CANCER CLINICAL TRIALS:
All you need to know

A booklet for patients with cancer

The future of cancer therapy

EORTC
European Organisation for Research and Treatment of Cancer

FOREWORD

If you have cancer, clinical trials may offer you additional treatment options. Your doctor may speak to you about clinical trials, but you can also freely ask your doctor about it. This booklet explains cancer clinical trials in all aspects which may be important to you.

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EORTC and Cancer Clinical Trials

WHAT IS THE EORTC?

EORTC is an international non-profit research association under Belgian law conducting clinical trials in Europe since 1962.

EORTC is the only organization which carries out clinical trials at international level for all types of cancer. These activities allow the compilation of data on a large number of patients, ensuring that valid and convincing statistics are available as quickly as possible.

WHAT IS EORTC'S MISSION?

The EORTC's mission is to improve the standard of cancer treatment and to facilitate the passage of experimental discoveries into-state-of-the-art treatment. As a result of such a comprehensive research program, more patients with cancer are being cured today than ever before, and many others are living longer with improved quality of life.

HOW BIG IS THE EORTC'S NETWORK?

The EORTC brings together a unique network of 2500 cancer specialists at more than 300 institutions around Europe to achieve its goals. They are about 6000 new patients entered in about 30 different EORTC clinical trials every year.

Studies conducted within the EORTC framework have led to increased survival rates for childhood cancers, Hodgkin's disease and leukaemia, melanoma, breast, uterine, prostate, testicular and bladder cancers, lung and larynx cancers, as well as many others including rare tumours (brain and sarcoma).

What are clinical trials?

WHAT IS A CLINICAL TRIAL?

In the field of cancer management, scientists and doctors are constantly looking to develop innovative, more effective and less toxic treatments to improve patient survival and quality of life. Clinical trial is a form of research done by doctors to confirm the safety and effectiveness of new promising treatment in patients. Many treatments used today are the result of past trials.

WHAT ARE THE OBJECTIVES?

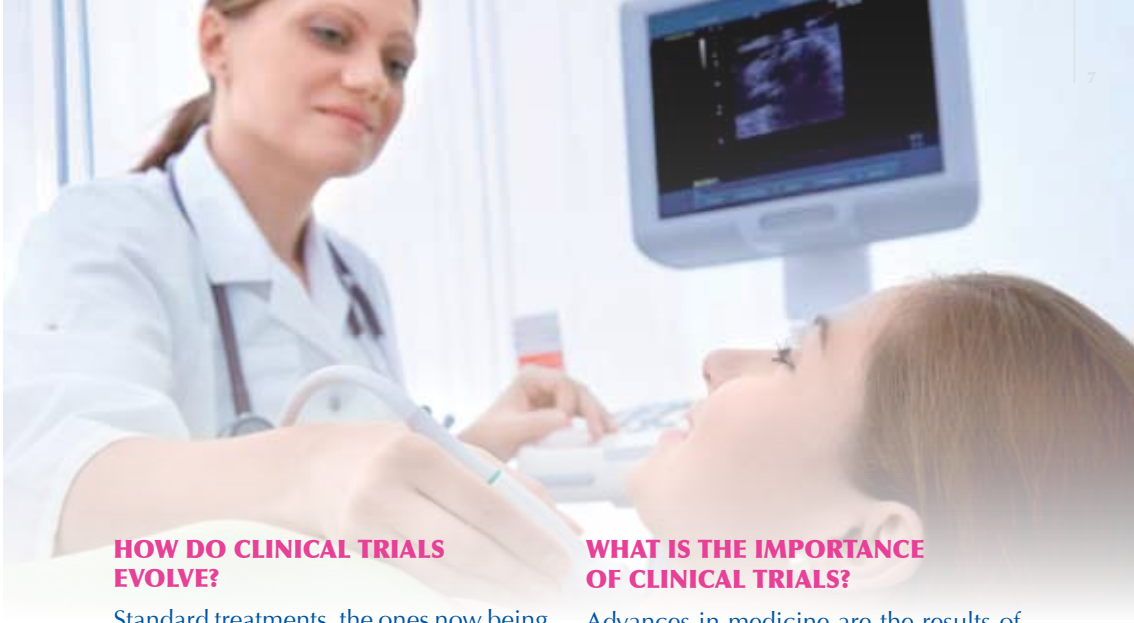
In cancer research, some clinical trials are aimed at evaluating new drugs while others optimize different therapeutic approaches including surgery, radiation therapy and combination of drugs already on the market.

However, with any new drug or treatment there may be risks as well as benefits. That is why clinical trials are closely monitored and usually conducted in hospitals or through the outpatient department.

WHY ARE CLINICAL TRIALS IMPORTANT?

As a patient with cancer, you may be asked to participate in a clinical trial. This booklet is written for you, your family and friends, to explain what clinical trials are and to help you understand how clinical trials are designed and carried out.

The time when cancer is diagnosed or when treatment options are being discussed is very difficult. Your doctor will talk to you about your disease and that will help you make the adequate decisions. It is often hard to remember or understand complex medical explanations. The information in this booklet is meant to complement what your doctors tell you. It provides answers to questions you might ask yourself.



HOW DO CLINICAL TRIALS EVOLVE?

Standard treatments, the ones now being used as reference or state-of-the-art treatment, are often the basis for building new, hopefully better, treatments. Many new regimens are designed on the basis of what has worked in the past.

If a new compound is well tolerated and works in a large number of patients, the tested drug is granted a license, making it available for all patients. Once the treatment is registered and authorized by competent authorities, doctors may wish to combine it with other treatments including surgery and/or radiation therapy.

WHAT IS THE IMPORTANCE OF CLINICAL TRIALS?

Advances in medicine are the results of new ideas and approaches developed through research. Scientific progress in a laboratory does not necessarily mean medical progress unless high quality clinical trials have been performed in patients to confirm the safety and the effectiveness of the new treatment.

If you take part in a clinical study, you will also be helping to advance medical science and thereby improving prospects for future patients.

CLINICAL TRIALS TAKE PLACE IN PHASES

After successful studies in laboratories and animals, a new treatment is evaluated through a series of clinical trials to test if it is safe and effective in humans. Clinical trials are the last steps to establishing better treatments and are conducted in different steps called phases, each designed to find out certain information.

Different phases may be proposed to patients depending on their general condition, the type and stage of their cancer. Each new phase of a clinical trial depends and builds on information from a previous phase.

PHASE I

A new research treatment is given to a small number of patients to determine dosage. The researchers watch the patients carefully for any harmful side effects. The new treatment has been thoroughly tested on animals in its laboratory stage but no one can predict how patients will react. For this reason, Phase I trials may involve significant risks. These are only offered to patients whose cancer has spread and who cannot be helped by other cancer treatments. Phase I treatments may produce anti-cancer affects, and some patients have been helped by these treatments.

PHASE II

The second step determines the activity of a new treatment on various types of cancer. There are about 40-80 patients entered in this phase. If a treatment has shown effectiveness against some types of cancer in Phase II, it moves on to Phase III.

PHASE III

Aims to compare a new treatment with standard treatment to see which is more effective. These Phase III trials usually require a large number of patients to provide significant clinical and statistical data.

PHASE IV

Aims to further assess the long term safety and effectiveness of treatments.

RANDOMIZATION

Some clinical trials test one treatment in one group.

Other trials compare two or more treatments in separate groups of patients who have similar conditions. From what is known at the time, any one of the treatments chosen may be of equal benefit to the patient. To find out the best, it is needed to compare them. People are put into different groups and each group receives a different treatment. To make sure groups patients are comparable, each patient is put into a group by chance (randomly). A computer program will place patients in one of the study groups. Neither patient nor doctor can choose the group. In this way the results can be validly compared.

How are patients protected?

WHAT IS A PROTOCOL?

To protect patients and to produce sound research results, treatments are carried out according to strict scientific and ethical principles. The treatment plan is described in a document called "protocol". The protocol outlines the purpose and procedures of the clinical trials. It indicates the number of patients participating in the trial, when relevant medical tests will be performed and which data are collected. The protocol must be followed by every doctor taking part in the research.

WHAT MEASURES ARE PUT IN PLACE TO PROTECT PATIENTS?

In addition to ethical and legal codes that govern medical practice, specific clinical trials laws provide additional protection to research participants in all participating countries. These safeguards include regular reviews of the protocol and the progress of each clinical trial by off-site researchers. Patients' safety is reviewed on an on-going basis in all trials.

Before being conducted, all clinical trials must first be approved an Ethical Committee (EC), whose mission is to ensure patient protection, safety and integrity.

EC are usually made up of scientists, doctors, clergy and other lay persons according to national laws. An EC reviews a study to see that it is well designed with the proper patient safeguards and that the risks are reasonable in relation to the potential benefits.

Some types of research are also reviewed and approved by competent authorities who monitor closely patient safety.

WHAT IS AN INFORMED CONSENT?

Patients learn about the details of a clinical trial from their doctor, but are also given information during the process of informed consent. This is an important process that ensures that the patient understands and makes his own informed decision to enrol. The patient indicates his intent by signing the informed consent form.

However, the process of informed consent goes on throughout the trial when the patient may be told of new findings from the clinical trial or informed of new risks. The patient may leave the trial at any time.

WHAT ABOUT PRIVACY?

According to international standards and national law, all data collected on a patient's health for the purpose of research will be kept confidential. The patient's identity will never be disclosed.

WHAT OF THE RESULTS?

At the end of the clinical trial, doctors and specialists in biostatics analyse the results and present them at scientific meetings, and in medical journals. Finals publications of trial results are reviewed by experts and by various government agencies for approval of new treatments if appropriate.

Patients can learn about trial results from their doctor. This helps to speed up the process of bringing better treatments to all cancer patients.

" The patient's identity will never be disclosed. "

Is a cancer trial risk-free?

WHAT ARE THE RISKS OR SIDE EFFECTS?

Treatments used in clinical trials can cause side effects and other health risks depending on the type of treatment and the patient's condition. Side effects vary from patient to patient. New and better ways of helping patients with these side effects are being found and used in all cancer treatments, including clinical trials.

Most side effects are temporary and will gradually fade away once treatment is stopped. For example, some anti-cancer drugs, whether standard or experimental, cause hair loss and nausea while others do not.

During treatment, the number of blood cells, called the blood count, may fall too low. Since this could lead to possible infections or other problems, patients have their blood count checked regularly. Fortunately, bone marrow has a great ability to replace blood cells, so that the blood count can usually return to normal.

Some side effects can be permanent and serious, even life-threatening. Other side effects may not appear until later, even after the treatment is over.

These "late" effects may include damage to a major organ such as the heart, lungs or kidneys, sterility or a second cancer. Doctors are concerned and trying to prevent these late complications by finding new and better treatments.

As a patient, there are a number of things to consider when deciding about your treatment. Cancer is a life-threatening disease, which causes symptoms of its own that are not related to the treatment. In each case, the unavoidable risks, and your condition, should be weighed against the potential risks and benefits of a new research treatment.

During the clinical trial, you will have to report all side effects to your doctor who will be able to help you.

WHY DO CANCER TREATMENTS HAVE SIDE EFFECTS?

Any medical treatment can carry the potential for side effects in some patients. Cancer treatments are particularly powerful, as they are designed to destroy dividing cancer cells. Such treatments can also affect healthy dividing cells which causes the side effects.

The challenge for doctors has been to develop treatments that eradicate cancer and maintain as best as possible the patient's quality of life.

WHAT IS BEING DONE TO FIGHT THESE SIDE EFFECTS?

Cancer researchers are trying to make cancer treatments more effective and lessen its side effects. Results of such efforts include:

- New anti-cancer drugs with fewer or milder side effects;
- Better anti-nausea medicine;
- More effective painkillers;
- Shorter periods of time on anti-cancer drugs for some diseases;
- Special ways to protect normal tissue during radiation therapy;
- New methods of surgery that are less extensive and less damaging to the body;
- Psychological support programs and information on ways to cope;
- Assessing quality of life: a new major concern of all health care providers.

Why should a patient be interested in a clinical trial?

WHY PARTICIPATE IN A CLINICAL TRIAL?

Patients take part in clinical trials for many reasons. They want the intense medical and scientific attention on their case, the opportunity to receive the most effective and up-to-date treatments. They may hope for a cure to the disease, a longer life expectation or just a way for feel better. At times, they may also want to contribute to a research effort that may help others in the future.

The patients in a clinical trial are among the first to receive new treatments before they are widely available. However, it is difficult to judge how the patient will react to the said treatment.

All patients in a clinical trial are carefully monitored during a trial and after. They have the guarantee to become part of a unique network of clinical trials carried out in Europe, sometimes in cooperation with the USA. Within this network, doctors and researchers pool their experience to design and monitor clinical trials and share their knowledge about cancer treatment.

WHO CAN JOIN A CLINICAL TRIAL?

Before you and your doctor make a decision about your treatment, your type of cancer will have to be diagnosed and "staged" to establish the extent of the disease.

Staging tells whether the disease has spread and how far. Deciding on treatments depends on many things, including the stage of your disease and your general health. You would mostly be referred to a trial by your own doctor or by a doctor who knows your case.

Each study concerns patients who have a similar disease. The eligibility guidelines are different from trial to trial and may include age, gender, the type and stage of cancer, medical history or

prior cancer treatments. Using these strict criteria helps produce reliable results and also excludes patients who might be harmed by a treatment.

WHAT IS IT LIKE TO RECEIVE TREATMENT IN A CLINICAL TRIAL?

You will receive your treatment in a cancer centre, hospital, clinic or a doctor's office. You may need to meet with a team of health and research professionals during the study. You may have more tests and more frequent doctor visits if you are in a clinical trial. This is to follow your progress, ensure your safety, as well as to collect data.

You will be given a treatment plan to carefully follow and you may be asked to fill out forms to evaluate your general feelings, particularly concerning your pain and other symptoms that affect your quality of life.

Throughout a clinical trial, a patient's personal doctor will be kept informed of the patient's progress. Patients are encouraged to maintain contact with their referring doctors.

"Within this network, doctors and researchers pool their experience to design and monitor clinical trials and share their knowledge about cancer treatment."

What trials are available for your type of cancer?

WHAT ARE YOUR CHOICES?

There many ways to find out what your treatment choices are. Talk to your doctor and get the opinion of cancer specialists. You should not be afraid to ask for a second opinion. Helpful treatment information can be obtained from the EORTC's network of specialists who have the latest information on clinical trials being offered in Europe for each type and stage of cancer.

WHAT IS BEST FOR YOU?

This is an important question. You should discuss your options with medical experts and with those closest to you. Talk to them and ask questions about the problems you will be facing. You need to understand what is going on to make the best choice for yourself. You may want to take a friend or relative along when you meet with your doctors. It may help if you plan what to ask and write your questions down. Remember there is no such thing as a stupid question.

As you decide about treatment, a clinical trial or other, remember that you are not alone. There are many people to help you – doctors, nurses, social workers, clergy, your family, friends, and other patients. Although it is your decision, they can help you think about it and decide what is best for you.

"Remember there is no such thing as a stupid question."

WHAT ARE THE IMPORTANT QUESTIONS YOU NEED TO ASK?

If you are thinking about taking part in a clinical trial, here are some important questions you should ask:

- Why is this trial being done?
- What does the trial involve? What kind of tests and treatments?
- What is likely to happen in my case, with, or without, this new treatment?
- What are my other options and their advantages and disadvantages?
- How could the trial affect my daily life?
- How often will I have to come to the hospital or clinic?
- What if I have other medical problems? Will I have to stop my regular medication?
- How long will I be in the trial?
- Will I have to be hospitalized? If so, how often and how long?
- Will there be any additional costs as compared to the standard treatment? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment or compensation would I be entitled to?
- What type of long-term follow-up care is part of the trial?
- Who has reviewed and approved this trial?
- Who is legally responsible for this trial (who is the sponsor)?

HOW TO FIND A CLINICAL TRIAL?

EORTC, pharmaceutical industries and other research organizations lead clinical trials. These trials take place in hospitals, clinics and large medical centers.

You can find all centers participating to EORTC clinical trials from EORTC web site. Alternatively, larger databases exist on the international (US National Cancer Institute, NCI US), European (EuraPharm EU CTR) and national level. You should also of course speak about this with your doctor.

USEFUL WEBSITES

EORTC:
http://www.eortc.org

NCI US:
http://www.cancer.gov/clinicaltrials/search

EudraPharm EU CTR:
http://eudrapharm.eu

Glossary

Adjuvant chemotherapy
One or more anti-cancer drugs used in combination with surgery or radiation therapy as part of the treatment of cancer. Adjuvant usually means «in addition to» initial treatment.

An adverse event
Any untoward medical occurrence in a patient or clinical investigation subject and which does not necessarily have a causal relationship with the treatment. An adverse event can therefore be any unfavourable and unintended sign, symptom, or disease temporarily associated with the use of a medicinal product or any treatment (surgery, radiation therapy), whether or not related to the investigational medical product, or treatment strategy.

Antibody
A protein produced by a plasma cell in the lymphatic system or bone marrow in response to a specific «antigen» (see antigen) which has stimulated the immune system. The antibody binds to the antigen which has stimulated the immune system. Once bound, the antigen can be destroyed by other cells of the immune system. See Immune System.

Antigen
A substance, foreign to the body, that stimulates the production of antibodies by the immune system. Antigens include foreign proteins, bacteria, viruses, pollen and other materials.

Biological therapy
Use of biologicals (substances produced by our own cells) or biological response modifiers (substances that affect the patient's defence systems) in the treatment of cancer.

Blood count
Measurement of the number of red cells, white cells, and platelets in a sample of blood.

Bone marrow
The inner, spongy core of bone that produces blood cells.

Cancer
A general term for more than 100 diseases characterised by abnormal and uncontrolled growth of cells. The resulting mass, or tumour, can invade and destroy surrounding normal tissues. Cancer cells from the tumour can spread through the blood or lymph to start new cancer growth in other parts of the body.

Chemotherapy
Treatment with anti-cancer drugs. Clinical trial or Clinical study – Research studies that involve human subjects. Each study tries to answer scientific questions and to find better ways to prevent and treat cancer.

Combination chemotherapy
Use of two or more anti-cancer drugs.

Combination therapy
The use of two or more modes of treatment – surgery, radiotherapy, chemotherapy, or immunotherapy – in combination, alternately or together, to achieve optimum results against cancer.

Control group
In clinical studies this is a group of patients which receives standard treatment, a treatment or intervention currently being used and considered to be of proven efficacy on the basis of past studies.Results in patients receiving newly developed treatments may then be compared to the control group. In cases where no standard treatmentyet exists for a particular condition, the control group receives no treatment but is carefully followed. No patient is placed in a control group without treatment if there is any beneficial treatment known for that patient.

Hormone
Chemical product of the endocrine glands of the body, which, when

secreted into body fluids, has a specific effect on other organs.

ICH
The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. The Guidelines for Good Clinical Practice is a result of this conference and is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.

Immune system
A complex network of organs, cells and specialised substances distributed throughout the body and defending it from organisms which cause infection or disease.

Immunotherapy
A form of biological therapy. An experimental method of treating cancer, using substances which stimulate the body's immune defence system.

Informed consent
The process in which a patient learns about and understands the purpose and aspects of a clinical trial and then decides voluntarily whether or not to participate. This process includes a document defining how much a patient must know about the potential benefits and risks of therapy before being able to agree to undergo it knowledgeably. Informed consent is required in all studies. If a patient signs an informed consent form and enters a trial, he or she is still free to leave the trial at any time, and can receive other available medical care.

Investigational new drug
A drug allowed to be used in clinical trials but not yet approved for commercial marketing.

Investigator
An investigator is the doctor who is an experienced clinical researcher who prepares a protocol or treatment plan and implements it with patients.

Metastasis
The transfer of disease from one part of the body to another. In cancer, metastasis is the migration of cancer cells from the original tumour site through the blood and lymph vessels to produce cancer growth in other tissues. Metastasis also is the term used for a secondary cancer growing at a distant site unless it is determined to be a new primary tumour.

Metastatic cancer
Cancer that has spread from its original site to one or more additional body sites.

Monoclonal antibodies
One of several new substances used in biological therapy. Monoclonal antibodies are antibodies of a single type. They are mass-produced and designed to home in on target cancer cells. Monoclonal antibodies are products of new scientific techniques and may prove useful in both cancer diagnosis and treatment.

Multimodality therapy
The combined use of more than one method of treatment, for example, surgery and chemotherapy.

Oncologist
A doctor who is a cancer specialist.

Placebo
An inactive substance resembling a medication, given for psychological effect or as a control in evaluating a medicine believed to be active. It is usually a tablet, capsule, or injection that contains a harmless substance but

appears to be the same as the medicine being tested. A placebo may be compared with a new drug when no one knows if any drug or treatment will be effective.

Protocol
The outline or plan for use of an experimental procedure or experimental treatment. Radiation therapy, also called.

Radiotherapy
Treatment using X-rays, cobalt-60, radium, neutrons, or other types of cell-destroying radiation. Radiosensitisers – Drugs being studied to try to boost the effect of adiation therapy.

Randomised clinical trials
A study in which patients with similar traits, such as extent of disease, are chosen or selected at random, to be placed in separate groups that are comparing different treatments. Because irrelevant factors or preferences do not influence the distribution of patients, the treatment groups can be considered comparable and results of the different treatments used in different groups can be compared. There is no way at the time for the researchers to know which of the treatments is best. It is the patient's choice to be in a randomised trial or not. See also Clinical trials.

Regression
A cancer that is growing smaller or disappearing, is said to be «in regression.»

Remission
When the signs and symptoms of cancer go away, the disease is said to be «in remission.» A remission can be temporary orpermanent.

Risk/benefit ratio
The relation between the risks and benefits of a given treatment or procedure. Ethical Committees and /or Institutional Review Boards (IRBs), located in the hospital or clinic where the study is to take place, determine whether the risks in a study are

reasonable with respect to the potential benefits. The patient must also assess the risk/benefit ration to decide if it is reasonable for him or her to take part in a study.

Side effects
(see adverse event)

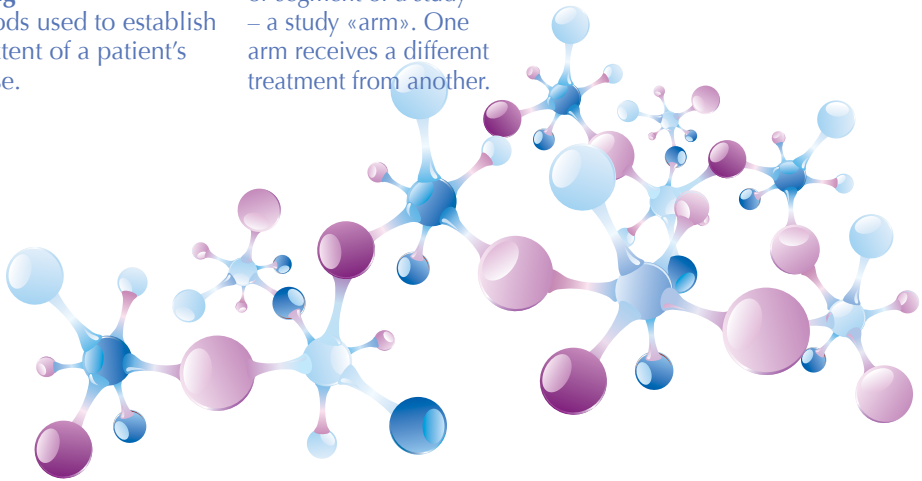
Staging
Methods used to establish the extent of a patient's disease.

Standard treatment
A treatment or other intervention currently beingused and considered to be of proved effectiveness on the basis of past studies.

Study arm
Patients in clinical trials are assigned to one part or segment of a study – a study «arm». One arm receives a different treatment from another.

Therapeutic
Pertaining to treatment.

Treatment group
The group that receives the new treatment being tested during a study.



Notes

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Or, have a look at the EORTC webpage on www.eortc.org or send an email at patient@eortc.be

For more information about EORTC, please contact:

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EORTC
1962 - 2012
50 years of Progress Against Cancer