HIV Clinical Trials

Pretty much everything we know about how HIV treatment depends on research—and not just any research, but clinical trials involving HIV-positive people. Today’s men, women and children living with HIV have yesterday’s clinical trial volunteers to thank for the highly effective, better tolerated and easier-to-take medications now available. Similarly, the future of our ability to respond to the needs of people living with HIV—whether its novel drugs for those starting therapy for the first time or in desperate need of new agents, new approaches to managing side effects or, best of all, a cure for the disease—depends greatly on people to continue enrolling in clinical trials today.

Of course, deciding to participate in a clinical trial isn’t only about altruism—putting the needs of others before our own. Though most people living with HIV today have an abundance of treatment options to choose from and do not need clinical trials to access life-saving therapy, this is not true for everybody. A growing number of people are at the end of their treatment rope, given that their HIV has developed resistance to most, if not all, of the approved meds. There are also individuals who cannot tolerate many available treatments and need access to alternative options or experimental drugs for side effects. And there is always interest in trying new compounds that are easier to take, work differently than any agents approved to date or are potentially effective against non-AIDS diseases that affect people living with HIV, such as cancers, hepatitis, mental health problems and heart disease.

Like all treatment decisions, deciding to join a clinical trial is a question that can only be answered through discussions with your health care provider and others you trust.

What is a clinical trial (or study)?
A clinical trial is a medical experiment that takes place in a hospital, a clinic or a doctor’s office. The experiment may test the safety and usefulness of a new drug, or it may test several different kinds of drugs or treatment strategies to see which one is better. Some clinical trials test drugs that treat HIV directly, while other trials test drugs that treat or prevent the opportunistic diseases and non-AIDS-related complications that commonly affect people with HIV. Studies may also test easier or more effective ways to take medications, or strategies to treat side effects of medications.

There are also trials under way contributing to research surrounding a cure for HIV/AIDS.

The first trials of a new drug performed in humans are known as Phase I studies and test the safety of the treatment. These studies may also look for early signs of effectiveness, such as viral
load reductions after the drug is taken for one or two weeks.

Once Phase I studies are completed, the drug moves into Phase II testing. These studies collect safety and dosing information and begin to see how effective the treatment is when taken for several months.

Phase III studies are larger, longer trials designed to confirm whether or not a treatment works and whether there are important safety issues.

The U.S. Food and Drug Administration (FDA) will review data from all of the trials, along with test tube and animal studies, to determine whether or not to approve the drug. Sometimes, an important new drug is granted “accelerated approval” by the FDA while the Phase III studies are still ongoing. Other times, the FDA requires all studies to be completed before an application for approval can be filed.

Finally, Phase IV studies may evaluate the approved drug in more people and different populations. Phase IV studies, also known as post-marketing studies, are also conducted to test several different approved treatments, to find out if one works better than others.

Unfortunately, some people living with HIV enter clinical trials to gain access to a doctor or clinic because they may not have any other options for receiving care. Some trials provide the equivalent of free care and medication, but some do require that approved meds be provided by the participant. Although participating in a study may be a useful part of your treatment, it is important to know that the main purpose of the trial is to test the treatment—not to provide the best possible medical care. Therefore, study participation is not a good substitute for regular doctor visits.

Most, though not all, clinical trials compare at least two different drugs or drug regimens. For example, a study might compare a new antiretroviral (ARV) in combination with older ARVs in one arm (or group) to a combination containing only older (but effective) ARVs in the second arm. When an experimental or new treatment is compared to already approved standard treatments, the second arm is known as the control group.

Another type of control used in clinical trials is known as a placebo—a fake, sugar or dummy pill—that contains no medicine but looks exactly like the tested treatment. Today, HIV clinical trials rarely use control arms in which only a placebo is given. This is because we already have effective treatments—an experimental drug or regimen needs to show that it works better, causes fewer side effects or is easier to take than drugs or regimens that are already available.

When studies compare different medicines, a computer may be used to randomly assign you to one of the treatment arms. This is known as randomization. This is important, as it prevents the researchers conducting the study from being biased—for example, assigning patients they already have a relationship with to receive the experimental treatment and those they don’t know to receive a placebo.
Additionally, you may not be told which treatment you are receiving. This is known as a blinded study because the participants don’t know whether they are in the control arm or in the arm receiving the studied treatment. When both the study participants and the doctors don’t know who is in the control group, the study is called double-blind, again to prevent clinical trial staff members from being biased. The government usually tries to carefully regulate clinical trials.

Why would I participate in a clinical trial?
People participate in clinical trials for several reasons. Some people participate in order to get a new and otherwise unavailable treatment. Some people participate in order to get free laboratory tests. Also, one of the most common reasons is that participation helps scientists find better treatments for HIV. Conversely, there may be reasons not to participate in a clinical trial. For instance, you may be asked to stop taking other medicines that are helping you. The treatments in the trial may have side effects, or be unsafe. Other treatments you may want to take in the future may not work as well because of drugs you took in a clinical trial. Studies may also require hospital stays, invasive tests or procedures. Or you may just not have the time and energy that a study might require.

Are clinical trials safe?
It depends. One purpose of a clinical trial is to measure the side effects, also called adverse events, associated with using a drug or combination of drugs. If the drug is very new, there may be unknown side effects—potentially serious or possibly fatal side effects. If you experience side effects, you may be taken off the drug or given a lower dose.

Also, new treatments may not work very well. This is important in HIV care because a weaker or less potent drug or regimen may cause your virus to develop resistance to certain meds.

As a general rule, the more people who have taken the treatment being studied, the more likely that researchers will understand and be able to explain the potential risks of the study.

Some studies today involve experiments that may not offer a personal benefit, but they are critical to research exploring curative treatment approaches. If you decide to enroll in these trials, make sure you understand fully what you are getting into.

Before you enroll in any clinical trial, all of the known risks, benefits rights and responsibilities should be explained to you. This is known as informed consent. During the informed consent process, you should received a detailed written explanation of the rules of the clinical trial. It should be written in plain, everyday language and should be translated for people who do not understand English. It is important to be sure that you understand everything in the informed consent document, and that you keep a copy for yourself. When you are ready, you will be asked to sign the document. You will receive a copy that has been signed by you and the person in charge of the study—the principle investigator (PI)—at the clinical trial site.

If you don’t understand something, ask questions! Don’t feel like you are asking too many questions or taking up too much time. Clinical trials need participants like you, and you have a
right to fully understand the commitment you are making. It might be helpful to write down the answers to your questions, so that you have the information later on.

However, it is important to know that some questions can’t be answered—after all, clinical trials are conducted to answer important questions. For instance, the side effects of a new treatment may not be known. In that case, the person explaining the trial to you may tell you what might happen, but may add that the researchers do not know for sure.

Remember, less is known about a drug being studied in Phase I or II.

Each trial has a set of rules. These rules are called the protocol—the blueprint of the study. The protocol includes rules about how often you will need to visit the study site, along with the tests that will be done. These rules should also be explained in the consent form. Again, it is important that you understand the protocol, and that you are pretty sure you will be able to follow it.

If there are any changes to the protocol, a new informed consent may be given to you to read and sign. Again, make sure you understand any changes that are being made along the way before you sign.

Know that the informed consent is not a binding contract—you have the right to withdraw from the study at any time, and for any reason.

Who is in charge of a clinical trial?
There are several people you should be able to trust when you enter a clinical trial. First, you’ll meet a study nurse or study coordinator. This will probably be the person you deal with most often. He or she will probably explain the informed consent to you, deal with medical tests and blood draws and handle any minor problems that may come up during the trial, such as helping you find transportation to the study site.

In addition, every study site will have a PI. The PI may give you medical examinations during the study, and he or she will be responsible for dealing with any serious medical problems that come up as a result of your study participation. Remember the PI may not know which arm of the study you are in.

Every study site also has an Institutional Review Board (IRB). The IRB is responsible for protecting the rights of participants in a trial. It must approve every trial that is conducted at that institution, and it must review the trial every few months. The IRB can stop a trial if it doesn’t do what it promised or if it exposes people to harm. You can complain to the IRB if you have a problem while in a trial.

Finally, there is the study’s Data and Safety Monitoring Board (DSMB), made up of experts who review the information (data) from the trial at different time points and who can delay or stop the study if there are safety concerns.
When you sign the informed consent, you should be given contact information for the study coordinator or study nurse, the principal investigator and the chairman of the IRB. That way, if any problems come up during the study, you can easily contact the right person.

As you can see, despite the unknown risks of being in a clinical trial, there are many safety checks and built-in mechanisms to protect you as the study participant.

How do I enter a clinical trial and what happens next?
First, the clinical trial team will screen you. This will likely involve some medical tests and lots of questions regarding your health and medical history, to determine whether or not you meet the inclusion or exclusion criteria. These are rules about who can and who can’t participate in this particular trial. For instance, a study may exclude people who are taking a particular medication or have less than 200 CD4 cells. If a study didn’t have criteria, it would be difficult to prove that something works in a given group of people.

If you qualify for the study, you will be given the informed consent to read and sign. Again, make sure you understand what is in the informed consent. You may be able to take it home in order to study it more thoroughly. Don’t feel pressured to sign the informed consent on the spot.

After you sign the informed consent, you are officially enrolled in the study. Usually you’ll be asked to have baseline blood draws—for example, lab tests to measure your viral load or CD4 cell count immediately before starting an experimental treatment—along with other assessments. This is required so investigators can use this information as a comparison to the tests performed at later time points in the trial.

What happens after that may vary widely depending on the type of study. For instance, you may be randomized to one of the treatment arms in the study and may not find out which group you’re in until after the trial has been completed. You may be randomized, but will know which study arm you in. Some studies will put everyone on the treatment being tested, which is known as an open-label trial.

You may be asked to come back often—maybe every week or two at first, followed by visits every few months—for more tests and more blood draws, for as long as the study in ongoing. By taking blood draws at intervals during the trial, comparisons can be made to your baseline tests to determine safety and effectiveness.

You will probably be asked about side effects you may have experienced, and you may be asked to report how adherent you were in taking the medication. Some clinical trial researchers may ask you to bring your medication bottles to the site, every time you visit, so they can count the number of pills left.

You may be given a quality of life document to fill out as well. This form looks at how the medications you’re using in the study affect things like your moods, activity levels and sleep patterns.
It is important that you continue to see your regular doctor after you enroll in the clinical trial. Ask the people running your study to communicate regularly with your doctor. Make sure that both you and your doctor get copies of any blood tests that are available. Discuss any side effects that you experience with your doctor. If you get sick during the trial, make sure to tell your study nurse or principal investigator.

Remember, it’s also important to have the phone number of a doctor or nurse involved with the trial whom you can call 24 hours a day, in case you have a problem in the middle of the night. Because the drugs in your trial may be experimental, a doctor in an emergency room may not know what to do if the drug makes you sick.

Usually, if the study was randomized and blinded, you will be told what treatment you were taking. If the study is ending, and if study results are available, you should be given those results. If you have been taking an experimental drug that is working for you, then you may be able to continue the drug indefinitely. However, this is not always the case—you may need to wait for it to be approved before you can access it again.

How can I find out about clinical trials?
Your doctor may suggest participating in a clinical trial. Other organizations and websites can help you find out about clinical trials. For instance, clinicaltrials.gov is a site run by the National Institutes of Health that has information about all HIV-related clinical studies in the United States. It also has “health information specialists” you can talk to at the toll-free number 1-800-HIV-0440 (1-800-448-0440).

If you receive HIV care at a major hospital, several of the health care providers there may be conducting clinical trials that may be of interest to you. Ask your HIV care providers for more information.

In the end, clinical trials have helped provide all the treatments we now have available to us. They have also helped us determine which drugs are the most effective, the safest to use and easiest to take. Whether you decide to enroll in a clinical trial or not should depend on many factors.

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