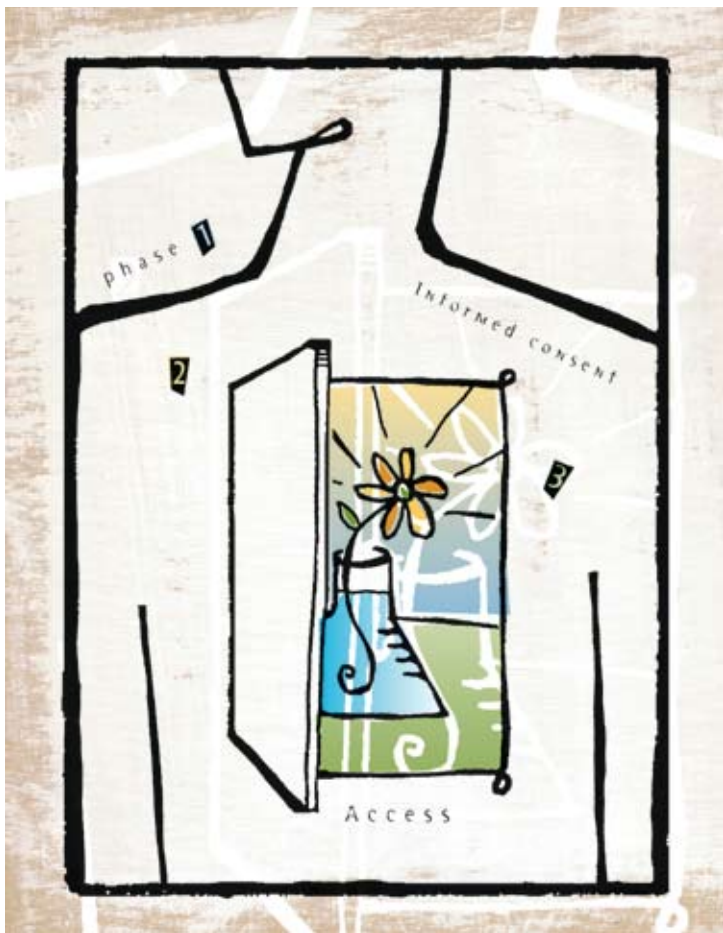


A Patient's Guide to Clinical Trials



Types of Trials ■ Phases ■ Informed **Consent** ■ Finding a Trial
■ After the Trial ■ **Drug Access** ■ Questions to Ask ■ **and More**

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A Patient's Guide to Clinical Trials

ONLY A SMALL NUMBER OF DRUGS DEVELOPED IN THE LABORATORY

complete the full clinical development program to be deemed safe and effective enough for the Food and Drug Administration to approve them—a **process that may take close to a decade**. But before FDA approval, a series of clinical trials must provide reliable data on the treatment's safety and potential benefit.

ONLY ONE in 1,000 compounds makes it from laboratory testing to human testing, where carefully designed studies for experimental treatments may contain a dozen or several thousand patients. Clinical trials provide data that may prove a new treatment is better than the standard therapy. They offer hope to patients with few options or those seeking treatments that may be more beneficial than the standard, one with fewer toxicities or one that is more convenient. Patients may also be motivated to join a clinical trial to further cancer research and help future cancer patients. **Although the number of patients enrolling in clinical trials has increased** in the past

decade, the increase in new treatments being developed mean more patients are needed to test new therapies. Unfortunately, only about 4 percent of cancer patients participate in trials. Participation may provide a potential benefit to science and future patients, and the patient may have the benefit of a potentially better therapy. **Online services, such as www.clinicaltrials.gov and www.cancer.gov**, provide information on researching and joining a trial, and provide search engines to find open trials. This pocket guide will serve as a tool to help you make an informed decision about whether joining a study is right for you.



Types of Trials

FOR EACH TYPE OF CLINICAL TRIAL, whether it is for a new injectable chemotherapy drug, a novel targeted agent or a preventive drug, investigators must design a plan to best study it. Clinical trials are done for novel experimental treatments, agents to prevent cancer, screening to detect cancer at an early stage, diagnostic tests as well as supportive care trials that study quality-of-life issues.

Most experimental compounds are first tested in the preclinical phase. Only one in 1,000 compounds ever make it through preclinical testing—laboratory trials that are conducted before a drug is tested on humans. The compound is usually first tested in cancer cells in a test tube or Petri dish to see if it is effective. Next, it is studied in animals to test if it is both effective and safe. Once a treatment moves to human testing, study investigators must decide how best to study the new therapy. Below are the different types of clinical trials.

- **Treatment trials** may include types of chemotherapy, radiation, targeted agents, surgery, gene therapy, immunotherapy or a combination of therapies.
- **Prevention trials** test new methods, such as chemoprevention medicines, vitamins, minerals or other supplements that scientists believe may lower the risk of a certain type of cancer. These trials look for the

best way to prevent cancer in people who have never had cancer or to prevent cancer from returning or a new primary cancer.

- **Screening trials** test the best way to find cancer, especially in its early stages, when it's the easiest to treat. Recent clinical trials are currently studying if computed tomography performed each year would find early-stage lung cancer in people at high risk.

- **Genetic studies** are also considered clinical trials. One genetic study called the Sisters Study will be looking for genetic and environmental risk factors for breast cancer. The trial is currently recruiting 50,000 women who may be at risk for breast cancer because one or more of their siblings had the disease. These types of trials may focus on genetic composition and how that affects cancer diagnosis, response to treatment and early detection. Researchers use the subject's blood and tissue to look for genetic abnormalities associated with certain types of cancer to help understand the role of genetics in cancer.

- **Supportive care trials** explore ways to improve comfort and quality of life for cancer patients. These trials study ways to reduce side effects, such as vomiting, fatigue, pain and sexual dysfunction and improve emotional and social functioning. Quality-of-life studies have examined integrative therapies, such as yoga, acupuncture, massage, natural herbs and vitamins as well as medication for sleep disorders and nausea.



Phases of Testing

ALTHOUGH AN INCREASING NUMBER of investigational cancer drugs are being approved by the FDA each year, the process is still lengthy and complex, beginning with a compound or idea that then must pass multiple hurdles before human testing can begin. Most clinical research of a new drug progresses in an orderly series of steps, called phases. This allows researchers to answer questions in a way that provides reliable information about the drug and protects the patients.

■ **Phase I:** Once a treatment clears preclinical testing in the laboratory, a phase I trial enrolls only a small number of patients. These early studies evaluate how a new drug should be given (orally or injected into the blood or into the muscle), how often it should be administered and the most effective dose with the fewest and least severe side effects. The drug regimen usually starts off very low and increases to the best dosage. Many patients who enter phase I trials have limited therapeutic options or do not improve with standard therapies. Treatments are often very experimental and may have a low likelihood of benefit. The primary thrust of phase I trials are safety and establishing a tolerated dosage. Fortunately, there are now more drugs in early studies that are designed based on an understanding of cancer biology and offer a greater probability of benefit.

■ **Phase II:** While a phase II trial continues

to test the safety of the drug, it also begins to evaluate how well the new drug works in a selected tumor type. These trials are usually limited to a specific tumor type that may have showed benefit with the treatment in earlier trials. Occasionally evidence in phase II trials shows such a significant benefit in a certain tumor type that a drug may go through an accelerated approval process by the FDA before completing the standard decade-long process.

■ **Phase III:** These studies either test a new drug, a new combination of drugs or a new surgical procedure in comparison to the current standard. Most patients choose to enter phase III studies more often than early-phase trials because of the availability, high number of patients needed, multiple locations and the higher probability that the treatment will work. Typically, a participant is randomly assigned to the standard treatment or the new treatment (called randomization). Some phase III trials are blinded, which means the patients may not know which treatment they are given to prevent bias. Those patients who are not randomized to the experimental treatment will receive the best standard treatment available. Phase III trials are often conducted at sites nationwide, including doctors' offices, clinics and cancer centers. Afterward, data from each site are pooled for the trial results.

Additional trials, though rare, are conducted after FDA approval to study the treatment's benefit and tolerability in a large population that may include several thousand patients.



Informed Consent

BEFORE THE INFORMED CONSENT MOVEMENT, clinical trials were many times performed on people without their detailed consent, including prison inmates, the mentally ill and concentration camp prisoners during World War II.

Developed after the trials of Nazi war criminals in the late 1940s, the Nuremberg Code was the first internationally recognized code of ethics regarding research in humans, which included voluntary participation. In 1981, the United States passed legislation requiring informed consent of all clinical trial participants to prevent patients from not knowing or misunderstanding their role in a clinical trial.

Informed consent is more of a process than a document, but before patients are allowed to participate in a clinical trial, they must sign an informed consent document that explains the purpose of the research, risks, benefits, alternative treatments and the patient's rights. It also provides an ongoing, open line of communication between the researchers and the patient.

Federal regulations protect patients by requiring voluntary informed consent. The informed consent document must clearly explain every aspect of the patient's choice regarding the trial. Typically, informed consent documents are written by the investigators conducting the research study and are approved by an Institutional Review Board, a committee that evaluates and approves all research studies before

they begin. The IRB monitors the trial and decides if any changes are necessary as the trial progresses. Although the board monitors the trial regularly, it also must continually approve the trial each year until the study is complete. If unexpected side effects develop or the treatment is discovered to possibly cause harm in the participants, the IRB can halt the trial at any time. If the treatment shows overwhelmingly positive results, the IRB can also prematurely stop the trial and allow all participants to cross over into the more effective treatment arm of the trial.

In addition to the IRB, many clinical trials federally funded through the National Institutes of Health require monitoring by an additional committee called the Data and Safety Monitoring Board. Comprised of doctors, patient advocates and statisticians, the board makes sure risks are kept to a minimum and data are complete and accurate. The DSMB has the power to stop a trial if negative or harmful results appear and can also stop the trial and allow all participants to cross over if a particular treatment works better than another. Another precaution is the FDA safety committee, which will inspect the trial, including records, research personnel, clinics and other clinical trial sites if complaints are lodged against a trial.

With about 75 percent of pediatric cancer patients enrolling in clinical trials, most parents will need to know the informed consent process. For these patients, informed consent is a shared decision between the parent and child. Children as young as 7 years

old are involved in some type of consent role in their care, but the parent must still read and understand the informed consent form and sign it to give legal permission for their child to participate in the trial. The ethical rule now is for the parent to provide informed consent, but for the child to agree to be a participant in the trial.

For all patients, the informed consent document should be easy to understand and should be written at an eighth-grade level, although some patient advocates still say patients may not fully understand all aspects of the clinical trial. For this reason, patients are encouraged to ask questions before and throughout the trial.

Patients should carefully read the entire consent form, ask questions of their doctors to gain a complete understanding of their treatment options and take the necessary time to reach a decision. If the patient's first language is not English, translation assistance is given to ensure understanding of the trial. The patient is allowed time to understand the information provided, to discuss the information with family, friends or physicians and to ask follow-up questions to the research team. As the trial progresses, the research team will continue to provide information and updates. It is important for patients to understand that since the treatments are experimental, outcomes and side effects are not always foreseeable, although any predicted risks should be explained in detail to the patient.

An informed consent document will include:

- A description of the research, its purpose,

how long the trial is expected to last, the procedures and treatments

- Risks and benefits of the treatment
- Other appropriate treatments that might benefit the patient
- A statement describing the extent to which the patient's identity is kept confidential
- A statement that participation in the trial is voluntary and that the patient may leave the trial at any time
- An explanation of any compensation or alternate medical treatments in the case of injury, what they consist of or where further information may be obtained
- The contact person if you have questions about the research or your rights as a patient, and the contact person in the event of a research-related injury

Patients should keep a copy of the informed consent document as a resource with their medical records. Patients may also ask for the full study design, which explains the clinical trial details. No informed consent document can ask patients to waive their legal rights or release the trial's research team, trial sponsor, drug manufacturer or institution from liability of negligence.



How to Find a Trial

UNFORTUNATELY, THERE IS NO ONE RESOURCE that contains every clinical trial for cancer patients. The process may involve searching through websites, calling pharmaceutical companies or asking your local cancer center or your doctor for information.

The NCI (www.cancer.gov) provides a comprehensive listing of clinical studies, providing more than 3,500 open trials. The site lists all NCI-sponsored trials and also provides links to NCI-recognized institutions and cooperative groups. The NIH's website (www.clinicaltrials.gov), another government-sponsored site, contains clinical trials for cancer and other diseases. Patients can also use this site to search by location, cancer type, disease stage, preferred treatment and other characteristics.

A clinical trial search should always begin with your oncologist, who should be able to tell you if something is available locally and give you resources on what is available in other parts of the country. Clinical trials are conducted at each of the 39 NCI-designated comprehensive cancer centers around the United States. Although it may be time-consuming to search for trials at each location, start with the one closest to home. If you are looking for a particular drug, contacting pharmaceutical companies directly is often the best source of information, but they may be concentrated in one location. Many nonprofit organizations also list active trials

for specific tumor types. (See opposite page for a listing of clinical trial resources and matching services.)

The earlier a drug is in the clinical trial process, the fewer places it is available. Patients may have better luck with late-phase trials that are conducted at various sites with enrollment often in the thousands and treatment that is more likely to be effective. Those with extremely rare cancers, patients facing recurrent disease and those who are not responding to the standard treatment regimen might find only a few institutions where a new approach to their disease is under investigation.

Other cancer patients are often a valuable source of information. Contacting local support groups through your hospital, physician or the American Cancer Society may turn up clinical trials. Cancer centers and cancer organizations often have message boards or e-mail lists where patients can talk to each other. Patients already enrolled in a trial are often willing to discuss their experiences. It's wise to be cautious, though. One person's experience may not be identical to yours.

Each trial has its own eligibility criteria and often has restrictions based on the type and stage of cancer, age, previous treatments received and current health status. It is best to keep your medical history handy when searching clinical trials because eligibility requirements may disqualify you from participating in certain trials. Once you've found trials you may qualify for, discuss them with your doctor and contact the study coordinators.

RESOURCES

General:

CenterWatch

www.centerwatch.com

Coalition of Cancer Cooperative Groups

877-520-4457

www.cancertrialshelp.org

EmergingMed

877-601-8601

www.emergingmed.com

National Cancer Institute

888-624-1937

www.cancer.gov

National Institutes of Health

www.clinicaltrials.gov

Cancer Centers:

Dana-Farber/Harvard Cancer Center

877-420-3951

www.dfcc.harvard.edu

Duke Comprehensive Cancer Center

888-275-3853

cancer.duke.edu

Fox Chase Cancer Center

888-369-2427

www.fccc.edu

Fred Hutchinson Cancer Research Center

800-804-8824

www.fhcrc.org

H. Lee Moffitt Cancer Center and Research Institute

888-663-3488

www.moffitt.usf.edu

Jonsson Comprehensive Cancer Center

310-825-5268

www.cancer.mednet.ucla.edu

Mayo Clinic Cancer Center

800-664-4542

cancercenter.mayo.edu

M.D. Anderson Cancer Center

800-392-1611

www.mdanderson.org

Memorial Sloan-Kettering Cancer Center

212-639-2000

www.mskcc.org

Roswell Park Cancer Institute

877-275-7724

www.roswellpark.org

Sidney Kimmel Comprehensive Cancer Center

410-955-5222

www.hopkinskimmellcancercenter.org

University of California, San Francisco Comprehensive Cancer Center

877-827-3222

cancer.ucsf.edu

Pharmaceutical:

Amgen Trials

805-447-1000

www.amgentrials.com

Novartis

888-669-6682

www.novartisclinicaltrials.com

Nonprofit Organizations:

Living Beyond Breast Cancer

610-645-4567

www.lbbc.org

Multiple Myeloma Research Foundation

www.multiplemyeloma.org

For more listings, visit

www.curetoday.com.



Costs

IN MOST TRIALS, the drugs under investigation are provided at no cost to the trial participant. Routine costs, such as hospital stays, outpatient appointments and tests accrued during a trial, are often covered by insurance or Medicare if the trial meets certain criteria.

Before joining a clinical trial, you should discuss the costs associated with the trial with the research team and ask what will be covered by insurance. Also, contact your insurance provider and discuss your coverage policy. Although insurers will not usually cover “experimental” treatments, recently passed legislation in several states requires insurance companies to cover routine medical care during a clinical trial. If an insurance company refuses coverage, appeal before the trial begins. Many companies will acknowledge a written letter by a doctor explaining the importance of the drug to a patient’s well-being and care. Non-treatment trials, including prevention or screening clinical trials, may not be covered by health insurance.

While many government-funded, late-phase trials are held in various sites across the country, many early-phase trials may be limited to a particular cancer center. Patients should consider the cost of travel and lodging, especially if the trial extends over several weeks or months and frequent trips are needed.

Some institutions can help with certain expenses. The NIH provides free travel for

those participating in NCI clinical trials in Bethesda, Maryland. The patient is only responsible for costs associated with the initial trip. The NIH also provides stipends to help with the cost of accommodations. Many private cancer centers also help patients find ways to alleviate some of the financial burden, including St. Jude Children’s Research Hospital, which provides free care to children with cancer. When you apply, ask who handles such issues for the institution.

Discounts and complementary airfare from major airlines, corporations and nonprofit air transportation organizations provide needed travel assistance including Angel Flight (www.angelflight.org), Mercy Medical Airlift (www.mercymedical.org) and Corporate Angel Network (www.corpangelnetwork.org). The National Patient Travel Helpline (800-296-1217) finds free or discounted air travel for those with a medical and financial need.

Housing may also be available through various nonprofit organizations or research centers if the patient must travel to the clinical trial site. The ACS has 22 Hope Lodge locations nationwide offering low-cost housing options for patients. The Ronald McDonald House offers housing for traveling pediatric cancer patients and their families. The National Association of Hospital Hospitality Houses (www.nahhh.org) provides information on more than 150 organizations around the country that provide free or discounted temporary housing (average is between \$5 and \$15 per day).



After The Trial

ONCE THE STUDY IS COMPLETED, there is no guarantee the patient may be given the option to continue on the drug, even if the patient has no other treatment options.

While some pharmaceutical companies may continue to offer the treatment, it may not be covered by insurance. Drug companies may only make a limited amount of drug for the trial, and as a result, there may not be enough after the trial is complete. There are special government programs that may provide the drug, and pharmaceutical companies may offer the drug through a compassionate use program (see “Drug Access”).

The data from the trial may be used to design future studies or be reviewed by the FDA for drug approval. It may take several months for the research team to compile data, but if the trial showed benefit, it may be announced through a medical journal or professional oncology meeting. Most clinical trial results found in medical and scientific journals are critiqued by medical professionals before publication to confirm the conclusions, which may also take time. Patients can find out information on the trial results from the research team or they can search PubMed (www.pubmed.gov), an online database of medical articles.

If the trial is one of many testing a particular treatment or it is a large, late-phase

trial, once an investigational drug is proven safe and effective, it may become the new gold standard. Sometimes, the trial results are inconclusive or the study design is flawed, causing researchers to work with the FDA to restructure the trial or determine how best to proceed with the next trial.

Previously, clinical trials that had either negative or inconclusive results or those that were halted early were not disclosed to the public or scientific community because their findings were not considered significant. This resulted in many duplicated trial efforts to test certain treatments and unidentified side effects. Currently, many pharmaceutical companies have clinical trial registries, a listing of all trial details and results, but there is no single, standardized registry. Some drug makers, including Eli Lilly and Roche, have published registries on their websites, listing all clinical trial results regardless of the outcome.

There is a goal to create a comprehensive, publicly available clinical trial database. Since February 2000, all federally and privately funded clinical trials of experimental treatments for serious diseases have been required to provide information to ClinicalTrials.gov's public clinical trial registry. Unfortunately, the information required is not comprehensive and the requirements have not been enforced. Within the next year, the World Health Organization will create a global clinical trial registry and www.clinicaltrials.gov will be improved so that researchers, patients and healthcare professionals can be fully informed about all clinical trials for a certain treatment.



Drug Access

PATIENTS MAY WAIT MONTHS OR YEARS for a drug to become available. For patients who have few treatment options and can't enroll in a clinical trial, compassionate use may be an acceptable alternative to a clinical trial. Some drug manufacturers sponsor voluntary programs either through expanded access or single-patient use that allows patients to receive investigational drugs before they have been approved.

Expanded access programs are typically designed to provide widespread access to a drug that has proven efficacy in clinical trials but is still awaiting FDA approval. They're similar to standard clinical trials with a specific treatment plan and certain FDA requirements, but they have less strict eligibility criteria.

Single-patient use offers an experimental drug to an individual patient, rather than a group. The FDA approves these uses on a case-by-case basis. Decisions are based on other treatments already available and the specific drug's effectiveness and toxicities shown in clinical trials.

Trying to get an unapproved drug through a compassionate use program can be frustrating, confusing and time-consuming and, unfortunately, only a few patients succeed. That's because there's no central database of these programs, drug companies may not have consistent procedures and federal policy is constantly evolving. In addition, many drug companies are hesitant to offer

compassionate use because they pay most of the costs, the drug may be in short supply, safety problems may arise that could hinder approval and alternative access could reduce participation in clinical trials. To qualify for compassionate use, patients typically must have exhausted standard treatment options, be ineligible for clinical trials and have a debilitating or life-threatening illness. To find compassionate use programs, patients should start with drug companies, cancer advocacy groups and clinical trial listing services. Compassionate use programs are offered at the discretion of a drug company, and the FDA can't compel a company to provide the drug.

Although patients may do most of the legwork tracking down a drug, their doctor must be the one to get formal approval from the drug company and the FDA for use of the drug. Detailed paperwork about the patient's situation, including medical history and previous treatments must be submitted by the patient's doctor. In some cases, the FDA turns around an approval in 24 hours, but in other cases, additional approval from an IRB is needed.

If a drug company turns down your request for individual use, try to get in touch with the right official, such as the medical director for oncology clinical development, to plead your case. If you're denied a spot in an expanded access program, check in regularly with the investigators or medical center for openings or new trials.

For a listing of current expanded access programs, visit www.curetoday.com.



Myth Versus Fact

PERVASIVE MYTHS about clinical trials may make you hesitant to volunteer. Here are the facts.

MYTH: Patients in clinical trials are little more than human guinea pigs.

FACT: Some people balk at participating in clinical trials because they fear that doctors and researchers will treat them as a set of symptoms rather than as a human being. But the overwhelming majority of cancer patients who have participated in clinical trials say the experience was positive and that they were treated with respect.

MYTH: Clinical trials are not safe. I'd be gambling with my health if I signed up.

FACT: New treatments are tested on human subjects only after there is valid scientific evidence that the treatments are likely to be effective and safe. If you take part in a phase III clinical trial, the drug or treatment has already been tested on small groups of patients for both safety and effectiveness.

MYTH: You should only agree to take part in a clinical trial if your cancer is terminal or there are no other treatment options available outside a trial.

FACT: Some clinical trials are reserved for cancer patients who have exhausted all the treatment options for their disease, but clinical trials of various types are open to patients at all stages of treatment. There are clinical trials that test ways of preventing a recurrence in breast cancer survivors, trials that look at cancer prevention in high-

risk populations and trials that compare different doses of chemotherapy drugs already in use.

MYTH: Cancer patients may be given a placebo in a clinical trial.

FACT: Placebos are not commonly used in clinical trials that test cancer treatments. Patients either receive the new treatment or the best standard of care. If there is no standard of care, patients may receive a placebo. In no case is a trial approved that would jeopardize a patient's health or offer them anything inferior to the best currently available treatment.

MYTH: If I join a clinical trial I won't be able to drop out.

FACT: This is not true. You may quit a clinical trial at any time.

MYTH: Researchers do not want to enroll older cancer patients.

FACT: Older patients are underrepresented in clinical trials, but not because researchers do not want to sign them up. Only 25 percent of participants in clinical trials are 65 or older, although 63 percent of all cancer patients are 65 or older.

MYTH: Researchers may not spell out all of the risks associated with a clinical trial.

FACT: The risks of a clinical trial are probably overstated as part of the informed consent process.

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Questions to Ask

- Why is this study being done?
- What is likely to happen to me if I do/don't participate?
- What are my other options (standard treatments, other studies)? What are the advantages and disadvantages?
- How much experience do you have with this particular treatment? With conducting clinical trials in general?
- What were the results in previous studies of this treatment?
- What kinds of tests and treatments does the study involve? How often are they done?
- What side effects might I expect from the study?
- Will I have to be hospitalized? If so, how often and for how long?
- Will I still be seeing my regular doctor?
- 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 remain 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?
- Can I choose to continue to get this treatment, even after the study ends?
- Will this require extra time or travel commitment on my part?
- How could the study affect my daily life?
- Are there others participating in the study whom I could speak to?

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A New Clinical Trial in Non-Hodgkin's Lymphoma

To evaluate whether treatment with rituximab plus sargramostim
will be more effective than rituximab alone

You may be eligible if you are an adult and have all of the following:

- Relapsed, follicular, B-cell non-Hodgkin's lymphoma
- Received 1 or more prior therapies for non-Hodgkin's lymphoma
- At least 1 measurable tumor documented by CT scan
- Additional criteria to be evaluated at screening visit

You are ineligible if you have any of the following:

- Rituximab-refractory disease (less than 6 months from last treatment with rituximab to relapse)
- Currently receiving treatment for another cancer
- Additional criteria to be evaluated at screening visit

By participating in this investigational study you may:

- Receive research medication
- Contribute to the growing knowledge of NHL treatment options

To learn if you may be eligible for the PREMIER clinical trial
and to locate a PREMIER study site near you, go to

www.nhl.onctrials.com

Or, call 1-888-BERLEX4 (237-5394) and press Option 7
for Clinical Trials





**A Phase III placebo-controlled
clinical trial to evaluate
bevacizumab in combination with
Tarceva® versus Tarceva® alone
in advanced Non-Small Cell Lung
Cancer [NSCLC]**

You may be eligible for this trial if you:

- Previously have been treated with chemotherapy for your NSCLC
- Are able to provide self-care and are up and about for more than 50% of your waking hours
- Are able to take oral medication
- Do not require treatment with full-dose warfarin or its equivalent

**For further information, please call 1-888-662-6728
or search for OSl3364g at www.clinicaltrials.gov**