, follow-up, etc.), but the results from that person are not included in the final study results.

In other cases, the studies may have already enrolled enough people and aren't taking more participants.

At times, there may be ways to get access to treatments that are in late phase clinical trials but not yet approved by the FDA. These are usually referred to as *expanded access* or *compassionate use* programs. In recent years the FDA has broadened these programs to allow some patients who urgently need these treatments to be able to get them. For more information, see our document, *Compassionate Drug Use*.

But it is not always easy to get access to these treatments. The programs are voluntary on the part of the company making the treatment. The company is not required to provide the treatment in these settings, and some companies may decide not to for various reasons (manufacturing issues, excess demand, etc.). Because of the amount of effort and paperwork involved, the process of trying to get an unapproved drug for compassionate use can be slow (weeks to months).

Some of these programs are described below. All require your informed consent, much the same as for any clinical trial.

Treatment use of an investigational new drug (treatment IND)

In some cases, if a treatment is showing promise in late phase clinical trials, the maker may apply to the FDA for a treatment IND (investigational new drug) status. This is much like setting up a new study, but it is meant mainly as a way for patients with no other options to be able to get the treatment before it is approved.

This is sometimes done when a person would not have met the eligibility criteria for the clinical trials or when the studies are already closed to further enrollment. The patient must have a life-threatening or severely debilitating condition for which there are no other treatment options.

Your doctor would need to get in touch with the treatment manufacturer to see if such a program exists and what would be needed for you to enter it. As with clinical trials, these programs have to have a protocol (written guideline or plan) that meets FDA approval, as well as approval by an institutional review board (IRB) in many cases.

The supplier may or may not charge for the treatment in question. It is important to find out beforehand whether you or your insurance company would pay for the treatment.

Single patient and emergency use of an investigational new drug

A *single patient IND* is used to get access to an unapproved treatment for one person with a serious condition who is not eligible for a clinical trial. It is much like a treatment IND in some ways. It does not require that the clinical trial protocol be followed, but it would probably require that your doctor spell out in detail the proposed treatment plan.

To get a single patient IND, your doctor would need to contact the manufacturer of the treatment to see if they would supply it. He or she would then need to have the proposed treatment protocol approved by the IRB and the FDA before treatment would be allowed to begin.

An *emergency IND* can be used when there isn't time to get approval from the IRB. Your doctor would need to contact the manufacturer to see if you can get the treatment, and then file the needed paperwork with the FDA. While IRB approval is not needed before starting treatment, the IRB would have to be notified of the situation and would have to approve future uses.

Summing it all up

Clinical trials can offer benefits for many people during their cancer experience. These may include access to newer or more treatment options, getting more involved medical

care, and having a greater sense of control over one's situation. But by their nature, clinical trials involve some possible risks and downsides, too, and they may not be right for everyone. Your decision on whether to look into or enter a clinical trial should be based on a realistic understanding of the possible risks and benefits.

If you are thinking about entering a clinical trial, there are many groups, including the American Cancer Society, who can help guide you through the information needed to make your decision.

Additional resources

More information from your American Cancer Society

The following information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

Clinical Trials: State Insurance Coverage Laws

Learning About New Cancer Treatments

Learning About New Ways to Prevent Cancer

Placebo Effect

Informed Consent (also available in Spanish)

Compassionate Drug Use

National organizations and Web sites*

Along with the American Cancer Society, other sources of information and support include:

National Cancer Institute
Toll-free number: 1-800-422-6237 (1-800-4-CANCER)
Web site: www.cancer.gov

> Offers general cancer information as well as information on clinical trials, deciding whether to take part, finding certain clinical trials, research news, and other resources.

Cancer Hope Network
Toll-free number: 1-877-467-3638
Web site: www.cancerhopenetwork.org

> Matches adult cancer patients with trained volunteers who have recovered from a similar cancer experience for telephone support. One program matches volunteers who have been on clinical trials with others who are considering taking part in a clinical trial.

Centers for Medicare & Medicaid Services (CMS)
Toll-free number: 1-800-633-4227
TTY: 1-877-486-2048
Web site: www.cms.hhs.gov

> A federal agency with the US Department of Health and Human Services that helps Americans and small companies by ensuring effective, up-to-date health care coverage and promoting quality care for beneficiaries. They help answer questions, give information, and refer callers to state Medicare offices and local HMO's with Medicare contracts.

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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