Clinical Trials: Questions and Answers

Key Points

- Clinical trials are research studies that test how well new medical approaches work in people (see Question 1).
- Every clinical trial has a protocol, which describes what will be done in the study, how it will be conducted, and why each part of the study is necessary (see Question 4).
- Informed consent is a process by which people learn the important facts about a clinical trial to help them decide whether to participate (see Question 6).
- Payment of patient care costs in clinical trials varies by health insurance plan and by study (see Question 11).

1. What are clinical trials, and why are they important?

Clinical trials are research studies that test how well new medical approaches work in people. Each study answers scientific questions and tries to find better ways to prevent, screen for, diagnose, or treat a disease. People who take part in cancer clinical trials have an opportunity to contribute to knowledge of, and progress against, cancer. They also receive up-to-date care from experts.

2. What are the types of clinical trials?

There are several types of clinical trials:

- **Prevention trials** test new approaches, such as medications, vitamins, or other supplements, that doctors believe may lower the risk of developing a certain type of cancer. Most prevention trials are conducted with healthy people who have not had cancer. Some trials are conducted with people who have had cancer and want to prevent recurrence (return of cancer), or reduce the chance of developing a new type of cancer.

- **Screening trials** study ways to detect cancer earlier. They are often conducted to determine whether finding cancer before it causes symptoms decreases the chance of dying from the disease. These trials involve people who do not have any symptoms of cancer.

- **Diagnostic trials** study tests or procedures that could be used to identify cancer more accurately. Diagnostic trials usually include people who have signs or symptoms of cancer.

- **Treatment trials** are conducted with people who have cancer. They are designed to answer specific questions about, and evaluate the effectiveness of, a new treatment or a new way of using a standard treatment. These trials test many types of treatments, such as new drugs, vaccines, new approaches to surgery or radiation therapy, or new combinations of treatments.

- **Quality-of-life (also called supportive care) trials** explore ways to improve the comfort and quality of life of cancer patients and cancer survivors. These trials may study ways to help people who are experiencing nausea, vomiting, sleep disorders, depression, or other effects from cancer or its treatment.

- **Genetics studies** are sometimes part of another cancer clinical trial. The genetics component of the trial may focus on how genetic makeup can affect detection, diagnosis, or response to cancer treatment.

  Population- and family-based genetic research studies differ from traditional cancer clinical trials. In these studies, researchers look at tissue or blood samples, generally from families or large groups of people, to find genetic changes that are associated with cancer. People who participate in genetics studies may or may not have cancer, depending on the study. The goal of these studies is to help understand the role of genes in the development of cancer.

3. Who sponsors clinical trials?

Government agencies, such as the National Cancer Institute (NCI) and other parts of the National Institutes of Health (NIH), the Department of Defense, and the Department of Veterans Affairs, sponsor and conduct clinical trials. In addition, organizations or individuals, such as physicians, medical institutions, foundations, volunteer groups, and pharmaceutical companies, also sponsor clinical trials.

NCI sponsors a large number of clinical trials and has a number of programs designed to make clinical trials widely available in the United States. These programs include the following:

- The **Cancer Centers Program** provides support to research-oriented institutions, including those that have been designated as NCI Comprehensive or Clinical Cancer Centers for their scientific excellence. More information is available in the National Cancer Institute-Designated Cancer Centers Database, which is available at http://www.cancer.gov/cancertopics/factsheet/NCI/cancer-centers on the Internet.

- The **Specialized Programs of Research Excellence (SPOREs)** bring together scientists and researchers to design and implement research programs that can improve prevention, detection, diagnosis, and treatment of specific types of cancer. More information about SPOREs is available at http://spores.nci.nih.gov/index.html on the Internet.

- The **Clinical Trials Cooperative Group Program** brings researchers, cancer centers, and doctors together into cooperative groups. These groups work with the NCI to identify important questions in cancer research, and design and conduct multisite clinical trials to answer these questions. Cooperative groups are located throughout the United States and in Canada and Europe. For more information, refer to the fact sheet *NCI's Clinical Trials Cooperative Group Program* at http://www.cancer.gov/cancertopics/factsheet/NCI/clinical-trials-cooperative-group on the Internet.

- The **Cancer Trials Support Unit (CTSU)** makes NCI-sponsored phase III treatment trials available to doctors and patients in the United States and Canada. Doctors who are not affiliated with an NCI-sponsored Clinical Trials Cooperative Group (see above) must complete an application process, which includes credential verification and site preparedness assessment, to become members of the CTSU's National Network of Investigators. CTSU members can enroll patients in clinical trials through the program's Web site, which is located at http://www.ctsu.org on the Internet. General information about the CTSU is also available on the program's Web site, or by calling 1–888–823–5923.

- The **Community Clinical Oncology Program (CCOP)** makes clinical trials available in a large number of communities across the United States. Local hospitals throughout the country affiliate with a cancer center or a cooperative group. This affiliation allows doctors to offer people participation in clinical trials more easily, so they do not have to travel long distances or leave their usual caregivers. The **Minority-Based Community Clinical Oncology Program** focuses on encouraging minority populations to participate in clinical trials. More information about the CCOP can be found in the NCI fact sheet *Community Clinical Oncology Program: Questions and Answers*, which is available at http://www.cancer.gov/cancertopics/factsheet/NCI/CCOP on the Internet.

- The **National Institutes of Health Clinical Center**, a research hospital located in Bethesda, Maryland, is part of the NIH. Trials at the Clinical Center are conducted by the components of the NIH, including the NCI. The NCI fact sheet *Cancer*

Clinical Trials at the National Institutes of Health Clinical Center: Questions and Answers has more information about the Clinical Center. This fact sheet is available at http://www.cancer.gov/cancertopics/factsheet/NCI/clinical-center on the Internet.

4. How are participants protected?

Research with people is conducted according to strict scientific and ethical principles. Every clinical trial has a protocol, or action plan, which acts like a "recipe" for conducting the trial. The plan describes what will be done in the study, how it will be conducted, and why each part of the study is necessary. The same protocol is used by every doctor or research center taking part in the trial.

All clinical trials that are federally funded or that evaluate a new drug or medical device subject to Food and Drug Administration regulation must be reviewed and approved by an Institutional Review Board (IRB). Many institutions require that all clinical trials, regardless of funding, be reviewed and approved by a local IRB. The Board, which includes doctors, researchers, community leaders, and other members of the community, reviews the protocol to make sure the study is conducted fairly and participants are not likely to be harmed. The IRB also decides how often to review the trial once it has begun. Based on this information, the IRB decides whether the clinical trial should continue as initially planned and, if not, what changes should be made. An IRB can stop a clinical trial if the researcher is not following the protocol or if the trial appears to be causing unexpected harm to the participants. An IRB can also stop a clinical trial if there is clear evidence that the new intervention is effective, in order to make it widely available.

NIH-supported clinical trials require data and safety monitoring. Some clinical trials, especially phase III clinical trials, use a Data and Safety Monitoring Board (DSMB). A DSMB is an independent committee made up of statisticians, physicians, and patient advocates. The DSMB ensures that the risks of participation are as small as possible, makes sure the data are complete, and stops a trial if safety concerns arise or when the trial's objectives have been met.

5. What are eligibility criteria, and why are they important?

Each study's protocol has guidelines for who can or cannot participate in the study. These guidelines, called eligibility criteria, describe characteristics that must be shared by all participants. The criteria differ from study to study. They may include age, gender, medical history, and current health status. Eligibility criteria for treatment studies often require that patients have a particular type and stage of cancer.

Enrolling participants with similar characteristics helps to ensure that the results of the trial will be due to what is under study and not other factors. In this way, eligibility criteria help researchers achieve accurate and meaningful results. These criteria also minimize the risk of a person's condition becoming worse by participating in the study.

6. What is informed consent?

Informed consent is a process by which people learn the important facts about a clinical trial to help them decide whether to participate. This information includes details about what is involved, such as the purpose of the study, the tests and other procedures used in the study, and the possible risks and benefits. In addition to talking with the doctor or nurse, people receive a written consent form explaining the study. People who agree to take part in the study are asked to sign the informed consent form. However, signing the form does not mean people must stay in the study. People can leave the study at any time—either before the study starts or at any time during the study or the follow-up period.

The informed consent process continues throughout the study. If new benefits, risks, or side effects are discovered during the study, the researchers must inform the participants. They may be asked to sign new consent forms if they want to stay in the study.

7. Where do clinical trials take place?

Clinical trials take place in doctors' offices, cancer centers, other medical centers, community hospitals and clinics, and veterans' and military hospitals in cities and towns across the United States and in other countries. Clinical trials may include participants at one or two highly specialized centers, or they may involve hundreds of locations at the same time.

8. How are clinical trials conducted?

Clinical trials are usually conducted in a series of steps, called phases. Treatment clinical trials listed in PDQ®, the NCI's comprehensive cancer information database, are always assigned a phase. However, screening, prevention, diagnostic, and quality-of-life studies do not always have a phase. Genetics clinical trials generally do not have a phase.

- **Phase I** trials are the first step in testing a new approach in people. In these studies, researchers evaluate what dose is safe, how a new agent should be given (by mouth, injected into a vein, or injected into the muscle), and how often. Researchers watch closely for any harmful side effects. Phase I trials usually enroll a small number of patients and take place at only a few locations. The dose of the new therapy or technique is increased a little at a time. The highest dose with an acceptable level of side effects is determined to be appropriate for further testing.

- **Phase II** trials study the safety and effectiveness of an agent or intervention, and evaluate how it affects the human body. Phase II studies usually focus on a particular type of cancer, and include fewer than 100 patients.

- **Phase III** trials compare a new agent or intervention (or new use of a standard one) with the current standard therapy. Participants are randomly assigned to the standard group or the new group, usually by computer. This method, called randomization, helps to avoid bias and ensures that human choices or other factors do not affect the study's results. In most cases, studies move into phase III testing only after they have shown promise in phases I and II. Phase III trials often include large numbers of people across the country.

- **Phase IV** trials are conducted to further evaluate the long-term safety and effectiveness of a treatment. They usually take place after the treatment has been approved for standard use. Several hundred to several thousand people may take part in a phase IV study. These studies are less common than phase I, II, or III trials.

People who participate in a clinical trial work with a research team. Team members may include doctors, nurses, social workers, dietitians, and other health professionals. The health care team provides care, monitors participants' health, and offers specific instructions about the study. So that the trial results are as reliable as possible, it is important for participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may continue to contact participants after the trial ends.

9. What are some of the benefits of taking part in a clinical trial?

The benefits of participating in a clinical trial include the following:

- Participants have access to promising new approaches that are often not available outside the clinical trial setting.
- The approach being studied may be more effective than the standard approach.
- Participants receive regular and careful medical attention from a research team that includes doctors and other health professionals.
- Participants may be the first to benefit from the new method under study.
- Results from the study may help others in the future.

10. What are some of the possible risks associated with taking part in a clinical trial?

The possible risks of participating in a clinical trial include the following:

- New drugs or procedures under study are not always better than the standard care to which they are being compared.
- New treatments may have side effects or risks that doctors do not expect or that are worse than those resulting from standard care.
- Participants in randomized trials will not be able to choose the approach they receive.

- Health insurance and managed care providers may not cover all patient care costs in a study.
- Participants may be required to make more visits to the doctor than they would if they were not in the clinical trial.

11. Who pays for the patient care costs associated with a clinical trial?

Health insurance and managed care providers often do not cover the patient care costs associated with a clinical trial. What they cover varies by health plan and by study. Some health plans do not cover clinical trials if they consider the approach being studied "experimental" or "investigational." However, if enough data show that the approach is safe and effective, a health plan may consider the approach "established" and cover some or all of the costs. Participants may have difficulty obtaining coverage for costs associated with prevention and screening clinical trials; health plans are currently less likely to have review processes in place for these studies. It may, therefore, be more difficult to get coverage for the costs associated with them. In many cases, it helps to have someone from the research team talk about coverage with representatives of the health plan.

Health plans may specify other criteria a trial must meet to be covered. The trial might have to be sponsored by a specified organization, be judged "medically necessary" by the health plan, not be significantly more expensive than treatments the health plan considers standard, or focus on types of cancer for which no standard treatments are available. In addition, the facility and medical staff might have to meet the plan's qualifications for conducting certain procedures, such as bone marrow transplants. More information about insurance coverage can be found on the NCI's *Clinical Trials and Insurance Coverage: A Resource Guide* Web page at http://www.cancer.gov/clinicaltrials/learning/insurance-coverage on the Internet.

Many states have passed legislation or developed policies requiring health plans to cover the costs of certain clinical trials. For more information, visit the NCI's Web site at http://www.cancer.gov/clinicaltrials/developments/laws-about-clinical-trial-costs on the Internet.

Federal programs that help pay the costs of care in a clinical trial include those listed below:

- Medicare reimburses patient care costs for its beneficiaries who participate in clinical trials designed to diagnose or treat cancer. Information about Medicare coverage of clinical trials is available at http://www.medicare.gov on the Internet, or by calling Medicare's toll-free number for beneficiaries at 1–800–633–4227 (1–800–MEDICARE). The toll-free number for the hearing impaired is 1–877–486–2048. Also, the NCI fact sheet *More Choices in Cancer Care: Information for Beneficiaries on Medicare Coverage of Cancer Clinical Trials* is

available at http://www.cancer.gov/cancertopics/factsheet/support/medicare on the Internet.

- Beneficiaries of TRICARE, the Department of Defense's health program, can be reimbursed for the medical costs of participation in NCI-sponsored phase II and phase III cancer prevention (including screening and early detection) and treatment trials. Additional information is available in the NCI fact sheet *TRICARE Beneficiaries Can Enter Clinical Trials for Cancer Prevention and Treatment Through a Department of Defense and National Cancer Institute Agreement*. This fact sheet can be found at http://www.cancer.gov/cancertopics/factsheet/NCI/TRICARE on the Internet.

- The Department of Veterans Affairs (VA) allows eligible veterans to participate in NCI-sponsored prevention, diagnosis, and treatment studies nationwide. All phases and types of NCI-sponsored trials are included. The NCI fact sheet *The NCI/VA Agreement on Clinical Trials: Questions and Answers* has more information. It is available at http://www.cancer.gov/cancertopics/factsheet/NCI/VA-clinical-trials on the Internet.

12. What are some questions people might ask their health care provider before entering a clinical trial?

It is important for people to ask questions before deciding to enter a clinical trial. Questions people might want to ask their doctor or nurse include the following:

The Study

- What is the purpose of the study?
- Why do the researchers think the approach being tested may be effective? Has it been tested before?
- Who is sponsoring the study?
- Who has reviewed and approved the study?
- What are the medical credentials and experience of the researchers and other study personnel?
- How are the study results and safety of participants being monitored?
- How long will the study last?
- How will the results be shared?

Possible Risks and Benefits

- What are the possible short-term benefits?
- What are the possible long-term benefits?
- What are the short-term risks, such as side effects?
- What are the possible long-term risks?
- What other treatment options are available?

- How do the possible risks and benefits of the trial compare with those of other options?

Participation and Care

- What kinds of treatment, medical tests, or procedures will the participants have during the study? How often will they receive the treatments, tests, or procedures?
- Will treatments, tests, or procedures be painful? If so, how can the pain be controlled?
- How do the tests in the study compare with what people might receive outside the study?
- Will participants be able to take their regular medications while in the clinical trial?
- Where will the participants receive their medical care? Will they be in a hospital? If so, for how long?
- Who will be in charge of the participants' care? Will they be able to see their own doctors?
- How long will participants need to stay in the study? Will there be follow-up visits after the study?

Personal Issues

- How could being in the study affect the participants' daily lives?
- What support is available for participants and their families?
- Can potential participants talk with people already enrolled in the study?

Cost Issues

- Will participants have to pay for any treatment, tests, or other charges? If so, what will the approximate charges be?
- What is health insurance likely to cover?
- Who can help answer questions from the insurance company or health plan?

13. What happens when a clinical trial is over?

After a clinical trial is completed, the researchers look carefully at the data collected during the trial before making decisions about the meaning of the findings and further testing. After a phase I or II trial, the researchers decide whether to move on to the next phase, or stop testing the agent or intervention because it was not safe or effective. When a phase III trial is completed, the researchers look at the data and decide whether the results have medical importance.

The results of clinical trials are often published in peer-reviewed, scientific journals. Peer review is a process by which experts review the report before it is published to make sure the analysis and conclusions are sound. If the results are particularly important, they may be featured by the media and discussed at scientific meetings and by patient advocacy groups before they are published. Once a new approach has been proven safe

and effective in a clinical trial, it may become standard practice. (Standard practice is a currently accepted and widely used approach.)

The National Library of Medicine's Web site offers links to resources for finding the results of clinical trials. It includes information about published and unpublished results. This resource can be found at http://www.nlm.nih.gov/services/ctresults.html on the Internet.

14. Where can people find more information about clinical trials?

In addition to the resources described in Question 3, people interested in taking part in a clinical trial should talk with their health care provider. Information about cancer clinical trials is also available from the NCI's Cancer Information Service (CIS). Information specialists at the CIS use PDQ to identify and provide detailed information about specific ongoing clinical trials. PDQ includes all NCI-funded clinical trials and some studies conducted by independent investigators at hospitals and medical centers in the United States and Europe.

People also have the option of searching for clinical trials on their own. The clinical trials page of the NCI's Web site, located at http://www.cancer.gov/clinicaltrials/ on the Internet, provides information about clinical trials and links to PDQ. Another resource is the NIH's ClinicalTrials.gov Web site. ClinicalTrials.gov lists clinical trials sponsored by the NIH, other Federal agencies, and the pharmaceutical industry for a wide range of diseases, including cancer and other conditions. This site can be found at http://clinicaltrials.gov on the Internet.

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Related NCI materials and Web pages:

- National Cancer Institute Fact Sheet 1.3, *Community Clinical Oncology Program: Questions and Answers*
  (http://www.cancer.gov/cancertopics/factsheet/NCI/CCOP)
- National Cancer Institute Fact Sheet 1.4, *NCI's Clinical Trials Cooperative Group Program*
  (http://www.cancer.gov/cancertopics/factsheet/NCI/clinical-trials-cooperative-group)
- National Cancer Institute Fact Sheet 1.13, *TRICARE Beneficiaries Can Enter Clinical Trials for Cancer Prevention and Treatment Through a Department of Defense and National Cancer Institute Agreement*
  (http://www.cancer.gov/cancertopics/factsheet/NCI/TRICARE)
- National Cancer Institute Fact Sheet 1.17, *The NCI/VA Agreement on Clinical Trials: Questions and Answers*
  (http://www.cancer.gov/cancertopics/factsheet/NCI/VA-clinical-trials)

- National Cancer Institute Fact Sheet 1.22, *Cancer Clinical Trials at the National Institutes of Health Clinical Center: Questions and Answers* (http://www.cancer.gov/cancertopics/factsheet/NCI/clinical-center)
- National Cancer Institute Fact Sheet 8.14, *More Choices in Cancer Care: Information for Beneficiaries on Medicare Coverage of Cancer Clinical Trials* (http://www.cancer.gov/cancertopics/factsheet/support/medicare)
- National Cancer Institute-Designated Cancer Centers Database (http://www.cancer.gov/cancertopics/factsheet/NCI/cancer-centers)
- *Taking Part in Cancer Treatment Research Studies* (http://www.cancer.gov/clinicaltrials/Taking-Part-in-Cancer-Treatment-Research-Studies)

For more help, contact:

NCI's Cancer Information Service
Telephone (toll-free): 1–800–4–CANCER (1–800–422–6237)
TTY (toll-free): 1–800–332–8615
LiveHelp® online chat: https://cissecure.nci.nih.gov/livehelp/welcome.asp

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