FRANKLY SPEAKING ABOUT CANCER

Understanding Clinical Trials

A GUIDE FOR PATIENTS AND CAREGIVERS

Not enough people living with cancer know about or participate in clinical trials. Anyone facing cancer should be aware that a clinical trial may be an important treatment option at some point during your care.

If you are considering participating in a clinical trial, or want to know more about how these studies work, this guide will help answer your questions and help prepare you to talk about clinical trials with your doctor.

CANCER SUPPORT COMMUNITY

IF YOU ARE THINKING ABOUT A CLINICAL TRIAL:

The decision to participate in a clinical trial is a very personal one. Your type of cancer, overall condition and priorities are all important in making that decision with your doctor and treatment team.

Here are some of the reasons why people decide to participate in a clinical trial:

- Hope—There are no guarantees in a clinical trial. It's a research study designed to test new treatments and learn whether they work, but for many people, trials do offer hope. This is particularly true if you are facing an advanced or difficult-to-treat cancer, or if you have stopped responding to other treatments.

- Access—Access to the most innovative therapies. All new cancer treatments are studied in clinical trials and many new agents and approaches are available only through trials before they are approved by the Food and Drug Administration (FDA).

- Care—People in clinical trials get the highest quality care and monitoring of their cancers.

- Physicians and treatment facilities dedicated to improving treatment—The doctors and cancer center that participate in clinical trials make a commitment to advancing cancer treatment and care.

- Progress—By participating in a clinical trial, you contribute to progress in treating cancer. This is true even if the trial does not work for you. Cancer research owes a huge debt to the patients who bring courage, optimism and commitment to being in trials.

Managing Expectations

Clinical trials are done for all types and stages of cancer. Some are designed to increase cure rates in cancers that already have effective means of treatment; others to enhance quality of life or even to prevent cancer. There are also trials in which the goal is to extend the life of people beyond what would be expected with standard therapy.

It is critical to have an open, honest discussion with your doctor and treatment team before you enroll in a trial. Ask all your questions—about the trial, its benefits, side effects, what you will need to do in terms of appointments and procedures, and what is important in your life and your goals.

Listen. Your doctor will provide the information you need about the trial and its possible outcomes. Bring someone with you to help you understand what is being said, take notes and talk things over with you.

Take time to think. In most cases, you have some time to think things over and talk to your family or other people who support you. You don't have to rush, and you don't have to do this alone.

If your cancer is advancing and you are not responding to treatment, you can feel afraid and upset. If you learn that your cancer is at high risk for recurring or spreading, you may be uncertain about being part of a trial. You may be looking for an outcome that is not realistic for the trial. All of these factors make it even more important to talk to your doctor about what to expect from the trial.

Being in a trial provides hope, but also means you have to accept some level of uncertainty. You are, in many ways, an explorer, and like anyone venturing into new territory, that comes with questions that can only be answered by the trial itself. By having an open, honest discussion with your doctor, you will make the decision that best fits your life and goals.

CSC's Open to Options® program can help you think about participating in a clinical trial and prepare you to talk with your doctor. See the resources at the end of this fact sheet for more information.

UNDERSTANDING CLINICAL TRIALS

A clinical trial is a research study that compares a new medicine or device with the standard of care—the best available established treatment.

Clinical trials are designed, implemented and evaluated using very clear guidelines and protocols. This is critical to assuring that the results of the study are valid and can be used to establish the best treatments, or standard of care, for patients facing cancer. Understanding how clinical trials work will help you make your decision.

Safety and Effectiveness

The goal of any clinical trial is to improve cancer treatment. That means helping people to live longer and better. Do the benefits that people receive outweigh negative effects of the treatment? The basic criteria for success or failure of a trial are safety and effectiveness.

The safety of a new drug or treatment is determined by its toxicity or the side effects it causes. These side effects often depend on the dose of the drug or the way it is given. They can range from minor to very severe.

Effectiveness means—does it work? Do those patients taking the new treatment live longer? Do they have a longer period of time before their cancer begins to grow or progress? Do their cancers shrink or disappear more than those of people taking the standard therapy? Does it help to make them feel better, even if for a limited time?

The ways in which safety and effectiveness are analyzed and evaluated are often very complicated and rely on many factors. These include results of scans and lab work, the doctor's observations, the patient's experience and a variety of statistical comparisons and analyses.

Who Participates in Clinical Trials?

There are clinical trials for every type and stage of cancer. There are even trials to help prevent cancers. Some studies are focused on decreasing the side effects of treatment or improving quality of life.

The majority of studies are designed to improve the treatment of people with diagnosed cancers. There are two major types of these trials:

- **ADJUVANT AND NEOADJUVANT TRIALS:** The goal of these studies is to reduce the chances that your cancer will recur or spread after primary treatment. Adjuvant trials are done immediately after primary treatment, neoadjuvant trials before primary treatment. You might consider participating in one of these trials if you have an aggressive type of cancer, your cancer has spread to lymph nodes or you have a large tumor.
- **TRIALS FOR MORE ADVANCED CANCERS:** Many trials are designed to improve treatment for people with recurrent cancer, meaning it came back after being treated previously, or metastatic cancer, meaning it has spread and can no longer be fully removed. You might consider participating in one of these trials if your cancer is diagnosed in a later stage or if it comes back or spreads after you have one or more other treatments.

Informed Consent

Before participating in a clinical trial, you will be asked to give your informed consent. This is a formal process in which the doctor or clinical trial coordinator reviews every aspect of the trial with you. You will be asked to sign a document that says you understand the trial and agree to being part of it. This is a very long, and often complicated document. This is a good opportunity for you to ask questions, and a good time to bring someone with you to the appointment to help fully understand what is being proposed.

Who Should Think about Being in a Trial?

Before the FDA approves a drug for use in clinical practice outside of clinical trials it goes through a series of clinical trials phases. Each phase builds on what is learned from the one before it, and each has different ways of recruiting patients and evaluating the results.

PRE-CLINICAL TRIALS: Every new drug, agent or treatment that is studied in a clinical trial has already undergone years of testing in the laboratory. These drugs have been shown to have great promise before they are ever given to a human being.

PHASE I: Once a drug is approved for human studies, it is tested in a small trial to determine the optimal safe dose. Phase I studies often involve patients with different kinds of cancer, or more recently, a single genetic change.

PHASE II: If a drug can be given safely to people on the Phase I trial, it is tested in a Phase II study. These are larger studies, usually for one or more specific types and stages of cancer. The goal of Phase II studies is to both determine the optimal dosing and provide an early assessment of whether the drug works.

PHASE III: These trials take place after a drug has shown good results in earlier studies. They are large studies, often involving hundreds, or even thousands of patients, in multiple centers in the United States and/or abroad. Patients on Phase III trials have specific types and stages of cancer. Many Phase III trials are randomized—meaning that patients are randomly assigned to receive either the new treatment or the established standard of care. These trials are designed to provide definitive evidence to support FDA approval of the drug or agent for use in the public.

PHASE IV: These trials take place after a drug is approved and are often called post-marketing trials. The goal is to make sure that no safety or other concerns come up after a drug is approved that may not have been seen in the pre-approval trials. It is important to follow patients for a number of years to determine if there are any long-term side effects or other issues that affect the way the treatment is used.

WHAT IS THE STANDARD OF CARE?

The standard of care is the accepted, common treatment approach for a given type and stage of cancer as determined by all the evidence available to researchers and doctors treating patients. This evidence comes from other clinical trials and from the outcomes and experiences of patients who receive that treatment. The standard of care is the basis of comparison for any clinical trial both for survival and side effects. Cancer treatment is always moving forward, so the standard of care often changes for many types of cancer. There are published guidelines that provide detailed information for doctors and patients on the standard of care for most cancers.

Measuring the Outcomes

Every trial has specific outcome measures that are used to determine the success or failure of the study. Your doctor will focus on your care and your response to the treatment. Researchers analyze the results of all the patients who participate in the study. They use one or more of these measures:

- **OVERALL SURVIVAL:** This simply means—do people on the new treatment live longer than expected compared to those receiving the standard of care?
- **DISEASE FREE SURVIVAL:** This means the amount of the time that all visible signs of cancer have disappeared.
- **PROGRESSION FREE SURVIVAL:** This means the time from the beginning of treatment until the cancer begins to grow or spread again.

For many adjuvant and neoadjuvant trials, the outcome measures are different.

- **COMPLETE PATHOLOGICAL RESPONSE:** This means that after the treatment, all visible signs of the cancer have disappeared. This is considered a very positive response.
- **PARTIAL PATHOLOGICAL RESPONSE:** This means that there is still some visible cancer after the trial, however, the disease has decreased from where it started, reflecting a partial response.

It is also very important to record, analyze and evaluate any side effects, also known as adverse events, you experience during the trial. Your treatment team will examine you for any physical signs and symptoms during the trial and report anything that happens. It is critical that you tell your doctors about anything that you notice—whether it be physical or emotional—while you are on the trial. The information you provide is valuable in assuring you get the best care. It is also important in assessing the side effects of the treatment.

SOME DEFINITIONS

Single agent trials: Test one drug or agent. Most new treatments are initially studied as single agents.

Combination trials: Trials using two or more drugs or agents taken together. These agents often use different mechanisms to attack the cancer.

Randomization: A process where patients are assigned either the experimental treatment or the standard of care. Your doctor has no role in deciding which treatment you will receive and it is done at random.

Access for Everyone

It is very important that everyone facing cancer has access to clinical trials. People of color, underserved populations, older people and women have been underrepresented in clinical trials. There are many reasons for this—historical, cultural and social. They include mistrust of the medical system, biases about how certain groups will respond to therapy, and the failure to address social, emotional and logistical barriers that keep some people out of trials.

It all begins with the conversation between the doctor and the patient, and in many cases, the family. If your doctor doesn't talk to you about clinical trials, ask. If you are not satisfied, seek a second opinion. If you have concerns about any issue related to being on a trial, bring it up directly with your doctor and your treatment team.

Getting the best cancer treatment means knowing about and having access to clinical trials. Don't settle for anything less.

Finding A Trial

At any given time, there are thousands of open clinical trials in cancer centers and hospitals across the country. Despite that, it can still be difficult for patients and caregivers to find a trial that is right for them. Here are some tips for finding a clinical trial.

- Know as much about your cancer as possible—the type, the stage, any previous treatments you have received, the results of any genetic testing you ever had.
- Keep your records together so you can get easy access to them.
- Expect to be confused if you try to find trials online—especially if you don't focus your search. The names of trials are very technical. They all have specific requirements that have to be met to take part in them. Trials open and close all the time and even good websites may not be up-to-date on their status.
- If you do search online, use www.clinicaltrials.gov, or go to the website of an advocacy group that works with your cancer. Some cancer centers also maintain lists of open trials by cancer site or have a protocol office you can call for help.

The best way to find a trial for you is to talk to your doctor. You can:

- Ask your doctor about trials at the center in which you are being treated. In general, academic medical centers and cancer centers offer more trials than community hospitals or private practices.
- If there are no trials available at your center, ask your doctor to help find a study in another institution that is right for you. Many doctors are willing to search for trials or talk to their colleagues for this purpose.
- If your doctor is not willing to help you find a trial, get a second opinion in a treatment facility that has the expertise and experience to offer these studies.
- If you find a potential study online, print out the information and bring it to your doctor for discussion.
- Nurse practitioners and nurses can be great sources of information about trials. They often have more time to spend with you and answer your questions.

If you are in a large cancer center, you are more likely to find a trial in your institution, but realize that in some circumstances finding a trial means changing doctors or treatment facilities. That can be hard. Patients often have strong attachments to their oncology teams. A trial in another center can also present travel and logistical problems. For many people, the benefit of being on a trial that offers hope and access to new therapies justifies the difficulties that come with changing doctors or having to travel longer distances.

Your doctors may discuss potential clinical trial options with you, but if that does not happen, you should ask about trials and whether you might be a good candidate for one. This is particularly important at key moments in your treatment, including diagnosis, recurrence or spread. Don't be afraid to ask. This is your life and your treatment.

New Models for Clinical Trials

The traditional clinical trial recruits patients with a certain type and/or stage of cancer, for example stage IV breast cancer, or stage III prostate cancer. This is done to compare how people with similar cancers respond to the treatment--apples to apples. Traditional trials also recruit a specific number of patients for each arm of the study and follow those patients for a set amount of time.

Today, there are new models of trials, which are the result of new treatments and new ways of thinking about cancer. Many of these trials recruit patients with a specific genetic mutation that can be targeted with a drug or agent—for example people with a BRAF or EGFR mutation. They may have several different kinds of cancer. In some instances, the targeted mutation occurs in a very small percentage of patients. This often

means that a large number of cancer centers participate in the study, and can mean that patients have to travel to these centers to be a part of the trial.

Researchers are also doing more studies that are "adaptive." This means that they monitor how patients in each arm of the study are doing, and if it becomes clear that one group has an advantage, the study is adapted. Patients are moved to the therapy that is working better. This provides a faster, more flexible way of evaluating new treatments and their results.

MYTHS, MISCONCEPTIONS AND BARRIERS

There are many reasons why people do not participate in clinical trials. Some are personal or medical, but others are the result of myths and misconceptions that people have about trials. Here are some of the most common:

- **THE GUINEA PIG.** Clinical trials are experimental studies—designed to learn something new, but you are not a guinea pig. A great deal is known about any drug or agent before it is given to human beings, and patients in trials receive excellent care and are monitored very closely.

- **THE PLACEBO.** It is very unusual for any patient in a cancer clinical trial to receive a non-active treatment or placebo. As noted, the basis of comparison for new treatments is the standard of care—the best known treatment. If you are concerned about this, ask your doctor about the treatments on the study arms.

- **COSTS OF CARE.** All of the costs of care during a trial are covered either by the trial's sponsor or by insurance. If you are concerned about indirect costs, such as transportation or child care, tell your treatment team and ask about resources to help with these expenses.

- **THE LAST DITCH TREATMENT.** There are some trials, usually phase I studies, that are for patients who have exhausted most or all of their treatment options, but there are many trials for patients at other stages of the journey. If your doctor offers you a trial, ask about its goals and what you can possibly expect in terms of outcomes.

Clinical Trials Resources

American Cancer Society's Clinical Trial Matching Service 800-303-5691 www.cancer.org/clinicaltrials

BreastCancerTrials.org 415-476-5777 www.breastcancertrials.org

CenterWatch 617-856-5900 www.centerwatch.com

Cancer Support Community 800-814-8927 www.cancersupportcommunity.org/clinicaltrials

National Cancer Institute's Clinical Trials Registry 800-422-6237 www.cancer.gov/clinicaltrials

National Library of Medicine's Clinical Trials Search www.clinicaltrials.gov

TrialsCheck www.cancertrialshelp.org/trialcheck

CANCER SUPPORT COMMUNITY RESOURCES

The Cancer Support Community's (CSC) resources and programs are available free of charge. To access any of these resources below call 888-793-9355 or visit www.cancersupportcommunity.org.

CANCER SUPPORT HELPLINE ®

Whether you are newly diagnosed with cancer, a longtime cancer survivor, caring for someone with cancer, or a health care professional looking for resources, CSC's toll-free Cancer Support Helpline (888-793-9355) is staffed by licensed CSC Helpline Counselors available to assist you Mon-Fri 9 am-9 pm ET.

OPEN TO OPTIONS ®

If you are facing a cancer treatment decision, this research-proven program can help you. In less than an hour, our trained specialists can help you create a written list of specific questions about your concerns for your doctor. Appointments can be made by calling 888-793-9355, visiting www.cancersupportcommunity.org or by contacting an Affiliate providing this service.

FRANKLY SPEAKING ABOUT CANCER ®

CSC's landmark cancer education series provides trusted information for cancer patients and their loved ones. Information is available through publications, online, and in-person programs.

AFFILIATE NETWORK SERVICES

Over 50 locations plus more than 100 satellite locations around the country offer on-site support groups, educational workshops, and healthy lifestyle programs specifically designed for people affected by cancer at no cost to the member.

CANCER EXPERIENCE REGISTRY®

The Registry is a community of people touched by cancer. The primary focus of the Registry is on collecting, analyzing and sharing information about the experience and needs of patients and their families. To join, go to www.CancerExperienceRegistry.org.

The Cancer Support Community and its partners provide this information as a service. This publication is not intended to take the place of medical care or the advice of your doctor. We strongly suggest consulting your doctor or other health care professionals to answer questions and learn more.

THIS PROGRAM WAS MADE POSSIBLE THROUGH CHARITABLE GRANTS FROM:

AMGEN Oncology

Celgene

AstraZeneca

Karyopharm Therapeutics

Pfizer

NOVARTIS

SPECIAL THANKS TO BIOMARIN