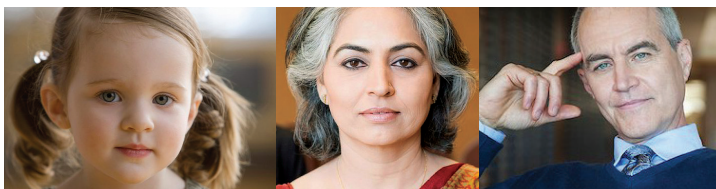


AMERICAN BRAIN TUMOR ASSOCIATION

Clinical Trials



American
Brain Tumor
Association®

Providing and pursuing answers®

ABOUT THE AMERICAN BRAIN TUMOR ASSOCIATION

Founded in 1973, the American Brain Tumor Association (ABTA) was the first national nonprofit organization dedicated solely to brain tumor research. The ABTA has since expanded our mission and now provides comprehensive resources to support the complex needs of brain tumor patients and caregivers, across all ages and tumor types, as well as the critical funding of research in the pursuit of breakthroughs in brain tumor diagnoses, treatments and care.

To learn more, visit abta.org.

We gratefully acknowledge Susan Chang, MD, director of Clinical Services, Neuro-Oncology Service of the Brain Tumor Research Center, Department of Neurological Surgery, School of Medicine, University of California, San Francisco, and the ABTA Clinical Advisory Committee for their review of this publication.

This publication is not intended as a substitute for professional medical advice and does not provide advice on treatments or conditions for individual patients. All health and treatment decisions must be made in consultation with your physician(s), utilizing your specific medical information. Inclusion in this publication is not a recommendation of any product, treatment, physician or hospital.

Clinical Trials

INTRODUCTION

This brochure describes how research studies, called clinical trials, are used to discover new ways to prevent, detect and treat brain tumors. Because clinical trials represent an additional treatment option for some, the following information explains what they are, how they work, and how you can find and evaluate a clinical trial to determine if it is right for you.

In general, there are several different types of clinical trials, including:

- Treatment trials
- Supportive care trials (also called quality-of-life trials)
- Prevention trials
- Early detection or screening trials
- Diagnostic trials

However, this brochure will focus primarily on clinical trials involving new treatments.

ABOUT CLINICAL TRIALS

A clinical trial is a research study conducted within a medical setting. It is an organized way of evaluating a new investigational treatment, such as a drug or device, to determine if it is safe and effective. Information derived from clinical trials add to our overall understanding of brain tumors and helps to identify new treatment options.

Clinical trial participants are patients who volunteer for this opportunity to obtain a treatment that otherwise wouldn't be available. During a clinical trial, participants receive either a new treatment, a new combination of existing treatments, or the currently-approved standard of care treatment (which is compared to a new treatment), or a currently available treatment that is used in a novel way.

No one knows in advance if the new treatment being tested in a clinical trial is as effective as, or better than, the standard therapy currently in use. The results of clinical trials are measured against the best standard therapy available for the particular condition.

Although researchers truly do not know whether the new treatment or the current treatment is the “best,” the new treatment being investigated must demonstrate some potential for success before a clinical trial is allowed to begin. That potential is based on previous laboratory experience, animal trials or the results of other clinical trials.

Trials are designed to answer the following questions about the new treatment:

- Is it safe? (Phase I)
- Is it effective? (Phase II)
- Is it more effective than standard treatment? (Phase III)

- Does it provide any benefit or advantage over standard treatment? Or is it the same or less effective than the standard treatment? (Phase IV)

WHY CLINICAL TRIALS ARE NECESSARY

Clinical trials play an important role in whether new treatments become available for public use. Many of the treatments available today are the result of clinical trials.

The U.S. Food and Drug Administration (FDA) requires any new treatment to be thoroughly evaluated and approved before being offered to the public. To gain FDA approval, the manufacturer of the treatment or device must submit full reports of the studies to show that the treatment or device is safe and effective for its intended use. Clinical trials act as the primary way for manufacturers to prove that their product is safe and effective.

HOW CLINICAL TRIALS BEGIN

If, after laboratory and animal studies, researchers believe a treatment or device will be safe and effective against a particular disease, the next step is to test it in humans. This is important because what works in the laboratory or in animals may not work in people. A clinical trial is designed to answer the crucial questions regarding the safety and effectiveness of the treatment in humans.

A clinical trial can be initiated by a researcher at a single medical facility or by an organization such as:

- National Institutes of Health (NIH)
- National Cancer Institute (NCI)
- National Institute of Neurological Disorders and Stroke (NINDS)

-
- Pharmaceutical, device or biomedical companies
 - Clinical cooperative groups or consortia

Before the clinical trial can begin, an application to conduct a trial of a new treatment must be approved by the FDA. The application includes a description of the treatment protocol and process the clinical trial will follow. If the trial is sponsored by an organization, such as the National Cancer Institute, then the protocol must also be approved by other review boards.

WHERE CLINICAL TRIALS ARE CONDUCTED

Clinical trials are primarily conducted by the U.S. government, pharmaceutical, biomedical or device companies and medical institutions. They often take place at cancer centers, university hospitals, major medical centers, and community medical centers.

CLINICAL TRIAL COSTS

The costs of clinical trials are covered by a variety of entities, including pharmaceutical companies, and are often supplemented by grants and scholarships, a patient's insurance, and the U.S. government.

The majority of clinical trials are paid for by the sponsor of the trial, which may be the U.S. government, a pharmaceutical company or a medical device company. The routine costs of care, such as surgery to remove the tumor or the usual follow-up MRI scans, may be covered by an insurance company with the patient paying their usual deductibles and out-of-

pocket expenses. Some, although not many, clinical trials provide small reimbursements to cover a patient's costs of participating in the trial, such as travel or parking.

In some instances, health insurance and managed care providers will not cover any patient costs in a clinical trial, nor expenses that occur because of side effects of treatment received in a clinical trial. This is because some health insurance plans define clinical trials as “experimental” or “investigational” procedures. As a result, the patient may be responsible for certain costs.

Before making a decision to enroll in a clinical trial, contact both the sponsor of the trial and your insurance company to learn what coverage is available to you.

HOW CLINICAL TRIALS ARE ORGANIZED

Each clinical trial follows a protocol—a detailed, written plan that explains why there is a need for the study, what it is intended to evaluate and how it will be conducted. The protocol is written by the clinical trial's principal investigator (the physician or scientist in charge of the trial) with input from other physicians, researchers, patient advocates and statisticians.

A protocol specifically includes:

- The reason (scientific rationale or basis) for conducting the trial
- Objectives of the study
- The number of participants that must be enrolled for the data to be meaningful
- Eligibility criteria—the types of tumors to be treated and their biomarkers, acceptable age ranges, health requirements and need for informed consent, and any exclusions due to previous treatments

-
- The treatments or devices to be used
 - A detailed explanation of how the treatment is to be given, its duration and schedule
 - Possible side effects and permitted interventions to ease the side effects
 - How patient progress is to be evaluated—required medical and neurological tests, questionnaires, scans and follow-up visits
 - The endpoints of the clinical trial—such as disease free survival (DFS), overall survival, quality of life (QOL), neurocognitive function, recurrence, time to progression (TTP) and toxicity/safety

Everyone enrolled in a clinical trial must meet the same eligibility criteria, receive the same treatment process and be evaluated the same way. This uniformity enables researchers to objectively measure the results of a new potential treatment. This means that patients involved in the same clinical trial will most likely have the same type of tumor, along with many other similarities, in order to ensure that the results are valid and not due to some other factor.

It is also important that an adequate number of patients be enrolled in the study to determine if effects (good and bad) are due to the treatment or to individual differences among the patients. The clinical trial protocol helps to ensure these types of issues are addressed.

Most clinical trials place participants into two groups: the investigational group (receives the new treatment) and the control group (receives the standard treatment or placebo). Participants are typically assigned to one of the two groups randomly, also known as a randomized clinical trial.

A randomized clinical trial (where participants are randomly assigned to each group) is considered the most reliable and impartial method for determining which treatment works best.

In a double-blind clinical trial, neither the doctor nor the patient knows which treatment is being given.

In a single-blind clinical trial, only the patients don't know which treatment they are receiving. At the end of the study, if one group has a better outcome than the other, the investigators will be able to conclude with some confidence that one treatment is better than the other. There are also non-randomized studies where patients with similar characteristics all receive the same investigational treatment.

Due to the seriousness of brain tumors, placebos are rarely used. If placebos are used in the trial, every patient must be informed of this possibility in advance of enrolling. Every patient must also receive, at minimum, standard therapy. No one in a brain tumor clinical trial will be "untreated."

CLINICAL TRIAL PHASES

Clinical trials are conducted in phases. Each phase focuses on answering a specific question about the new treatment.

Phase I

A phase I clinical trial is designed to answer the question: How much of the new treatment can be safely given and what is the best way to give it?

The research team monitors the patient carefully to assess the side effects of the treatment. The tumor-fighting effects are also evaluated, but this is not the primary purpose of a phase I study.

Some of these clinical trials are dose escalation studies—

studies in which the dosage of the treatment is increased gradually to most effectively determine a safe dosage. The result of this type of study is a determination of the point at which a balance is reached between dose and acceptable side effects. The trial typically lasts between a few months and a year, and involves a small group of about 20 patients. When a balance is reached between dosage and acceptable side effects, the treatment moves into a phase II study. The clinical trial is stopped if unacceptable side effects occur.

If the treatments under investigation are already well known for treatment of other diseases, but the correct dosage for brain tumors has not been determined, phases I and II may be combined in the same trial.

Phase II

A phase II trial is designed to answer the question: Is the new treatment effective against a specific type of tumor?

An effective treatment causes tumors to shrink in size or stop growing. There are very specific guidelines used in phase II trials to evaluate the effectiveness of the response to treatment. With a complete response (CR), the tumor or tumors disappear on scan. A partial response (PR) means that the tumor has shrunk in size by the amount described in the guidelines. Stable disease (SD) means little or no change in size of the tumor. Progressive disease (PD) means that the size of the tumor has increased per the guidelines.

A phase II brain tumor clinical trial might last as long as two years and require about 75 patients, but can vary depending on the study design. Patients are monitored according to the protocol outline and side effects are carefully evaluated.

If a positive response occurs in enough patients to be statistically significant (results which are not due to chance or error), research will move to a phase III trial. If the treatment is found to be ineffective, testing stops. If testing ceases, patients enrolled in the trial may be offered other treatment options or participation in another clinical trial.

Phase III

A phase III trial is designed to answer the following questions:

Is this new treatment more effective than already approved standard treatments?

Are there fewer side effects than the standard treatment?

Also, if the new treatment is as effective as standard treatment, does it offer some other advantage? For example, is the new treatment given orally rather than intravenously or is it safer to administer?

A phase III trial usually involves hundreds or even thousands of participants so the effectiveness of the different treatments can be statistically measured and compared on a large scale.

Once a new treatment has been proven successful in a phase III trial, an application for FDA approval can be submitted. If data from the clinical trials meet the FDA's standards, the treatment will be approved for use.

Phase IV

A phase IV trial might be required by the FDA to evaluate side effects that were not apparent in the phase III trials or to answer unresolved questions. This phase is conducted after the treatment has already received FDA approval. Again, large numbers of participants are enrolled in this type of trial.

YOUR RIGHTS AND PROTECTIONS AS A CLINICAL TRIAL PARTICIPANT

Leaving the Trial

You may end your participation in a clinical trial at any time for any reason. If you decide you want to leave the study, you have the right to learn about other treatment options. After leaving the trial you may remain with physicians at the trial treatment facility, return to your regular doctor to receive another treatment or consult with other experts.

Informed Consent

Prior to any kind of treatment, you have a right to know the exact nature of the treatment: the known risks, the prospects of success and if there are standard therapies. Informed consent means that the information must be explained to you by a member of the trial treatment team, all your questions must be answered and you must fully understand the explanation. You will be asked to sign a consent form once you are satisfied that you have all the information you need and have decided to participate in the study. Parents or guardians may sign for minors. Minors might be given an assent form which provides information appropriate to their age and allows them to be involved in the process.

Ongoing Monitoring

You will be closely monitored by medical professionals throughout the study to monitor changes in your overall health, not just your brain tumor. A data monitoring committee looks at the statistical parts of the study and alerts researchers if side effects outweigh the benefits of the treatment. If additional information about the treatment is learned during the study, you will be kept informed.

Clinical trials are monitored and overseen by several entities to ensure that participants' rights and safety are protected. These entities include the clinical investigator, Institutional Review Board, Data Safety Monitoring Board, and government agencies, such as the FDA.

Privacy

The study administrators must make every effort to keep your personal and health-related information confidential. To do this, most of your records will be identified by a number, rather than your name.

Risk Assessment

Institutional Review Boards (IRBs) composed of experts and lay people at hospitals and research institutions throughout the U.S. work to ensure you are not exposed to any unnecessary risks during the clinical trial. Clinical trials sponsored by the National Cancer Institute (NCI) and some drug companies will have their own Data Monitoring Committee (DMC) or Data Safety Monitoring Board (DSMB) to review the potential risks.

HOW LONG DOES IT TAKE A SPONSOR TO COMPLETE A CLINICAL TRIAL?

The answer to this question depends on the phase of the trial and the number of people participating. Phase I trials can last from several months to a year but involve small numbers of people. Phase II trials may take up to two years to complete. Phase III trials often require several years to enroll and monitor the progress of the hundreds or thousands of study participants.

However, if a particular clinical trial is of interest to many people, the trial may “accrue” participants faster than expected, helping to accelerate the anticipated timeframe.

HOW RESULTS OF CLINICAL TRIALS ARE MADE KNOWN

After all patients have been treated and followed for the prescribed length of time, the results are analyzed. It is the sponsor's obligation to distribute the results as quickly and widely as possible. In reality, this can take months or even years. Trial results are made known in several ways:

- A poster or presentation at a scientific medical meeting
- An article published in a scientific journal (this may take months before the article appears in print; some journals make available electronic versions of the article as soon as they are reviewed)
- Electronic bulletins from the National Cancer Institute (NCI)
- New trials citing results of the prior study
- An application to the FDA for a New Drug Application (NDA)
- Word of mouth among the researchers or sponsors
- News media reports, press releases, etc.

HOW TO FIND CLINICAL TRIALS

The best options for finding clinical trials are to ask your healthcare team for direction or seek out clinical trials on your own.

Ask Your Healthcare Team

Since your doctors know your physical condition, it makes good sense to talk with them about treatment

options. One of your physicians may already be an investigator in a trial located near your home. Or, your physician may know of clinical trials for which you would qualify. Additionally, your healthcare team can contact their colleagues in the field or specialists at brain tumor referral centers on your behalf. Don't hesitate to ask for their advice and help.

Seek Out Clinical Trials on Your Own

If you decide to pursue clinical trial information on your own, let your doctor know of your desire to learn more about clinical trials as a treatment option. Contact the ABTA for guidance on how to find a clinical trial that is right for you. You may also visit clinicaltrials.gov to search for available clinical trials. Then, collect all your diagnostic information. Ask your doctor's office staff to help you obtain the correct information.

You will need to know the following:

- The exact spelling of the tumor
- The location of the tumor within the brain or spine
- The biomarkers of your tumor (commonly found in a pathology report)
- The size of the tumor
- The number of tumors
- The type of treatments you've already received (biopsy or surgery, radiation therapy, chemotherapy, etc.). If you've received chemotherapy or radiation, you'll need to know the specifics: type of radiation or drug, dose and dates of treatment.

Eventually, you will need copies of your medical records. When you find a clinical trial of interest to you, the clinical trial coordinators will provide a list of the

records they need for review, such as copies of scans (and which dates), laboratory tests, operative reports, pathology reports, pathology slides, etc.

Your medical records belong to you and there should be no problem in getting the copies you need (although you may be charged copying fees, postage, etc.). Be aware, though, that copying costs are sometimes expensive. In a few states, medical records are released only to another physician.

HOW TO KNOW IF YOU'RE ELIGIBLE FOR A CLINICAL TRIAL

Every clinical trial has its own eligibility requirements, called inclusion and exclusion criteria. Some of these requirements include, but are not limited to, the following:

- Tumor type
- Age and/or gender requirements
- Certain tumor types or biomarkers
- Previous treatments allowed (or not)
- Medical history
- Minimum performance status required (performance status expresses a person's ability to function and perform normal daily activities—see the Zubrod and Karnofsky Performance scale below).

If you are considering a specific clinical trial, seek out as much information as you can about that new treatment. Because phase I trials are just beginning their testing, very little information may be available. On the other hand, a considerable amount of information is available by the time a clinical trial reaches phase III. You can search the medical literature for more information about the treatment on websites such as the National Institutes of Health National Library of Medicine PubMed® (pubmed.gov) and Google Scholar (scholar.google.com).

ZUBROD (AND KARNOFSKY) PERFORMANCE SCALES

- 0 Fully active, able to carry on all pre-disease activities without restriction (Zubrod 0 equates to a Karnofsky score of 90–100)
- 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. For example, light housework, office work (Karnofsky score 70–80)
- 2 Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours (Karnofsky score 50–60)
- 3 Capable of only limited self-care, confined to bed or chair 50% or more of waking hours (Karnofsky score 30–40)
- 4 Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair (Karnofsky score 10–20)

CONTACT THE STUDY COORDINATOR FOR THE CLINICAL TRIAL(S) IN WHICH YOU HAVE INTEREST

Call the contact number for the clinical trial location you are interested in, or ask your doctor to call for you. A clinical trial coordinator, protocol assistant, research associate, or nurse may accept telephone or e-mail inquiries to verify that the trial is still open. Before you call, make a list of questions that concern you most and that you need answered before you can make a decision.

Some of the most common questions include:

- Why is the new treatment thought to be effective? Has it been tested before?
- When did the trial begin?
- How many people have been treated so far?
- How many participants have my type of tumor?
- What are the known possible side effects? Are they temporary or permanent? Can they be controlled or lessened some way (medications, diet, etc.)? How could they affect my daily activities?
- How is the treatment administered and where will the treatment take place? Can it be given close to my home?
- How many treatments will there be? How long will each one take?
- Will the study doctors work with my regular doctors while I participate in the study?
- Will I have to be hospitalized as part of the study?

- Am I eligible for this study?
- How and when will I be notified if I am eligible for the clinical trial?
- What costs will be covered by the clinical trial sponsor?
What costs will be covered by my health insurance?
What costs will be my responsibility?

A definitive answer on eligibility may require copies of your medical records, including blood test reports, operative reports, scans, pathology reports, etc. Find out which documents are needed to determine your eligibility, and the best way to send them.

Ask for a copy of the complete protocol and the informed consent form. The informed consent form includes information about the hoped-for benefits, the known risks and reported side effects of the new treatment. The protocol is probably the only document that contains the full rationale for the study. It documents the reason the study is being done and the results of earlier testing on the new drug or device. Some clinical cooperative groups offer their complete protocols at their website; if not, request it from a research associate or investigator associated with the clinical trial.

RIGHT TO TRY AND EXPANDED ACCESS

Some people are not eligible for clinical trials due to reasons outside their control, including, their treatment history, their medical history, trial-specific inclusion criteria, trial funding, or other factors.

The **Right to Try Act** and **Expanded Access** are two ways patients can get access to a clinical trial or other investigational treatment even if they do not meet the eligibility requirements. By using either of these options,

the costs of a clinical trial or investigational treatment may not be covered by a trial sponsor, so it is important for the patient to understand which costs he or she will be responsible for.

RIGHT TO TRY LAW

The Right to Try Act was signed into law in 2018. Through this law, a patient may be admitted to a clinical trial that he or she would not normally be eligible for, or be prescribed a non-FDA approved medication that has been studied in a clinical trial.

For a treatment to be used under Right to Try laws, it must have passed FDA phase I clinical trial testing. The patient must have a life-threatening disease or condition and have first tried all other approved treatment options. Also, the patient (or their legally authorized representative) must obtain and provide to a physician the written informed consent regarding the trial.

The costs of an investigational treatment provided under Right to Try law may not be covered by a clinical trial sponsor or health insurance, so it is important for the patient to understand potential costs. Additionally, there may be risks to trying a treatment under the Right to Try Act. Speak with your doctor about the risks of these treatments.

EXPANDED ACCESS/COMPASSIONATE USE

Expanded Access (also called Compassionate Use) provides patients that have life-threatening diseases or conditions with access to a non-FDA approved investigational treatment. The patient must have no

other generally accepted treatment options available, and must not be eligible for a clinical trial. A licensed physician must oversee the treatment and work with the parties testing the investigational treatment. The FDA must approve a patient's request to use an investigational treatment under Expanded Access. The costs of an investigational treatment provided under Expanded Access may not be covered by a clinical trial sponsor or health insurance, so it is important for the patient to understand which costs he or she will be responsible for. Additionally, there may be risks to trying a treatment under Expanded Access. Speak with your physician about the risks of these treatments.

DECIDING

Once you've learned about the clinical trials that are available, and have talked with your doctor about the standard treatment therapies available, it becomes time to decide the next course of action. You should now have enough information to make your decision about whether it is in your best interest to participate in a clinical trial.

Remember, clinical trials are medical research—they can't promise you'll be cured, or even helped, by the treatment being studied. There are pros and cons to investigational treatments, just as there are for all the other treatment options. Discuss the results of your research with your doctor, your family and others whose judgment you value and trust. If you have researched your options well, you should be able to make an educated choice on how to proceed. Also, the patient (or their legally authorized representative) must obtain and provide to a physician the written informed consent regarding the trial.

AMERICAN BRAIN TUMOR ASSOCIATION INFORMATION, RESOURCES AND SUPPORT

Brochures

Educational brochures are available on our website or can be requested in hard copy format for free by calling the ABTA. Most brochures are available in Spanish, with exceptions marked with an asterisk.

General Information

About Brain Tumors: A Primer for Patients and Caregivers

Brain Tumor Dictionary*

Brain Tumors Handbook for the Newly Diagnosed*

Caregiver Handbook*

Tumor Types

Ependymoma

Glioblastoma and Anaplastic Astrocytoma

Medulloblastoma

Meningioma

Metastatic Brain Tumors

Oligodendroglioma and Oligoastrocytoma

Pituitary Tumors

Treatment

Chemotherapy

Clinical Trials

Conventional Radiation Therapy

Proton Therapy

Stereotactic Radiosurgery*

Steroids

Surgery

AMERICAN BRAIN TUMOR ASSOCIATION INFORMATION, RESOURCES AND SUPPORT

Information

ABTA WEBSITE | ABTA.ORG

Offers more than 200 pages of information, programs, support services and resources, including: brain tumor treatment center and support group locators, caregiver resources, research updates and tumor type and treatment information across all ages and tumor types.

Education & Support

- **ABTA Educational Meetings & Webinars**
In-person and virtual educational meetings led by nationally-recognized medical professionals.
- **ABTA Patient & Caregiver Mentor Support Program**
Connect with a trained patient or caregiver mentor to help navigate a brain tumor diagnosis.
- **ABTA Connections Community**
An online support and discussion community of more than 25,000 members.
- **ABTA CareLine**
For personalized information and resources, call 800-886-ABTA (2282) or email info@abta.org to connect with a CareLine staff member.

Get Involved

- Join an ABTA fundraising event.
- Donate by visiting abta.org/donate.

Contact The ABTA

CareLine: 800-886-ABTA (2282)

Email: info@abta.org

Website: abta.org

AMERICAN BRAIN TUMOR ASSOCIATION

8550 W. Bryn Mawr Avenue, Suite 550

Chicago IL 60631

For more information:

Website: abta.org

CareLine: 800-886-ABTA (2282)

Email: info@abta.org



American
Brain Tumor
Association®

Providing and pursuing answers®