

WHY SHOULD YOU READ THIS BOOKLET?

Patients with cancer may be asked to participate in a clinical trial. If you are a patient, a family member or friend, this booklet is for you. Our goal is to explain you what clinical trials are and to help you understand how they are set up and carried out.

We know how difficult it can be to understand and remember complex medical information, especially when cancer is being diagnosed and treatment options are being presented. However, this information is important to help you make adequate decisions. This booklet is meant to complement what your doctors tell you, providing answers to many of the questions you may have.



For more information about EORTC, please have a look at the EORTC webpage on www.eortc.org or send an email at communication@eortc.org.

CANCER CLINICAL TRIALS All you need to know

A booklet for people affected by cancer



A MESSAGE FROM THE CEO

Clinical trials may offer additional treatment options for people with cancer. Sometimes doctors talk to their patients about clinical trials, but patients can also ask their doctors about them. This booklet aims to provide an overview of all aspects of clinical trials in cancer that might be relevant for people whose life has been affected by cancer.



Denis Lacombe
EORTC Chief Executive Officer

TABLE OF CONTENTS

CANCER CLINICAL TRIALS: All you need to know

EORTC and cancer clinical trials	01
About clinical trials	03
Clinical trials phases	05
Safety of patients	07
Risks of cancer trials	11
Taking part in a clinical trial	13
Finding the right trial	17
Glossary	21

EORTC & CANCER CLINICAL TRIALS

WHAT IS THE EORTC?

EORTC is an international and independent non-profit cancer research organisation conducting clinical trials in Europe since 1962.

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

WHAT IS EORTC'S MISSION?

The EORTC mission is to increase people's survival and quality of life by testing new therapies, leaving no patient behind. Thanks to such initiatives, 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:

- **3100** cancer specialists
- **+750** institutions
- **48** countries
- **± 210245** patient entries
- **± 1193** EORTC studies
- **60 years** since its establishment

Studies conducted within the EORTC framework have led to increased survival rates and/or optimization of therapeutics (i.e. sometimes, less aggressive surgery or replacing surgery by radiotherapy) 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, such as brain tumours and sarcoma.



ABOUT 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. A clinical trial is a form of research done by health care professionals and other researchers to evaluate if a new, promising diagnosis or treatment approach is safe for patients and can improve their condition. Many treatments available today are the result of past trials.

WHAT ARE THE OBJECTIVES OF A CLINICAL TRIAL?

Some clinical trials in cancer research aim at evaluating new drugs and treatments, while others optimize or combine different treatment options, including surgery, radiotherapy, translational research, combinations of modalities and supportive care already available on the market.

However, with any new drug or treatment there may be risks as well as

benefits. Therefore, in order to minimize the risks associated with the use of new drugs or treatments, clinical trials are closely monitored and usually are conducted inside health care facilities such as hospitals.

HOW DO CANCER TREATMENTS 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 treatment approaches are designed based on what worked in the past.

If new drugs, other treatments, and new technologies are well tolerated and work well for many patients, a license is granted, making them available for all patients. Once they obtain such a licence, doctors may wish to combine them with other treatments including surgery and/or radiotherapy.

WHY ARE CLINICAL TRIALS IMPORTANT?

Advances in medicine result from new ideas and approaches developed through research. Scientific progress in laboratories cannot translate to

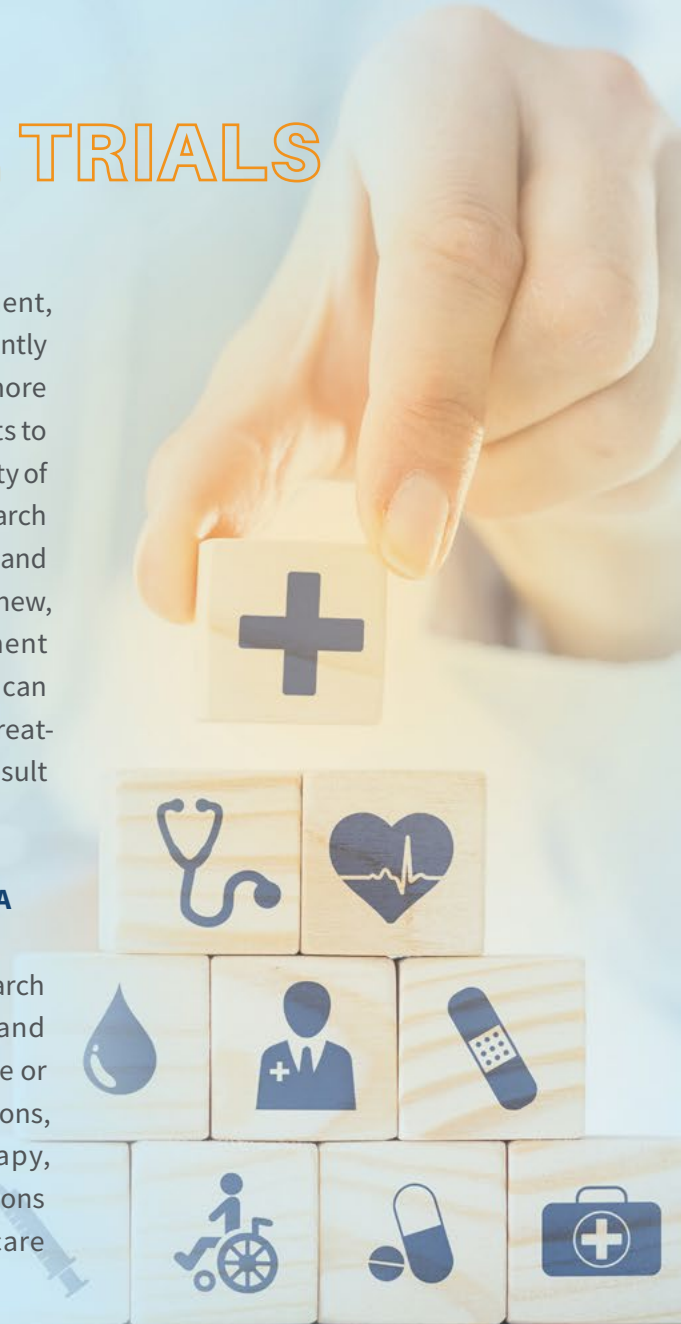
improvements for patients unless high quality clinical trials have been carried out in humans to confirm that the new treatment works and is safe. If you take part in a clinical trial, you will also help to advance medical science and improve prospects for future patients.

CLINICAL TRIALS TAKE PLACE IN PHASES

After successful studies in laboratories, a new treatment is evaluated through a series of clinical trials to test whether it is safe and effective for humans. Clinical trials are conducted in different phases, each designed to obtain a specific information.

Patients may be offered to participate in one or more different phases, depending on their general condition, what type of cancer they have and how advanced it is.

Each new phase of a clinical trial depends and builds on information from a previous phase.



CLINICAL TRIAL PHASES

PHASE 01

A new research treatment has been thoroughly tested in the laboratory (also referred to as pre-clinical research), but no one can predict how humans will react. The new treatment is therefore given to a small number of patients to determine its safety. The researchers watch the patients carefully for any harmful side effects. 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 already available. Usually, new cancer treatments are not tested on healthy patients.



PHASE 03

This step aims to compare a new treatment with a standard treatment to see which works better. Such Phase III trials usually require many patients to provide significant clinical and statistical data.



RANDOMIZATION

Some clinical trials test one treatment in one group of people. Other trials compare two or more treatments in separate groups of patients who have similar conditions. To find out which is the best treatment among the ones that have been chosen, clinicians need to compare them.

People are put into different groups and each group receives a different treatment. To make sure patient groups are comparable, patients are split into groups 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.

PHASE 04

This step aims to further study the long-term safety and effectiveness of treatments after their approval and being licensed.



PHASE 02

This second step determines if the new treatment works for treating specific cancers in specific settings (for example before or after surgery, during radiotherapy, as palliative treatment) and to further assess safety. About 40-80 patients enter this phase. If a treatment has been shown to work against some types of cancer in a safety manner in Phase II, it moves on to Phase III trials.

SAFETY OF PATIENTS



WHAT IS A TRIAL PROTOCOL?

In order to protect patients and to produce sound research results, treatments in clinical trials 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 trial. It indicates the number of patients participating in the trial, relevant medical tests to perform, and data to collect. The protocol must be followed by every doctor, other health care professionals and researchers 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. These safeguards include regular reviews of the protocol and the progress of each clinical trial by other researchers. Patients’ safety is continuously monitored in all trials.

Before the start, all clinical trials must first be approved by an Ethical Committee (EC), whose mission is to ensure patients' protection, safety, and integrity.

ECs are usually composed of scientists, doctors, clergy, and other lay persons according to national laws. An EC reviews study protocol documents to check whether they are well designed with the proper patients' safeguards and that the risks are reasonable in relation to the potential benefits.

Some types of studies are also reviewed and approved by competent authorities that closely monitor patients' safety.

all their questions answered by the team. This is the informed consent process, an important step to ensure that patients understand what the clinical trial is about and make their own informed decision whether to take part in it or not. Patients give their consent by signing the informed consent form.

However, the process of informed consent continues throughout the trial when the patients may be informed of new findings from the clinical trial or of new risks.

Patients may leave the trial at any time without affecting the following follow up or treatments.



The patient's identity will never be disclosed.

WHAT IS AN INFORMED CONSENT?

Patients learn about the details of a clinical trial from their doctor, but they also receive written information and are given time to read it carefully, discuss with other people, and to see

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 to other parties besides the treating doctor.

WHAT ABOUT THE RESULTS?

At the end of the clinical trial, doctors, other health care professionals, scientists and specialists in biostatistics

analyse the results and present them at scientific meetings, and in medical journals. Publications of trial results are reviewed by experts and by various government agencies for the approval and reimbursement of new treatments, if appropriate.

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



RISKS OF CANCER TRIALS

WHAT ARE THE RISKS OR SIDE EFFECTS?

Like any treatment, treatments used in clinical trials can cause side effects and other health risks depending on the type of treatment and the patient's condition. For example, some anti-cancer drugs, whether standard or experimental, may cause hair loss and nausea, while others do not. Side effects vary from patient to patient and most of them are temporary and will gradually fade away once the treatment is complete. New and better ways of helping patients with these side effects are being explored and used in all cancer treatments, including clinical trials.

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

Cancer itself is a life-threatening disease, which causes symptoms that are not necessarily related to the treatment. In any case, the unavoidable risks and patients' condition should be balanced with the potential risks and benefits of a new research treatment.

During the clinical trial, patients will have to report all side effects to their medical team who will be able to help.

WHY DO CANCER TREATMENTS HAVE SIDE EFFECTS?

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 regenerate blood cells, so that the blood count can usually return to normal.

Any medical treatment can potentially cause side effects in some patients. Some cancer treatments are particularly strong, as they are designed to destroy cancer cells while those are replicating. Such treatments can also affect healthy cells, and this causes the side effects.

One of the challenges that doctors and researchers encounter is the development of treatments that cure or control cancer while preserving the patient's quality of life.

WHAT IS BEING DONE TO REDUCE THESE SIDE EFFECTS?

Cancer researchers are trying to make cancer treatments more effective and reduce the side effects. The results of such efforts include:

- New anti-cancer drugs with fewer or milder side effects;
- Better supportive care and treatments, like antiemetics (directed to avoid or reduce nausea and vomiting), painkillers, psychological support and rehabilitation programs and information on ways to cope;
- Shorter periods on anticancer drugs for some diseases;
- Special ways to protect normal tissue during radiation therapy;
- New methods of surgery that are less invasive and less damaging to the body;
- Assessing patients 'quality of life and assessing fragility, particularly in elderly patients are now major concerns of all healthcare providers.



TAKING PART IN A CLINICAL TRIAL

WHY PARTICIPATE IN A CLINICAL TRIAL?

Patients take part in clinical trials for many reasons. Some want to have a better understanding of their case and the opportunity to receive the most effective and up-to-date treatments. Others are motivated by a hope for a cure of the disease and longer life expectation, or a better quality of life. Another reason is patients' willingness to contribute to research that may help others in the future.

Patients in a clinical trial are among the first to receive new treatments or new treatment combination before they are widely available (i.e., when efficacy and safety are demonstrated). However, it is difficult to predict how each patient will react to the trial 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 patients participating in clinical trials carried out all over the world. Within this network, doctors and researchers combine their experience to design and monitor clinical trials and share their knowledge about cancer treatment.

WHO CAN JOIN A CLINICAL TRIAL?

Before patients and their doctors decide on a treatment, cancer, including its type and stage, should be diagnosed. Staging tells whether the disease has spread in the body and to what extent. The decision to choose a certain treatment depends also on the patients' general health. Patients would mostly be referred to a trial by their doctor or by a doctor who knows their case.

Each study involves patients who have a similar disease. The criteria determining who can take part in a specific study are different from trial to trial and may include age, gender, type and stage of cancer, medical history, or previous cancer treatments. The application of such criteria helps to produce reliable results and exclude patients who might not benefit from the treatment.

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

Patients will receive their treatment in a cancer centre, hospital, clinic, or a doctor's practice. Patients may need to meet with a team of health-care and research professionals during the study, and they may also need to undergo more tests and more frequent doctor visits if they are in a clinical trial. This is needed to follow up on the response of their cancer to treatment, ensure their safety, as well as to collect data.

Patients will receive a schedule of visits, tests, response assessment and, in the case of oral drugs, a treatment plan to carefully follow. They may also be asked to fill out forms to evaluate their general state, particularly concerning pain and other symptoms that affect their quality of life.

Throughout a clinical trial, the patient's family doctor (general practitioner) can be kept informed of the patient's response to treatment. Patients are encouraged to maintain contact with their family doctors.

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Within our network, doctors and researchers combine their experience to design and monitor clinical trials and share their knowledge about cancer treatment.

FINDING THE RIGHT TRIAL



WHAT ARE YOUR CHOICES?

There are many ways to find out what are the treatment choices available. Patients can talk to their doctor, get the opinion of cancer specialists and should not be afraid to ask for a second opinion.

Helpful treatment information can also 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. Please consult the EORTC website for more information or scan the QR code under: "Useful Websites".

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 concerns you might have. 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 doctor(s). It may also help if you prepare your questions in advance or even write the questions down. Remember, there is no such thing as a stupid question.

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

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

USEFUL WEBSITES



(i)



(ii)



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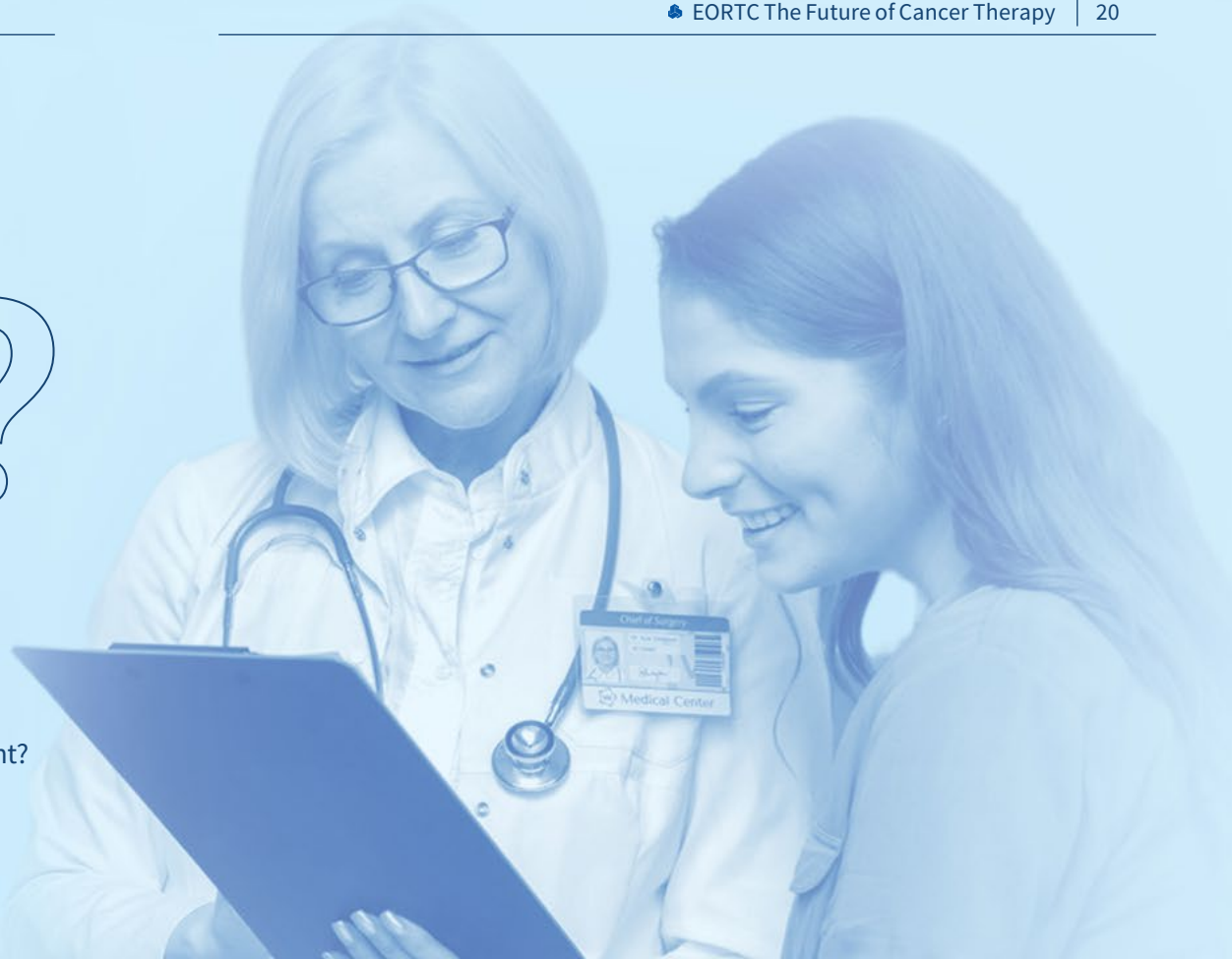
- (i) EORTC
- (ii) EORTC database of clinical trials
- (iii) EORTC patient involvement
- (iv) Database of clinical trials



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 taking my regular medication?
- For how long will I be in the trial?
- Will I have to be hospitalised? If so, how often and for 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 because 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?



HOW TO FIND A CLINICAL TRIAL?

Organisations such as the EORTC, pharmaceutical companies and other research organizations lead clinical trials. These trials take place in hospitals, clinics, and large medical centres.

You can find all centres participating in EORTC clinical trials on the EORTC website. Alternatively, larger databases exist at the international (US National Cancer Institute, NCI US), European (European Clinical Trials Register, Clinical Trial Information System) and national levels. You can also discuss it with the cancer specialist that is taking care of your case.

GLOSSARY

Adjuvant treatment	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 unwanted event that may be related to the use of a drug or a treatment. It can be any unfavourable and unintended sign, symptom, or disease associated with the use of a drug or a treatment (surgery, radiation therapy), whether related to them or not.
Antibody	A protein produced by plasma cells in the lymphatic system or bone marrow in response to a specific «antigen» (see antigen) which has stimulated the immune system (see 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.
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.
Blinding	A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

Blood count	Measurement of the number of blood cells, i.e. 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 diseases in which abnormal cells divide without control and can invade nearby tissues. Cancer cells can also spread to other parts of the body through the blood and lymph systems.
Carcinoma	A cancer that begins in the skin or in tissues that line or cover internal organs.
Chemotherapy	Treatment directed to kill cells that divide fast, as cancer cells.
Clinical trial / Clinical study	Research study that involves human subjects. Each study aims to answer scientific questions and to find better ways to prevent and/or treat cancer and/or to support cancer treatments.
Combination chemotherapy	The use of two or more chemotherapy drugs.
Combination / multimodality therapy	The use of two or more modalities of treatment – surgery, radiotherapy, chemotherapy, or immunotherapy – in combination, alternately or together, to achieve optimal results against cancer.
Control group	In clinical studies, this is a group of patients who receive a standard treatment, that is a treatment or intervention currently being used and considered to be of proven efficacy based on past studies. Results observed in patients receiving newly developed treatments may then be compared to those of the control group. In cases where no standard treatment yet exists for a particular condition, the control group receives no treatment but is carefully monitored. For ethical reasons, 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 pathogens, cancer cells and other entities that can cause diseases.
Immunotherapy	A type of therapy that uses substances which stimulate the immune system to help the body fight cancer, infection, and other diseases.
Informed consent	The process in which patients learn about and understand the purpose and aspects of a clinical trial and then decide voluntarily whether to participate. This process includes a document describing what patients 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 patients sign an informed consent form and enter a trial, they are 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	A medical doctor who is an experienced clinical researcher and who prepares and carries out a protocol or treatment plan and implements it with patients in a clinical trial. The investigator is part of study team composed of other scientists, nurses, and other research staff.
Leukaemia	A cancer that begins in blood-forming tissue, such as the bone marrow, and causes the production of too many abnormal blood cells, thereby preventing the normal functioning of blood cells.
Lymphoma & multiple myeloma	Cancers that begin in the cells of the immune system.
Melanoma	A skin cancer that develops in the cells (melanocytes) that produce melanin.
Metastasis	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.
Neoadjuvant treatment	Any treatment that is given for cancer (like chemotherapy, hormone therapy or radiotherapy) before the main treatment, usually surgery, with the goal of making the main treatment more likely to be successful.

Oncologist	A doctor who is a specialist in cancer treatment. Oncologists can specialise in different cancer treatments, such as radiation, medical oncology or surgery.
Palliative care	An interdisciplinary medical caregiving approach aimed at optimizing quality of life and mitigating suffering among people with serious, complex, and sometimes terminal illnesses.
Palliative treatment	Any anticancer treatment like chemotherapy, hormone-therapy or radiotherapy, target therapy, immunotherapy) given for advanced and incurable disease. The goals are improving survival and quality of life, in many cases treating advanced cancer as a chronic disease.
Placebo	An inactive substance resembling a medication, given 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 new drug may be compared with a placebo when no one knows if any drug or treatment will be effective.
Protocol	The outline or plan for testing of an experimental procedure or experimental treatment.
Radiation therapy / radiotherapy	A treatment using X-rays, cobalt-60, radium, neutrons, or other types of cell-destroying radiation.
Radiosensitisers	Drugs that are being used to boost the effect of radiation therapy.
Randomised clinical trials	A study in which patients with similar traits, such as extent of disease, are selected randomly, 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. At the time the patient enters a clinical trials researchers do not know which of the treatments is most optimal. It is the patient's choice to be in a randomised trial or not. See also Clinical trials.
Regression	A decrease in the size of a tumour or in the extent of cancer in the body.
Remission	When the signs and symptoms of cancer go away, the disease is said to be «in remission». A remission can be temporary or permanent.
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 based on information submitted by the sponsor. The patient must also assess the risk/benefit ratio to decide if it is reasonable for them to take part in a study.
Sarcoma	A cancer that begins in bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.
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 being used and considered to be of proved effectiveness based on past studies.
Study arm	Patients in clinical trials are assigned to one part or group 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.

