Clinical Trial Basics

An information booklet to complement the IKCC My treatment, My Choice decision aids for people with renal cell carcinoma (kidney cancer)

IKCC
International Kidney Cancer Coalition

Kidney Cancer: My Treatment, My Choice Decision Aid ©

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An information booklet to support you in the shared decision-making process with your healthcare team

Insert local patient support organisation logo here

This workbook belongs to:

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This information booklet is intended for patients to use alongside the advice of their healthcare team.
It does not support any course of treatment over another.
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Clinical Trial Basics:
Information booklet

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Contents

Foreword

Perhaps you are reading this because you are considering taking part in a clinical trial for kidney cancer yourself, or someone you care about is trying to make this decision. We understand that the medical language and the information about clinical trials can be overwhelming. One of the strongest beliefs of the International Kidney Cancer Coalition (IKCC) is that patients and their families have an essential role to play in healthcare decision-making that affects their lives.

There has never been a time with so many new discoveries in kidney cancer. Clinical trials have demonstrated the benefits of new treatments that could potentially be used to improve outcomes after surgery.

There are now more choices and patients can receive different treatments or combinations of treatments. Clinicians are getting more experienced and knowledgeable, and the choice of treatments for kidney cancer, both within the healthcare system and through participation in clinical trials, is increasing. Thanks to clinical trials, the use of robotic removal of part of the kidney, better tools to predict how well patients respond to treatment, and the role of treatment before and after surgery are all evolving rapidly. The basic biological mechanisms of kidney cancer are being untangled with the promise of biomarkers, new diagnostics, and drug targets.

We are very excited to be participating in this rapidly changing and expanding field of medicine which promises real gains in the very near future. This can only be achieved through clinical research relying on patients to take part in clinical trials for new treatments.

This information booklet was written by a collaborative team of patients, patient advocates and medical professionals who have supported thousands of kidney cancer patients worldwide.

You may find that this booklet contains a lot of medical information and new terms. If you find it difficult to read all at once, it might be helpful to read it in sections or re-read it again at another time. For more information, and to help you understand the medical terms that are used, please also read our 'Kidney Cancer Basics' booklet, which includes 'My Kidney Cancer Dictionary' or see the glossary on page 42 of this booklet.

We hope that you find this booklet helpful as an introduction to the basics of clinical trials, and it will support you with your decision to take part in a clinical trial in the future.

Dr. Rachel Giles,
Chair, International Kidney Cancer Coalition
www.ikcc.org

Dr. Michael A.S. Jewett,
Chair, IKCC Medical Advisory Board
www.ikcc.org

About this information booklet

This information booklet is for people diagnosed with a type of kidney cancer called renal cell carcinoma (RCC), including all subtypes of RCC and stages of RCC. It is for people who are considering taking part in a clinical trial and would like more information about clinical trials. There are clinical trials available at all points throughout the treatment pathway, e.g., before and after surgery, and for patients who have already been treated with one or more medicines.

There are different types of treatment for people who have RCC. You will probably have many appointments with your healthcare team and receive a lot of information about your treatment options. One of these options might be to take part in a clinical trial. You will be faced with new challenges, concerns, and questions, that we hope will be addressed in this booklet.

Access to clinical trials for RCC is different around the world. It depends on which country you live in, or what your national healthcare system or insurance plan offers patients with kidney cancer. You will need to take this into consideration when deciding whether to take part in a clinical trial.

This booklet covers all the different types of clinical trial available for kidney cancer. Clinical trials are used to test several things, such as:

- The risks and causes of cancer, such as how genetics, lifestyle and other factors can increase the risk of cancer
- Medicines or lifestyle changes to prevent cancer or reduce the risk of developing cancer
- Tests for screening people for cancer in the general population
- Tests or scans for diagnosing cancer
- New medicines/treatments/devices or combinations of medicines, new doses, or different ways of giving treatment
- Quality of life of patients on a particular medical treatment.

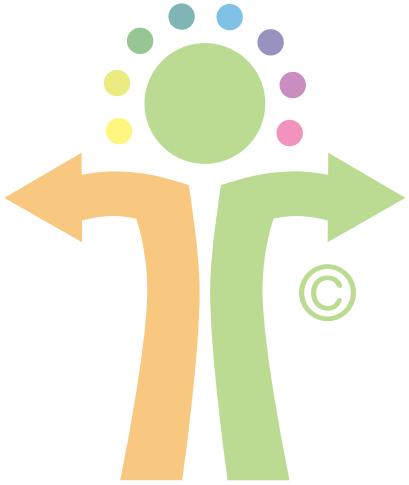
This booklet aims to help guide you through your conversations with your healthcare team and provides:

- Information about why new treatments need to be tested in clinical trials
- What is a clinical trial?
- Information about the ethics of clinical trials
- What are the different types of clinical trial and research studies?
- Who conducts clinical trials and where?
- Information about data management and reporting

Having kidney cancer can be overwhelming. Learning about the disease and access to treatment options can empower you to become an informed patient and help you make the best decisions about your care and the various treatments available to you.

You are the most important and powerful person involved in your own healthcare. Only you understand the impact of these decisions on your life.

You may find this booklet useful when discussing clinical trials with your family or healthcare team.



Why do new treatments need to be tested?

All new medical treatments, medicines and devices need to be vigorously tested to ensure they are safe and effective for treating medical conditions and diseases in humans. Treatments are tested both in the laboratory and in the clinic. Before a new medicine is given to humans, laboratory and animal tests are done to ensure they are safe for human use. They are then tested in the clinic in medical research studies involving people; these are called clinical trials.

Before new medical treatments, medicines and devices can be given to patients they need to be tested for:

- Safety and efficacy
- Finding the best dose to use
- Regulatory requirements
- Comparison to standard care.

All clinical trials and research studies involving humans are written following guidelines from the International Conference on Harmonization (ICH) Good Clinical Practice (GCP). ICH GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve humans. It aims to provide a common standard to help with the approval of clinical trial data by regulatory authorities.

Safety and efficacy

One of the main aims of clinical trials is to make sure the new medicines, medical treatments or devices are safe to use in humans and that they don't cause serious or unacceptable side effects that impact the quality of life of the patients. Also, the new medicine, medical treatment or device must be more (or equally) effective at treating the disease or condition under consideration than currently available treatments/standard care.

Clinical trials are also used to look at the impact of the new medicine, treatment, or device on your day-to-day life, for example how often you need to travel to hospital, and how the side effects influence you physically.

Finding the best dose to use

Clinical trials are also used to find the most effective dose of a new medicine. These trials are done early in the development process and are called phase 1 trials. Small numbers of patients are given a very small dose of the medicine. If all is well, the dose is gradually increased with each new group of patients until the researchers find the dose that is best tolerated. The researchers monitor the side effects and how the patients feel until they find the best dose. These studies are sometimes called dose escalation studies.

Why do new treatments need to be tested?

Regulatory requirements

Pharmaceutical companies use the data collected during laboratory testing (usually on animals) and clinical trials to form a product license application. This application is submitted to the regulatory authority in each individual country to obtain a license to market and sell the drug. In general, it can take 10-15 years to complete the trials on new medicines and for the medicine to get to the marketplace.

In some countries, new medicines, treatments, or devices need to be assessed for use within their national health service once a product license has been obtained. This is for reimbursement purposes and involves information about the cost of the treatment, as well as safety and efficacy.

Comparison to standard care

Later in the development process, clinical trials compare the new medicine, treatment, or device to what is currently available for the treatment of the cancer, i.e., standard care. These trials involve large numbers of patients and aim to find out which treatment works best, more about side effects and how the treatment affects a patient's quality of life.

Not all clinical trials are successful in finding a new and better treatment. Sometimes, the results from clinical trials show that the new medicine, treatment, or device does not work or is not as good as standard care. Sometimes it has worse side effects than existing treatments. However, this information is still useful for researchers and doctors, and adds to our knowledge of cancer and how best to treat it.

What is a clinical trial?

What is a clinical trial?

A clinical trial is a rigorously controlled and regulated medical research study involving people. Clinical trials find new ways to prevent, diagnose or treat disease. Clinical trials test new treatments or devices in people with cancer to make sure they are safe and effective at treating cancer. They also compare different treatments and treatment strategies. All new treatments must go through clinical trials before their benefits and risks can really be known.

What are clinical trials used for?

Clinical trials can be used to look at:

- The risks and causes of cancer, for example lifestyle factors and/or genetics
- New and better ways of preventing, screening, and diagnosing cancer
- New ways of treating cancer, such as new types of treatment, new combinations of treatments, or different ways of giving treatment
- Side effects to treatments and ways of controlling them
- The effect of a treatment on the quality of life of patients.

Clinical trials are also used to detect disease earlier, sometimes before there are symptoms, prevent a health problem, or improve quality of life for people living with a life-threatening disease or a chronic health problem.

Researchers also sometimes run clinical trials to study the role of caregivers and support groups.

How are clinical trials planned?

Researchers or doctors working in the pharmaceutical industry, devices industry, hospitals, charities, or government research institutes think of something they would like to investigate. These ideas come from laboratory work, experience that they have with patients or the public, or from the results of previous clinical trials or research. The idea could involve:

- A new medicine, medical treatment, or device
- A different combination of treatments
- Using an existing treatment for a different condition
- Testing a new way of giving an existing treatment or using a device.

Writing the protocol

The team interested in the research write a detailed plan or protocol that describes the medicine, treatment, or device under investigation, the conduct of the trial, and the patients who will be included in the trial. This protocol will be used by everyone involved in running the clinical trial. The protocol contains a lot of detailed information, such as:

- The aims of the clinical trial and why the researchers want to do the trial
- Who can take part in the clinical trial (eligibility)
- A description of the medicine, treatment, or device under investigation and how it is taken
- How many people are needed to show that a new medicine, treatment, or device is better than what is currently available
- A description of the visits that are needed during the trial and the tests that are required at each visit before, during and after treatment
- A description of the potential side effects to the medicine, treatment, or device and how to report any side effects to the trial team
- A timeline for the conduct of the clinical trial. Some clinical trials can take many years to complete, depending on how effective the treatment is
- How and when the results of the trial will be analysed and reported.

Patient involvement in clinical trial design and patient information

Some government health agencies, charities and pharmaceutical companies engage patients and caregivers in the design and implementation of clinical trials and the development of patient information materials. This can help ensure:

- The patients included in trials are those that are likely to experience benefits that are greater than the possible risks
- The endpoints included in the trial capture the experiences and outcomes of the treatment most important to patients and their caregivers
- The trial is conducted in such a way as to enhance patient experience and ease the burden on patients and their caregivers.

Patients can provide input to the design and implementation of trials that improve patient recruitment and retention. Their input can identify potential barriers to participation and retention of patients and support development of appropriate solutions, such as:

- Changing the design of the trial to ensure that patients see value in the aim of the study
- Development of key messages and patient information materials to improve patient recruitment

- Input to the practical aspect of the trial, such as transport to and from hospital, and format, location, scheduling, length, and timing of assessments
- Providing patient-friendly materials or incentives to improve engagement and retention of patients in the trial, especially for long and complicated trial designs
- Identifying solutions to help with the participation of specific patient populations in the trial, perhaps by geographic location or subtype of cancer.

Who decides the clinical trial sites?

Once the protocol has been finalised, hospitals with the right expertise and equipment can sign up so they can recruit patients to the trial. If the trial is sponsored by a pharmaceutical company or run by a contract research organisation (CRO) or charity, appropriate hospitals with the right expertise, patient populations, and equipment are approached. Hospitals are invited to see if they are interested in taking part and have enough time and resources to do so. Trials run by government health agencies are usually presented to the hospitals who work regularly with these health agencies to determine if they can take part. Often, the government health agency is in or linked to a local hospital or clinical research unit where most of their trials take place.

The hospital staff involved with the trial will usually receive training from the research team. This takes the form of investigator meetings, where a drug brochure (containing all the available information about the medicine, including results from preclinical and clinical studies), protocol and case report forms (the forms used for recording patient information and test results) are discussed in detail.

Who funds clinical trials?

Clinical trials involve several different organisations and can be very expensive to run. The money is needed for:

- Treatments, procedures, equipment, and tests
- Research staff to recruit the patients, carry out the tests, run the trial and collect the data
- In the case of early phase clinical trials, ward beds and facilities for the duration of the treatment
- Administrative costs of obtaining all the necessary approvals, overseeing the protocol, data collection, reporting serious side effects, production of results, and writing the report
- Staff and computer technology to enter the data onto a database, collate the data, analyse the results, and write the report
- The cost of extra tests or hospital stays for patients taking part.

Clinical trials are conducted in hospital departments, GP surgeries, or specialist phase 1 units, depending on the phase of the trial and the patient population under investigation. There will be a team of doctors, scientists, nurses, and other medical and healthcare professionals running the clinical trial, which will be led by a doctor with several years research experience (the principal investigator).

Funding for all these activities can come from multiple sources, or from a single source, including:

- ***Pharmaceutical companies*** fund a large amount of cancer research and run their own clinical trials for the medicines that they have developed. They also sometimes give a grant or supply the drug free of charge for trials run by other organisations. If a pharmaceutical company is running the trial, they must pay the hospital for the costs of tests and patient stays
- ***Charities*** Many charities fund cancer research. For example, Cancer Research UK (the single largest funder of cancer research in the UK), the Howard Hughes Medical Institute in the USA, and Institut Pasteur in France
- ***Government*** funds health research and coordinates cancer research nationally through organisations such as the National Institutes of Health (NIH) in the USA, the National Institute for Health Research (NIHR) in the UK (funded by the Department of Health and Social Care), and the Australian National Health and Medical Research Council (NHMRC). The money for tests and costs of hospital stays often comes from the government
- ***International organisations*** Some trials are funded by organisations from other countries, such as the European Organisation for Research and Treatment for Cancer (EORTC), and the National Cancer Institute (NCI) in the USA.

Approval for clinical trials

Regulatory approval

Before a trial can start, it is reviewed by the regulatory body of the country where the trial is taking place to ensure strict regulatory guidelines are being followed in the design and planned conduct of the trial. For example, in the European Union, all clinical trials of new medicines, medical treatments and devices need to be authorised by an organisation called the European Medicines Agency (EMA). This is called Clinical Trial Authorisation (CTA).

Ethics approval

Once a trial has received regulatory approval, it is then reviewed by a Research Ethics Committee (or Ethical Review Board). This is to ensure that the patient's rights are protected, and the highest standards of clinical practice will be observed to ensure the safety of the patient.

Research ethics committees and how they operate

The trial protocol must be approved by a Research Ethics Committee to make sure it is in the best interest of the patients and the procedures can be completed without adversely impacting on their lives. The trial protocol is reviewed by the Research Ethics Committee located in the hospital or health authority where it is proposed to carry out the trial.

Each Research Ethics Committee consists of people who are not involved with the trial in any way. Some Research Ethics Committee include members of the public who are not researchers or healthcare professionals.

Research Ethics Committees make sure that the rights, safety, dignity and wellbeing of the patients are protected. They assess each trial protocol against a set of standards.

They look at things like:

- The aim of the trial and how important the issue is for patients
- How the research team plan to recruit people for the clinical trial
- Whether the likely benefits of taking part in the trial are greater than the possible risks
- The qualifications and experience of the clinical research team running the trial
- Whether the trial protocol has been peer reviewed
- If the patient information sheet is complete and easy to understand
- If extra information, such as doctor's letters, patient questionnaires or forms are well written in patient-friendly language.

The Research Ethics Committee then decides if the trial is safe and ethical to do, and whether it can go ahead in the hospital or health authority that they represent. If the Committee come across any problems with the trial protocol or accompanying documentation (e.g., the patient information sheet), they can ask the research team to make the appropriate changes before they give approval for the trial to start.

After the trial has started, the researchers need approval from the Research Ethics Committee to change the protocol. They must also keep the Committee informed of any serious unexpected side effects that occur during the trial. The Committee can stop the trial at any time if they have any concerns about the welfare of the people taking part.

Research Ethics Committees are sent a copy of the trial results and trial report at the end of the trial.

Specialist committees

For some trials, approval is needed from other specialist committees in addition to the Research Ethics Committee to go ahead. For example, a trial that uses a treatment or CT scans that expose people to high levels of radiation might need a certificate from a specialist committee to enable them to start the trial.

Hospital approval

In some countries, each hospital that wants to take part in the trial must also get approval from their Research and Development (R&D) department. This is sometimes called a site-specific assessment to make sure that the hospital has the staff, time, equipment, and expertise to carry out the trial safely, and that they are not already running a trial recruiting similar patients. Once this approval has been given, the hospital staff (doctors, research nurses, pharmacists, and radiographers) can be trained on the trial protocol.

Once all the necessary approvals are in place (regulatory, ethics and hospital), the trial can then start to recruit patients.

Patient information sheets and consent forms

Patient information sheets and consent forms for clinical trials are written following guidelines from the International Conference on Harmonization (ICH) Good Clinical Practice, which aim to provide uniform standards for the development of new medicines for humans.

Patients must be given sufficient information to allow them to decide whether they want to take part in a clinical trial. A patient information sheet should be written in simple, non-technical language and be easily understood by the patient. The use of short words, sentences, and paragraphs is recommended to improve readability. Some government health agencies, charities, and pharmaceutical companies involve patients and caregivers in the development of patient information sheets to ensure patients can understand them.

The following table lists what should be covered in the patient information sheet and consent form for a clinical trial:

Approval for clinical trials

Study title	This should be simplified and self-explanatory in patient-friendly language
Invitation paragraph	Explains that the patient is being asked to take part in a clinical trial, why the trial is being done, and what it involves. The patient will also be asked to consider discussing the trial with friends, relatives, and their GP if they wish, and to ask for more information if they need it
What is the purpose of the clinical trial?	The background and aim of the trial, including the duration
Why have I been chosen?	An explanation of how the patient was chosen for the trial and how many other patients will be taking part
Do I have to take part?	An explanation that taking part in the trial is entirely voluntary, that patients are free to withdraw at any time and without giving a reason, and this will not affect their care
What will happen to me if I take part?	Detail about what will happen to the patient during the trial, including the length of the trial, how often they will need to visit the hospital, what tests are required at each visit (blood tests, scans, assessments), travel expenses and the patient's responsibilities. For randomised trials, explain the randomisation process for putting patients into treatment groups and the chance of them getting the study medication/ treatment. For blinded trials, explain that the patient will not know which treatment group they are in. For double blind trials, neither the patient nor the doctor will know. Explain what a placebo is for placebo-controlled trials

What do I have to do? Are there any lifestyle restrictions?	Tell the patient if there are any dietary restrictions, whether they can continue to take any regular medication, drive, take part in sport, refrain from giving blood, and what happens if they get pregnant. Remind the patient that they should take the study medication regularly
Study medication or device	A short description of the medicine or device and stage of development. Dose of the medicine and method of administration. Patients should be given a card (like a credit card) with details of the trial to always carry with them
What are the alternatives for diagnosis or treatment?	Patients should be told what other treatments are available
What are the side effects of taking part?	For any new medicine possible side effects should be explained and the procedure for reporting side effects to the trial team. Known side effects should be listed in patient-friendly language
What are the possible disadvantages and risks of taking part?	All possible risks or disadvantages should be listed, especially the potential harm to an unborn child. Women who are at risk of pregnancy may be asked to have a pregnancy test before taking part in the trial and use effective contraception during the trial. If a woman becomes pregnant during the trial, she should immediately tell her doctor
What are the possible benefits of taking part?	Possible benefits of the trial should be explained without being coercive
What if new information becomes available?	If additional information becomes available during the trial the patient needs to be kept informed and the consequences of this new information, e.g., withdrawal from the trial

What happens when the research study stops?	If the treatment is not available after the end of the trial or if the trial is stopped, this should be explained to the patient along with alternative treatments
What if something goes wrong?	How complaints about staff or the trial are handled by the researchers. In some countries this will include no-fault compensation arrangements
Will my taking part in this study be kept confidential?	Patient permission will be needed to allow restricted access to their medical records and to the information collected about them during the study. All information collected about them will be kept strictly confidential
What will happen to the results of the research study?	What will happen to the results of the trial and when they will be published. Can the patients have a copy of the published results, and will they be told which treatment they received? Patients will not be identified in any report/publication
Other information	Who is organising and funding the research (pharmaceutical company, government health agency, charity) and whether the researchers have been paid? Contacts for further information. Version number and date of the patient information sheet
Consent form	Title of trial and name of researcher. Place to sign to indicate that the patient has read and understood the patient information sheet for the trial and has had the opportunity to ask questions; that they understand participation is voluntary and they are free to withdraw at any time, without giving any reason, and without medical care or legal rights being affected; that their medical notes may be looked at and they give permission for this; and they agree to take part in the trial

Patient confidentiality and data protection

Clinical trial researchers need to keep all patient information that is generated, collected, processed, and stored during the trial confidential. Information from which patients can be identified must not be sent outside the research team unless the need can be justified AND the patient has given consent AND the research ethics committee has given approval for the patient to give consent.

Patient information must be kept confidential in line with the requirements of the local country's Data Protection Act or General Data Protection Regulation (GDPR).

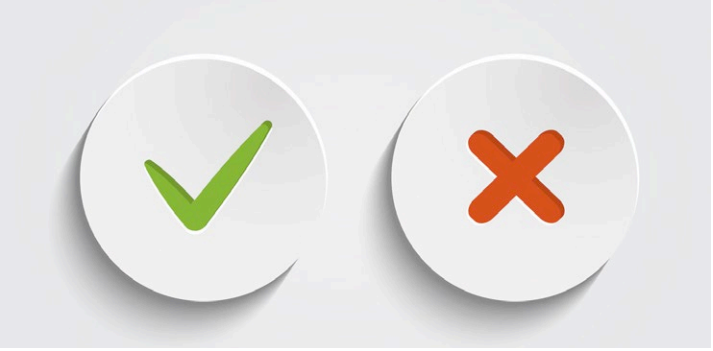
Pharmaceutical companies, government health agencies and charities must have mechanisms for patients to:

- Access their own information
- Give appropriate consent for the collection and processing of their personal data/information
- Have a procedure for the deletion of personal data/information that is no longer of use or if consent is withdrawn
- Allow them to request that the processing of their personal data/information is stopped.
- Have clear procedures for handling information requests from the media
- Allow the purpose and quality of information to be monitored and maintained to ensure that it is appropriate for the purposes intended.

Data protection policies are in place at pharmaceutical companies, government health agencies and charities to ensure that:

- Information is protected against unauthorised or unlawful access
- Confidentiality of information is assured
- Technical integrity of information is maintained
- Regulatory requirements and guidelines are met
- Information technology systems prevent the release of information (by accident or deliberate or criminal act) and ensure their safe use
- Information that can be used to identify a person is restricted to authorised users only.

What are inclusion and exclusion criteria and why are they needed?



All trials have entry conditions called inclusion/exclusion criteria or eligibility criteria. The inclusion/exclusion criteria define the attributes that patients must have to make it possible to accomplish the aim of the trial and make it safe for them to take part. Once the trial is up and running, patients who fit the criteria can take part.

Inclusion criteria are characteristics that the patients must have if they are to be included in the trial. Exclusion criteria are those characteristics that don't allow the patients to enter the trial. Inclusion and exclusion criteria may include factors such as age, gender, type and stage of disease, previous treatment history, the presence or absence of other medical, psychosocial, or emotional conditions and sometimes race and ethnicity.

Defining inclusion and exclusion criteria increases the likelihood of producing reliable and reproducible results, minimises the chance of harm to the patients, and guards against exploitation of vulnerable people.

What are the different types of clinical trials?

What are the different types of clinical trials?

Medical research studies involving people are called clinical trials. There are two main types of clinical trials - interventional and observational.

Interventional trials aim to find out more about an intervention like a new medicine, medical treatment, or device. In some trials all patients receive the new treatment, in other trials patients are put into different treatment groups, the results from which are compared.

Observational studies aim to observe what happens to patients in different situations. There are no treatments or interventions; however, the researchers observe the people taking part, but they don't influence what treatments the patients have.

There are different types of clinical trials within these two groups.

Pilot and feasibility studies

Pilot and feasibility studies are usually run before the start of a larger clinical trial to:

- See if it is possible to carry out the trial on a larger scale
- Look at how the main parts of the larger trial will work on a smaller scale (a pilot study).

Feasibility studies

Researchers might carry out a feasibility study before starting a much larger clinical trial to see if the larger trial can be done. Feasibility studies look at things such as:

- The patient population, and whether the research team are likely to recruit enough patients for the larger clinical trial
- The design of the clinical trial, and whether people would be willing to be allocated to treatment groups at random (randomisation)
- The assessments and hospital visits needed for the trial, and whether people can complete them
- The length of the larger clinical trial, and whether people would be willing to stay in the trial until the end.

Feasibility studies are not sufficient to answer any of the research questions of the main clinical trial but may give some indication of the outcome of the trial.

Pilot studies

Pilot studies are scaled down versions of the larger clinical trial and help test whether the main parts of the clinical trial will work.

Pilot studies may help answer the research question, and sometimes form the first part of the main clinical trial. The data generated from the pilot study can be used when the results from the main clinical trial are analysed.

Investigational clinical trials

There are 4 phases of investigational clinical trials, which are described in the table below:

Phase 1 clinical trials	The first studies in humans	Small numbers of patients or healthy volunteers (usually male). Used to investigate whether the new medicine is safe for human use. Can be used to find the most effective dose of medicine to use for patients
Phase 2 clinical trials	Investigates the safety and efficacy of a medicine in larger numbers of patients (100s)	Focuses on the effectiveness of the medicine at different doses, and its safety in patients. When phase 2 is completed, the decision will be made whether the medicine can be taken into phase 3 development if there is a very good chance of the drug meeting the strict safety and efficacy guidelines stipulated by the regulatory authorities

Phase 3 clinical trials	Involve large numbers of patients (1000s), usually on a global scale	Compare the efficacy and safety of the new medicine with either the standard existing treatment or placebo (dummy treatment). Can also study the new medicine in different patient populations and different doses and combinations of medicines. Usually randomised and sometimes blinded so that the patients (and the doctor in the case of double-blind trials) do not know which treatment they are receiving to avoid a biased interpretation of the results. Data obtained from phase 3 clinical trials are used to demonstrate the benefits of the new medicine over the current standard of care
Phase 4 clinical trials	Collect information on the use of the new treatment when used in routine patient care (i.e., after a product license has been granted for marketing)	For example, a new medicine may be assessed to see how it is being used in the clinic together with other effective treatments to treat a particular disease or medical condition in a select group of patients

Observational clinical trials

In an observational study, the researchers do not intervene in the care of the patient, but simply observe and record what happens. Observational studies often use questionnaires and surveys to record information about the lifestyles, quality of life and care of the people in the studies. Observational studies may look at the causes and patterns of disease.

There are two main types of observational study: case control studies and cohort studies.

Case control studies
These are retrospective studies in which groups of patients with a certain characteristic are compared to groups of patients without that characteristic, e.g., being overweight. The aim is to see whether exposure to any factor occurs more or less frequently in the cases (being overweight) compared to the control group.

An example of a case control study would be the comparison of smoking habits in people with lung cancer (cases) and people without lung cancer (controls) to determine a link between smoking and lung cancer.

Cohort studies
Cohort studies follow a group of people over time to assess the incidence of a disease (or some other event). Cohort studies are used to describe the effect of being exposed to one or more risk factors on the incidence of the disease. Cohort studies can be prospective (planned) or retrospective (historical).

Cohort studies can be used to assess the relationship over time between exposure to certain risk factors and the development of the disease. They can also be used to assess cause and effect, although randomised clinical trials are preferable for this. However, for rare diseases, the cohort may have to be very large with a long follow-up, resulting in an expensive study and many people being lost-to-follow-up.

Screening and prevention trials

Screening trials

Screening is done to detect cancer before it has started to cause symptoms i.e., for the early diagnosis of cancer. Screening is used to detect cancers, either in the general population (for example, breast cancer screening), or in people with a higher risk of developing cancer (for example, bowel cancer screening in older people). Some countries have regular screening programmes for the more common cancers, such as breast, bowel, cervical and prostate cancer; however, there are currently no screening programmes for kidney cancer.

Screening trials are used to determine the reliability of new tests to detect types of cancer, or to try to find out if there is a benefit to people in diagnosing cancer earlier.

Prevention trials

Prevention trials are used to determine whether a particular intervention (e.g., special diet, regular exercise) can prevent cancer from developing. They are carried out with people who do not have cancer, and can be done with the general population, or a group of people at higher risk of developing cancer.

Translational research

Translational research is research that applies findings from basic science to enhance human health and well-being. In a medical research context, translational research aims to 'translate' findings in basic research into medical practice and meaningful health outcomes.

Translational research is often referred to as from 'bench-to-bedside' research: Research from laboratory experiments through clinical trials to treating the patient. Translational research uses knowledge from basic science to produce new drugs, devices, and treatment options for patients.

Translational research helps turn early innovations into new health products. Research in universities, pharmaceutical companies and charities produces many new discoveries and inventions, which have the potential to improve health; however, turning these ideas into useful products can be extremely difficult.

Researchers need to bring together the right combination of medical, scientific, and business expertise to develop the product and position it within the market. To be able to do this, they need to anticipate what the market will be looking for, and how the product will be introduced alongside the competition. Translational research helps to overcome these obstacles, bridging the gap between basic research and a deliverable product.

Basket trials

A basket trial involves a single new medicine or a combination of medicines that is studied across multiple types of cancer defined by disease stage, histology, number of prior therapies, genetic or other biomarkers, or demographic characteristics.

Placebo-controlled trials

A placebo-controlled trial is a trial in which there are two (or more) groups. One group gets the active treatment, the other gets the placebo. A placebo is a dummy substance without any activity, but the patient (and often the research team) cannot distinguish it from the active treatment. Everything else is the same between the two groups, so that any difference in their outcome can be attributed to the active treatment.

Side effects in clinical trials

Side effects in clinical trials

Side effects (called adverse events in clinical trials) are unwanted or unexpected symptoms or feelings that occur after taking medicine. Side effects can be relatively minor, such as a headache, fatigue, nausea, or a dry mouth. They can also be life-threatening, such as severe bleeding or irreversible damage to the liver or kidneys.

If you experience a side effect, write it down immediately so that you can report it to your doctor accurately. Call your clinical trial team right away if you have any problems with trial medicines or if you are worried that the medicine might be doing more harm than good. Your doctor may be able to treat the side effect so that you can stay in the clinical trial or change the dose of the trial medication. If the side effect is severe, sometimes a different medication, lifestyle change, dietary change, or other measure may help to minimise it. However, this might lead to you being unable to continue in the study and you may need to be withdrawn.

Reporting side effects during clinical trials

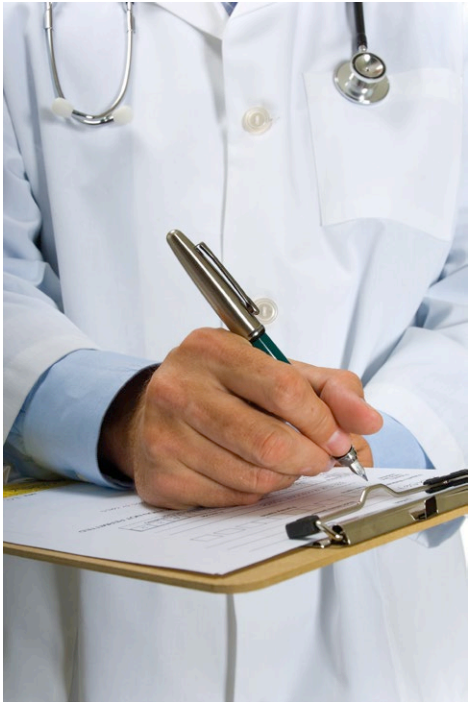
It is important that you contact your clinical trial team if you think you have a side effect after using a trial medicine or device. They will tell you if you need any medical care. They will also consider if you need to change your treatment or if you need a different treatment, and whether you can continue in the trial.

More severe side effects that occur during clinical trials must be reported to the Research Ethics Committee (or Ethical Review Board) that approved the study by the researchers immediately (at least within three days).

It is important for patients to identify the impact of new medicines, treatments, or devices, particularly on their quality of life. This adds to the overall knowledge of the safety of a new medicine, treatment, or device and the patient experience. The patients' role in reporting side effects is key to improving the safety of clinical trials. This also helps to protect other patients in the clinical trial against any immediate hazard to their health or safety.

During the trial, the research team must report all unexpected serious side effects to the regulatory body that approved the clinical trial. Reports of serious side effects in double-blind trials must be unblinded. The research team must also submit an annual review of the safety of the new medicine to the regulatory body, which includes details of all unexpected serious side effects that have occurred during the clinical trial, along with a safety summary for the new medicine. The annual review of safety must also be sent to the Research Ethics Committee.

For clinical trials of medical devices, only reports of serious side effects that are related to the trial or unexpected (i.e., not listed in the protocol) should be notified to the Research Ethics Committee within 15 days of the research team becoming aware of them.



Grading of severity of side effects

The National Cancer Institute (NCI) has established a standardised way to measure the seriousness of a side effect. The Common Toxicity Criteria for Adverse Events (CTCAE) is used by the clinical trial team to record the severity of a side effect in a clinical trial. It can be found on the National Cancer Institute website. Side effects are graded on a scale from 1 to 5, as follows:

Grade 1	Mild	No symptoms (asymptomatic) or mild symptoms. Clinical or diagnostic observations only. Treatment not needed
Grade 2	Moderate	Minimal, local, or non-invasive treatment needed. Limited age-appropriate activities of daily living, e.g., preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
Grade 3	Severe	Medically significant but not immediately life-threatening. Hospitalisation or extended hospitalisation. Disabling and limiting self-care activities of daily living, e.g., bathing, dressing, and undressing, feeding oneself, using the toilet, taking medications, and not bedridden
Grade 4	Life-threatening	Urgent treatment or intervention needed
Grade 5	Death	Death related to the side effect of the trial medication, treatment, or device

Grade 1 side effects are mild and generally not bothersome. Grade 2 are bothersome and may interfere with doing some activities but are usually not dangerous. Grade 3 are serious and interfere with a person's ability to do basic things like eat or get dressed and may also require medical intervention. Grade 4 are usually severe enough to require hospitalisation. Grade 5 side effects are fatal.

Most clinical trials and doctors focus on grade 3 side effects or higher, because these are the most dangerous. Grade 2 side effects, however, can significantly impact the patient's quality of life, even if they may not be medically dangerous. For example, a grade 1 headache is mild. A grade 2 headache keeps the patient from doing things like shopping or cooking. A grade 3 headache keeps the patient from getting out of bed, even to go to the bathroom.

Data management and reporting of clinical trials

Data management is the collection, storing and using data securely and efficiently. In clinical trials, data about patients, clinical trial tests and observations, side effects and response to medicines, treatments and devices are collected, recorded, stored, and analysed. They are then reported to help people and organisations use the data within strict data protection regulations to make decisions about new treatments for the benefit of patients.

How are the data collected and analysed?

Data collection and collation

Clinical trial data are collected on case report forms (CRFs). Case report forms are printed, optical or electronic documents designed to record all the information required by the protocol on each trial patient. Each patient in the trial will have their own case report form.

It is the responsibility of the clinical trial team to complete the case report form and make sure it is kept up to date throughout the clinical trial. In multicentre clinical trials, all sites need to be given instructions (a completion guide) on how to complete the case report forms in a standard way.

Case report form pages are arranged in order of patient visits and should include the following:

- Inclusion/exclusion criteria checklist with tick boxes
- If informed consent has been taken or date informed consent taken
- Demographics of the patient (e.g., age, gender, ethnicity)
- Relevant medical history
- Results of physical examination
- Baseline data
- Primary and secondary endpoints
- Results of various laboratory tests, scans, and ECG etc.
- Dosing and compliance data
- Side effects
- Concomitant medications
- Withdrawal form
- Serious Adverse Event Reporting Form (if available)

During the clinical trial, a proportion of the case report forms (about 10%) are audited by someone not directly involved in the trial (a clinical research associate from a pharmaceutical company, government health agency or charity) to make sure the data are an accurate reflection of what is recorded in the patient's hospital notes.

Most organisations will have a formal data management strategy that describes the activity of the data managers, the technology that is used to capture the data (electronic, optical, paper), the regulatory requirements, and the aims of the organisation for collecting and analysing the data.

Data monitoring committee

The data monitoring committee is a group of people who are not directly involved with the clinical trial. They keep an eye on how things are going during the trial, and make sure everything is running safely. They have the authority to change parts of the trial, or even stop the trial, if they feel they need to.

Analysis of the results

When all patients have been treated in the trial, the research team will look at the data and analyse the results. They will look at things like:

- How well the treatment worked compared to standard practice
- What were the side effects to treatment and when did they occur?
- How the treatment affected quality of life.

They will then draw conclusions about the treatments tested in the trial and make recommendations for future research.

If the results of the trial show a new medicine, treatment or device is better than the existing treatment, it may be licensed so that doctors can give it to patients. This is quite a long and complicated review process, and sometimes depends on the results of more than one trial.

This review process ensures that the new medicine, treatment, or device is safe, effective, the benefits outweigh any potential risks to patients, and it is better than existing treatments. This process is carried out by government agencies, such as the Food and Drug Administration (FDA) in the USA and the European Medicines Agency (EMA) in the European Union. They look at all new medicines to give them a marketing authorisation (or license).

Once a medicine or treatment is licensed, some countries with national health systems might carry out a health technology assessment (HTA) to see if it can be used within their national health system. For example, in England, the National Health and Care Excellence (NICE) decides whether a new medicine or treatment should be available within the English and Welsh National Health Service (NHS) and the

China National Health Development Research Centre makes decisions for the Chinese National Health Service.

After licensing, the regulatory bodies continue to collect information about the new medicine, treatment, or device to see how well it is working and information about side effects. They continue to check the safety and effectiveness of the new medicine, treatment, or device.

Dissemination of clinical trial results

The research team will write a clinical trial report to explain the findings from the clinical trial. The report will contain information on how well a treatment works (the end points of the clinical trial). For example, the main aim of a trial (primary end point) might be to find out how long people live after different treatments, or how long before the cancer comes back. Secondary end points could be what happens to the medicine in the body (pharmacokinetics and pharmacodynamics), or how safe is the medicine or treatment (side effects), or the effect of the new medicine or treatment on quality of life.

Clinical trial reports never contain any names or other details that could identify patients. They are all confidential.

Sometimes the results show that the new treatment is not better than the existing treatment. But even when a trial shows a treatment isn't useful for a particular cancer, it adds to our knowledge and understanding of cancer and how to treat it.

Many research teams publish the results from clinical trials in a medical journal or present them at a conference, to share what they have learnt.

Glossary

Active surveillance:
A way of monitoring cancer that is slow growing or indolent, rather than treating it straight away. During this time, regular testing is undertaken to check the growth and spread of the cancer. Some patients find this treatment approach difficult to understand; however, many tumours, particularly in older people, do not cause problems for the patient, and active surveillance enables them to avoid the debilitating side effects of some cancer treatments. Also called watch and wait and watchful waiting.

Adverse event:
Undesired effect that may or may not be related to treatment, such as dizziness, or a rash. A symptom caused by the treatment is a side effect. Serious adverse events are reported to the national regulatory authority.

Aetiology study:
A type of study that investigates the cause of a specific disease or tries to understand why a disease gets worse or better. Aetiological studies do not have to be clinical trials. Sometimes they can involve following up for a long time to see who develops the disease and what factors may have caused the disease to get worse or get better.

Baseline:
An initial measurement that is taken at the start of a study or just before the start of treatment. It is used for comparison over time to look for changes. For example, the size of a tumour will be measured before treatment (baseline) and then afterwards to see if the treatment had an effect.

Basket trial:
A trial involving a single medicine or treatment that is studied across multiple types of cancer, which all share a certain characteristic (e.g., the same mutation or biomarker).

Bias:
When a particular design or analysis is likely to favour a particular outcome and would, therefore, make those results unreliable. Bias can distort the results and could lead to unsafe or ineffective treatments being licensed for use, or useful treatments being overlooked. One way to avoid bias is by using randomisation and by 'blinding' patients and their caregivers.

Blinded:
Clinical trial patients do not know which treatment they are receiving. This helps prevent bias. See also 'double blind clinical trial'.

Case control study:
A type of observational study that is used to identify factors that may contribute to a medical condition by comparing people with a condition/disease (the 'cases') with people who do not have the condition/disease but are otherwise similar (the 'controls').

Case Report Form (CRF):
A paper or electronic questionnaire specifically used in a clinical trial to collect data from each participating patient.

CAT scan:
Computerised axial tomography scan. See definition for computerised tomography.

Cause:
Something that brings about a disease or a cancer, e.g., smoking is a cause of lung cancer.

Centre activation:
A centre can start to recruit patients into a clinical trial. This can only happen when the centre has completed all the necessary paperwork and the staff are aware of their responsibilities for the clinical trial.

Clinical equipoise:
The assumption that there is not one 'better' investigational treatment (for either the control or experimental group) during the design of a randomised controlled trial (RCT). A true state of clinical equipoise exists when one has no good basis for a choice between two or more treatment options.

Clinical trial:
A rigorously controlled research study that finds new ways to prevent, diagnose or treat disease. Clinical trials test new treatments and other interventions in people with cancer to make sure they are safe and effective at treating cancer. They also compare different treatments and treatment strategies. All new treatments must go through clinical trials before its benefits and risks can really be known.

Closed:
Usually refers to when recruitment of new patients into a clinical trial is stopped. Existing patients who are already in

the study continue to be followed up as part of the trial. This follow-up can continue for many years if the trial has been designed to look at long-term results. When follow-up for all patients has been completed and the data collected, the trial data can be analysed and reported. Usually, no more information is collected on the patients unless specific ethics approval is granted for the researchers to do so.

Cohort:
A group of people with a shared characteristic.

Cohort study:
A study of a group of people who share a characteristic, such as age, condition, or stage of cancer, often used to identify the causes of diseases, and to help develop clinical trials for new treatments.

Committee for Medicinal Products for Human Use:
The committee at the European Medicines Agency responsible for preparing opinions on questions concerning medicines for human use.

Common Toxicity Criteria for Adverse Events (CTCAE):
A grading system used by the clinical trial team to record the severity of a side effect (adverse event) in a clinical trial.

Compliance data:
A set of basic security practices for healthcare organisations that will help safeguard sensitive patient data, and satisfy compliance requirements from the government, e.g., Health Insurance Portability and Accountability Act (HIPAA) in the USA and the Data Protection Act in the United Kingdom.

Concomitant medication:
One or more medicines taken at the same time as the trial medicine.

Consent form:
A form used to record the written consent of a patient to take part in a clinical trial.

Contract Research Organisation (CRO):
A company that provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis.

Cross-over trials:
Clinical trials in which two different treatments are being compared, one in each of two groups of patients. After a period, the patients cross over to have the treatment that the other group of patients received.

CT (or CAT) scan or computerised tomography:
A special type of X-ray examination in which a series of X-ray pictures of your body are taken from different angles. A computer puts the pictures together to give a detailed image of the inside of your body.

Data and safety monitoring committee:
A group of people not directly involved with the clinical trial who keep an eye on how things are going during the trial, and make sure everything is running safely.

Disease-free survival:
Length of time after treatment during which no cancer is found. Can be reported for an individual patient or for a study population. Sometimes also called relapse-free survival.

Disease progression:
The course that a disease takes over time. When doctors talk about progress of disease, unfortunately they mean it has got worse.

Dose escalation study:
A study that determines the best dose of a new medicine or treatment.

Double blind clinical trial:
The patient, their doctor, and the researchers running the trial do not know which treatment is received by the individual patient until all data have been recorded. This helps prevent bias.

Drug brochure (investigator's brochure):
A comprehensive document summarising all the information available about the medicine under investigation in a clinical trial.

Effectiveness:
The degree to which something is successful at producing the desired result or effect.

Efficacy:
The ability to produce the desired result or effect.
Eligibility criteria: Clearly defined criteria for who is eligible to take part in a clinical trial and who is not. These criteria are described in the inclusion and exclusion criteria of the trial.

Endpoint:
In clinical trials, an event or outcome that can be measured to see whether the medicine or device being studied benefits patients.

Ethical Review Board (or Research Ethics committee):
A committee of healthcare professionals and lay people who review clinical trials and research studies to ensure they are conducted to appropriate ethical standards. Recruitment for a clinical trial cannot start until ethics committee approval has been granted.

Evidence base:
A collection of the best available scientific research currently available about a health condition. This is used to make decisions about how best to treat and provide care for individuals with that condition, or to prevent it.

Exclusion criteria:
These determine who is not eligible for a clinical trial. For example, many trials exclude women who are pregnant, or who may become pregnant, to avoid any possible danger to a baby, or people who are taking a drug that might interact with the treatment being studied (see also eligibility criteria and inclusion criteria).

Feasibility study:
A small-scale study carried out before starting a much larger clinical trial to see if the larger trial can be done.

Five-year survival:
A statistic indicating the percentage of people with a particular type of cancer who are living 5 years after the initial cancer diagnosis.

Good Clinical Practice (GCP):
An international quality standard for the conduct of clinical trials. Randomised clinical trials are required by law to conform to GCP.

Half-life:
The period it takes for half of the total amount of a substance or drug to be eliminated from the body.

Health economics:
In some clinical trials the cost of all aspects of the treatments being compared is examined. This is particularly important when there is more than one effective approach to treating a condition.

Inclusion criteria:
A set of criteria that clearly indicate who can join a clinical trial or research study, e.g., the condition and stage of disease they are already at, and their age. See also eligibility criteria and exclusion criteria.

Informed consent:
Written permission given before surgery, clinical trials, research or other kinds of treatments and tests. The individual, or a parent or guardian, must understand the treatment and legally agree to any risks involved.

Interim analysis:
An analysis of trial data, which is undertaken before the end of the trial.

International Conference on Harmonization (ICH) Good Clinical Practice:
An international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve humans. It aims to provide a common standard to help with the approval of clinical trial data by regulatory authorities.

Intervention:
A measure that is introduced and evaluated through a clinical trial with the aim of improving health. It could be a treatment (e.g., drug A vs. drug B), a treatment strategy (e.g., a drug vs. a surgical technique), a different screening approach, or prevention measure.

Interventional trial:
A type of clinical trial in which patients are put into groups that receive one or more intervention or treatment so that researchers can evaluate the effects of the interventions on the health of the patients.

Investigational drug:
A substance that has been tested in a laboratory and has regulatory approval to be tested in people in clinical trials. A drug may have a license for use in one disease/condition but be considered investigational in other diseases/conditions. Also called an experimental drug.

Karnofsky index:
A scale for the measurement of the general wellbeing and activities of daily life of cancer patients. Patients are scored from 100 to 0, where 100 is “perfect” health, and 0 is death. Doctors occasionally assign performance scores in between standard intervals of 10. The primary purpose of the Karnofsky index was to evaluate a patient’s ability to tolerate and survive chemotherapy for cancer.

Kidney cancer:
Cancer that forms in tissues of the kidneys, including renal cell carcinoma (RCC), transitional cell carcinoma (TCC) (also called renal pelvis carcinoma), and Wilms’ tumour, a rare

type of kidney cancer that usually develops in children under the age of 5.

Leibovich score:
A scoring algorithm that can be used to predict the risk of kidney cancer reappearing after it has been resected. The scoring system is based on the stage of the primary tumour, spread to the lymph nodes, tumour size, nuclear grade, and tumour necrosis. A low score (0-2) has a low risk, whereas a high score (6-11) has a high risk of relapse.

Multidisciplinary team (MDT):
A group of health care and social care professionals who provide different services for patients in a co-ordinated way. Members of the team may vary and will depend on the patient's needs and the condition or disease being treated.

NED or No Evidence of Disease:
Medical phrase to indicate that the doctors are not able to detect any sign of disease or cancer with current testing methods.

Objective response:
A measurable response, usually assessed with a CT scan.

Observational study:
A study that observes a group of patients over a period and measures certain outcomes (e.g., the causes and patterns of disease, and whether a particular factor causes cancer or not, e.g., the effect of certain exposures (e.g., tobacco smoke, long duration of HIV infection). The study does not contain any attempt to affect the outcome.

Off-label:
The legal use of a prescription drug to treat a disease or condition for which the drug has not been licensed for use.

Open label trials:
A clinical trial in which patients and their doctors know which treatment (or treatment strategy) they are receiving.

Outcome measures:
Outcomes are measures of health, e.g., response to treatment, occurrence, or recurrence of disease, a measure of wellbeing.

Overall survival:
The length of time from either date of diagnosis or start of treatment that people diagnosed with cancer (or another disease) are still alive.

Pharmacodynamics:
The biological effect of medicines within the body and their mechanism of action.

Pharmacokinetics:
How medicines move around the body.

Partial response:
A decrease in the size of a tumour or in the extent of the cancer in response to treatment. This is also called partial remission.

Patient information sheet (or materials):
Leaflets or other materials, e.g., videos that provide sufficient information, in an understandable format to support patients in making the right decision for them to take part in a clinical trial, or to for them to decline participation.

Physical examination:
The process by which a doctor investigates the body of a person for signs of disease.

Pilot study:
A scaled down version of a larger clinical trial to help test whether the main parts of the clinical trial will work. The results from a pilot study can be used in the larger clinical trial.

Positron emission tomography (PET) scan:
A procedure in which a small amount of radioactive glucose is injected into a vein and a scanner is used to make detailed computerised pictures of areas inside the body where the glucose is used. Because cancer cells often are very active and need more glucose than normal cells, the radioactive glucose accumulates in cancer cells and these areas are highlighted on the scan.

Placebo:
A dummy treatment that is designed to be harmless and to have no effect. It looks, smells, and tastes like the treatment being tested, so that patients do not know if they are taking the dummy treatment or the treatment itself, i.e., they are blinded to the treatment they are taking. The effects of the active drug are compared to the effects of the placebo.

Placebo-controlled trial:
A trial in which there are two (or more) groups. One group gets the active treatment, the other gets the placebo.

Everything else is the same between the two groups, so that any difference in their outcome can be attributed to the active treatment.

Primary end point:
The main endpoint or outcome of a clinical trial.

Principal investigator:
A healthcare professional with several years research experience who is responsible for the management, conduct, and reporting of the clinical trial and for managing any collaborative relationships.

Product license:
A license that allows the manufacturer to market and sell a product.

Prognosis:
The likely outcome or course of a disease. The factors that affect a patient's prognosis include the type of cancer, its stage, grade, and response to treatment but also patient characteristics, for example their age.

Prognostic factor:
A situation or condition, or a characteristic of a patient, which can be used to estimate the chance of recovery from a disease, or the chance of the disease recurring (coming back).

Progression:
Increase in the size of a tumour or spread of cancer in the body.

Progression-free survival (PFS):
The length of time a patient lives without their cancer getting worse (progressing). PFS is a measurement used in clinical trials to help determine whether a new treatment is effective.

Progressive disease:
Cancer that is growing, spreading, or getting worse.

Protocol:
The plan for a research study or clinical trial. Protocols need to be approved by an ethics committee before the study begins to recruit patients. They provide information on the question being addressed by the study, the treatments under investigation, the eligibility criteria, and the visit schedule and type of tests for trial patients.

Quality of life:
As well as measuring the physical effects of a treatment (for example changes to blood pressure), some trials try to assess the impact of treatments on people's quality of life. For example, a 'quality of life' study might ask about; mood and general sense of wellbeing, fatigue, sleep patterns, and ability to carry out daily activities.

Randomisation:
Used in randomised controlled trials. It is decided at random which treatment or treatment strategy a trial patient will receive. This ensures that each patient has the same chance of receiving the treatments or strategies being compared and avoids one treatment being given to someone because they are, for example, elderly or very sick. Randomisation ensures that the groups of people being compared in a trial are as similar as possible, except for the treatment they receive. This in turn ensures that differences seen between these groups after they have started their treatment are likely to be due to the treatments being compared.

Randomised controlled trial (RCT):
A clinical trial in which the patients are assigned by chance to different treatment groups; neither the researchers nor the patients can choose which group they are in. Randomisation allows a fair comparison between trial groups to be made.

Recurrence:
Cancer that has returned after a period during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumour, or to another place in the body.

Regression:
A decrease in the size of a tumour or the extent of cancer in the body.

Regulatory body:
A government organisation that establishes national standards for medicines and ensure that these standards are adhered to. Regulatory bodies also grant product licenses for new medicines.

Relapse:
The return of the signs and symptoms of cancer after a period of improvement.

Relative survival:
A specific measurement of survival. For cancer, the rate is calculated by adjusting the survival rate to remove all causes of death except cancer. The rate is determined at specific time intervals, such as 2 years and 5 years after diagnosis.

Remission:
If a cancer is in remission, there is no sign of it on scans or during an examination. Doctors use the word 'remission' instead of cure when talking about cancer because they cannot be sure that there are no cancer cells at all in the body.

Response:
An improvement in disease related to treatment.

Response rate:
The percentage of patients whose cancer shrinks or disappears after treatment (responds to treatment).

Risk:
The chance that a person will get cancer. It is also used to describe the chance that the cancer will come back or recur.

Screening:
A way of finding out if people have a higher chance of having a health problem, so that early treatment can be offered, or information given to help them make informed decisions.

Secondary end point:
Clinical endpoints or outcomes from clinical trials in addition to the primary end point.

Shared decision-making:
A process that ensures individuals are supported to make decisions that are right for them. It is a collaborative process through which a clinician supports a patient to reach a decision about their treatment. The conversation brings together the clinician's expertise, such as treatment options, evidence, risks and benefits, and the patient's preferences, personal circumstances, goals, values, and beliefs.

Side effects:
Side effects are other effects on the body that may be related to the treatment or caused by something other than treatment. For example, a drug used to treat lung cancer may also cause a skin rash.

Stable disease:
Cancer that isn't changing, i.e., the tumour(s) is not growing, and no new tumours have developed.

Standard care:
Treatment that is accepted by medical experts as a proper treatment for a certain type of disease and that is widely used by healthcare professionals.

Stage/staging:
A system used to describe the size of a tumour and the extent of spread of the cancer throughout the body.

Survival rate:
The percentage of people in a study or treatment group who are alive for a given period after diagnosis. This is commonly expressed as 1- or 5-year survival rates.

Symptom:
An indication that a person has a condition or disease. Examples of symptoms include headache, fever, fatigue, nausea, vomiting, and pain.

Systemic:
Affecting the entire body. Also used to describe the supply of medicines through the circulatory system (blood) to the entire body.

Systemic treatment/therapy:
A treatment that is delivered to the entire body through the circulatory system (blood). Most cancer drugs are systemic treatments.

TNM staging:
A system for staging cancer based on the presence of tumours (T), lymph node involvement (N) and metastases (M). Also called AJCC staging.

Toxicity:
The extent to which something is poisonous or harmful.

Trade name:
The name of a drug under which it is licensed and sold. Also called the brand name.

Translational research:
Research aimed at translating results from basic science into results that directly benefit humans.

Trial/treatment arm:
One of the groups to which trial patients are assigned to in a randomised controlled trial. The group of people receiving the current standard care are usually referred to as the control arm.

Trial phases:
Clinical trials are conducted in phases from phase 1 through phase 4. Phase 1 trials aim to test safety and usually involve a small number of people. Phase 2 trials aim to evaluate effectiveness, and usually involve a larger number of people. Phase 3 trials aim to compare two or more treatments or treatment strategies and monitor side effects. Results from phase 3 trials are used to license treatments for use by patients. Phase 4 trials are post-marketing studies and collect further information on use of treatments in clinical practice.

Tumour:
A swelling, or lesion formed by an abnormal growth of cells. Tumour is not synonymous with cancer and a tumour can be benign (not cancerous) or malignant (cancerous).

Tumour burden/load:
The number of cancer cells, the size of a tumour, or the amount of cancer in the body.

Ultrasound scan:
A real-time, moving test that uses sound waves to detect and differentiate between tumours and cysts. A small probe producing sound waves is rubbed over the area of interest and the sound wave echoes are detected by the probe and turned into a picture of the organs and structures inside your body by a computer.

X-ray:
A type of electromagnetic radiation used to make images. The image is recorded on a film, called a radiograph. The parts of your body appear light or dark due to the different rates that your tissues absorb the X-rays. Calcium in bones absorbs X-rays the most, so bones look white on the radiograph. Fat and other soft tissues absorb less and look grey. Air absorbs least, so lungs look black.

Acknowledgements

The IKCC My Treatment, My Choice decision aid series was conceived by and written in collaboration with kidney cancer patients for the benefit of patients worldwide.

The IKCC is an independent international network of patient organisations that focus exclusively, or include a specific focus on, kidney cancer. It is legally incorporated as a Foundation in the Netherlands. The organisation was born from a very strong desire among various national kidney cancer patient groups to network, cooperate and share materials, knowledge, and experiences.

As part of the My treatment, My Choice series of decision aids, this Clinical Trial Basics booklet has been developed by the IKCC working in partnership with Action Kidney Cancer, a kidney cancer charity based in the UK.

Contributors
Richard Barker, kidney cancer patient
Rose Woodward, patient advocate
Dr Andreas Schmitt, oncologist, Royal Marsden Hospital, UK
Dr Sharon Deveson Kell, medical writer

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International Kidney Cancer Coalition

Registered Address: Stichting IKCC
't Ven 30
1115HB Duivendrecht,
The Netherlands

Email: info@ikcc.org
Website: www.ikcc.org

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