Cancer Association of South Africa (CANSA)

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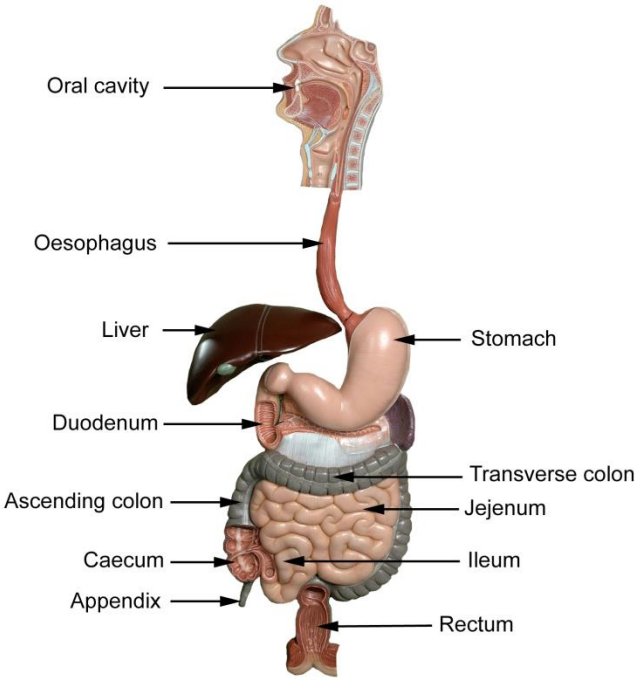
Fact Sheet on Gastrointestinal Stromal Tumour

Introduction

The human gastrointestinal tract (GI tract, or GIT) is an organ system that is responsible for consuming and digesting foodstuffs, absorbing nutrients and fluids, and expelling waste. The gastrointestinal tract consists of the stomach and intestines, and is divided into the upper and lower gastrointestinal tracts.



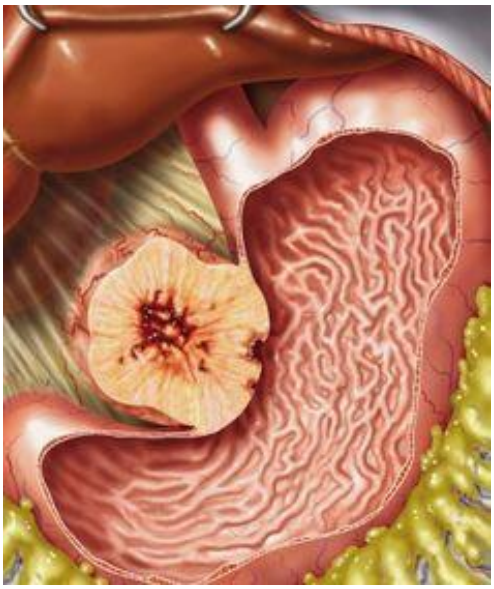
[Picture Credit: GI Tract]

The GI tract is conventionally divided into upper (mouth to ileum) and lower (caecum to anus) GI tract. From the point of view of GI bleeding, however, the demarcation between the upper and lower GI tract is the duodenojejunal (DJ) junction; bleeding above the DJ junction is called upper GI bleeding, and that below the DJ junction is called lower GI bleeding.

For the purposes of endoscopy, the upper GI tract includes the oesophagus, stomach and duodenum [oesophagogastroduodenoscopy (EGD) or upper GI endoscopy UGIE], and the lower GI tract includes the anus, rectum, colon, and caecum (anoproctosigmoid colonoscopy or lower GI endoscopy). The small intestine (jejunum and ileum) is relatively inaccessible to endoscopy.
(MedScape).

Gastrointestinal Stromal Tumours

Gastrointestinal stromal tumours (GISTs) are uncommon (rare) tumours of the GI tract. It is a type of sarcoma. These tumours start in very early forms of special cells found in the wall of the gastrointestinal (GI) tract, called the *interstitial cells of Cajal* (ICCs). ICCs are cells of the autonomic nervous system, the part of the nervous system that regulates body processes such as digesting food. ICCs are sometimes called the 'pacemakers' of the GI tract because



they signal the muscles in the digestive system to contract to move food and liquid through the GI tract.

[Picture Credit: GIST Tumour]

More than half of GISTs start in the stomach. Most other GISTs start in the small intestine, but GISTs can start anywhere along the GI tract. A small number of GISTs start outside the GI tract in nearby areas such as the omentum (an apron-like layer of fatty tissue that hangs over the organs in the abdomen) or the peritoneum (the layer of tissue that covers the organs and lines the walls of the abdomen).

Not all GISTs are cancerous. Some are benign (not cancerous) and do not grow into other areas or spread to other parts of the body.
(American Cancer Society; Cancer Research UK).

Incidence of Gastrointestinal Stromal Tumour (GIST) in South Africa
The National Cancer Registry (NCR) of 2012 does not provide any information regarding the incidence of Gastrointestinal Stromal Tumour (GIST).

Symptoms of Gastrointestinal Stromal Tumour (GIST)
People with early stage GIST often do not have any symptoms. Early stage GIST may be found when people are having tests for other medical conditions. Most GISTs are diagnosed in later stages of the disease.

The symptoms of advanced GIST are likely to include:

- Pain or discomfort in the belly (abdomen)
- A feeling of fullness
- Being sick (wanting to vomit)
- Blood in stools or vomit
- Feeling very tired
- A low red blood cell count (anaemia)

Other medical conditions apart from GIST can cause these symptoms. If one has these symptoms one should see a doctor. GIST is rare, so it is more likely to be caused by something less serious, but it is always best to have it checked out by a medical doctor.
(Cancer Research UK).

Risk Factors for Gastrointestinal Stromal Tumour (GIST)
The majority of GISTs develop for no known reason, called sporadic. Doctors are rarely able to find a specific risk factor for patients diagnosed with a GIST. The following are some of the risk factors:

Age - GISTs most often occur in people older than 50

Sex - GISTs are slightly more common in men than in women

Family history - GISTs rarely run in families, and having a family member with a GIST does not always increase one's risk of developing the disease. Hereditary syndromes that *can* increase the risk of GISTs include neurofibromatosis Type 1 (NF1) and Carney-Stratakis dyad. Carney-Stratakis syndrome is a familial syndrome characterised by gastrointestinal stromal tumours (GIST) and paragangliomas, often at multiple sites. It is a very rare syndrome. It presents at a young age (median age: 19 years) with an apparently equal ratio of male and female patients.

Genetics - Most often, a GIST, including non-hereditary tumours, develops because of genetic mutations or changes. The two most common genes affected are called *KIT* and *platelet-derived growth factor receptor* (*PDGFR*). Increasingly, researchers are finding other mutations, such as a protein called succinate dehydrogenase (SDH), or *BRAF*, a gene occasionally changed in people with melanoma or colorectal cancer. Testing for these mutations may be available at hospitals that specialise in treating a GIST. Researchers continue to look for specific genes and other syndromes that may be related to the development of GISTs and which may be used to help choose a patient's treatment options.

Because no non-hereditary, preventable risk factors have been found, there is no good way to prevent GIST development (Cancer.Net; Orpha.Net).

[Picture Credit: GIST Cancer]

Diagnosis of Gastrointestinal Stromal Tumour (GIST)
No laboratory test can specifically confirm or rule out the presence of a Gastrointestinal Stromal Tumour (GIST). The following tests are generally ordered in the workup of patients who present with nonspecific abdominal symptoms; abdominal pain; or complications of a GIST-like haemorrhage, obstruction, or perforation:

- Complete blood cell count
- Coagulation profile
- Serum chemistry studies
- BUN (blood urea nitrogen) and creatinine - urea nitrogen forms when protein breaks down
- Liver function tests (amylase and lipase values)
- Bloodtype, screen, and crossmatch
- Serum albumin

Other Tests:
Plain abdominal X-ray
Barium and air (double-contrast) X-ray series
Computed tomography (CT) scans of the abdomen and pelvis: MRI can depict tumours and yield information about surrounding structures
Positron emission tomography (PET) scanning
Endoscopy
Biopsy of tissue:

- Biopsy provides definitive diagnosis
- Biopsy may be required when preoperative therapy is needed in cases where the tumour is unresectable or only marginally resectable
- Biopsy may not be necessary if the tumour is surgically resectable and preoperative medical therapy is not required

(E-medicine).

Staging of Gastrointestinal Stromal Tumour (GIST)

The most common system used is the TNM system of the American Joint Committee on Cancer (AJCC). This system is based on 4 key pieces of information:

- **T** describes the size of the primary **tumour**, measured in centimetres (cm).
- **N** describes whether the cancer has spread to nearby (regional) lymph **nodes** (this is very rare for GISTs).
- **M** indicates whether the cancer has **metastasized** (spread) to other organs of the body. If a GIST does spread, most often it is within the abdomen, such as to the liver. Less often, it may spread to the lungs and bones.
- The **mitotic rate** is a measure of how fast the cancer cells are growing and dividing. It is described as either low or high. A low mitotic rate predicts a better outcome.
- Numbers or letters appear after T, N, and M to provide more details about each of these factors:
- The numbers 0 through 4 indicate increasing severity.
- The letter X means "cannot be assessed" because the information is not available.

T categories for GIST

TX: The primary (main) tumour cannot be assessed.
T0: No signs of a primary tumour.
T1: The tumour is 2 cm or less across (about 4/5 of an inch).
T2: The tumour is larger than 2 cm across but not larger than 5 cm (about 2 inches).
T3: The tumour is larger than 5 cm across but not larger than 10 cm (about 4 inches).
T4: The tumour is larger than 10 cm across.

N categories for GIST

NX: Regional (nearby) lymph nodes cannot be assessed.
N0: The cancer has not spread to nearby lymph nodes.
N1: The cancer has spread to nearby lymph nodes.

M categories for GIST

M0: The cancer has not spread (metastasized) to distant organs or sites.
M1: The cancer has spread to distant organs or sites (like the liver or the lungs).

Stage Grouping

Once the T, N, and M categories have been determined, this information is combined, along with the mitotic rate, in a process called *stage grouping*. The overall stage is expressed in Roman numerals from I (the least advanced) to IV (the most advanced). The stage grouping depends on where the tumour starts.

GIST that starts in the stomach or the omentum*

*The omentum is an apron-like layer of fatty tissue that hangs over the organs in the abdomen

Stage IA: T1 or T2, N0, M0, low mitotic rate: The tumour is no larger than 5 cm across (T1 or T2). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is low.

Stage IB: T3, N0, M0, low mitotic rate: The tumour is larger than 5 cm but not larger than 10 cm across (T3). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is low.

Stage II: One of the following applies:

- **T1 or T2, N0, M0**, **high mitotic rate:** The tumour is no larger than 5 cm across (T1 or T2). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is high.
- **T4, N0, M0, low mitotic rate:** The tumour is larger than 10 cm across (T4). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is low.

Stage IIIA: T3, N0, M0, high mitotic rate: The tumour is larger than 5 cm but not larger than 10 cm across (T3). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is high.

Stage IIIB: T4, N0, M0, high mitotic rate: The tumour is larger than 10 cm across (T4). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is high.

Stage IV: One of the following applies:

- **Any T, N1, M0, any mitotic rate:** The tumour can be any size (any T) and the cancer has spread to nearby lymph nodes (N1). It has not spread to distant sites (M0). The tumour can have any mitotic rate.
- **Any T, any N, M1, any mitotic rate:** The tumour can be any size (any T) and it may or may not have spread to nearby lymph nodes (any N). The cancer has spread to distant sites, such as the liver or the lungs (M1). The tumour can have any mitotic rate.

GIST of the small intestine, oesophagus, colon, rectum, or peritoneum**

**The peritoneum is a layer of tissue that covers the organs and lines the inside walls of the abdomen. Tumours in these locations are more likely to grow quickly than GISTs that start in the stomach

Stage I: T1 or T2, N0, M0, low mitotic rate: The tumour is no larger than 5 cm across (T1 or T2). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is low.

Stage II: T3, N0, M0, low mitotic rate: The tumour is larger than 5 cm but not larger than 10 cm across (T3). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is low.

Stage IIIA: One of the following applies:

- **T1, N0, M0, high mitotic rate:** The tumour is no larger than 2 cm across (T1). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is high.
- **T4, N0, M0, low mitotic rate:** The tumour is larger than 10 cm across (T4). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is low.

Stage IIIB: T2 to T4, N0, M0, high mitotic rate: The tumour is larger than 2 cm across (T2 to T4). The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0). The mitotic rate is high.

Stage IV: One of the following applies:
- **Any T, N1, M0, any mitotic rate:** The tumour can be any size (any T) and the cancer has spread to nearby lymph nodes (N1). It has not spread to distant sites (M0). The tumour can have any mitotic rate.
- **Any T, any N, M1, any mitotic rate:** The tumour can be any size (any T) and it may or may not have spread to nearby lymph nodes (any N). The cancer has spread to distant sites, such as the liver or the lungs (M1). The tumour can have any mitotic rate.

(American Cancer Society).

Treatment of Gastrointestinal Stromal Tumour

Different types of doctors often work together to create a patient's overall treatment plan that combines different types of treatments. This is called the multidisciplinary team.

Descriptions of the most common treatment options for GISTs are listed below.

Treatment options and recommendations depend on several factors, including the type and stage of tumour, possible side effects, and the patient's preferences and overall health. The care plan may also include treatment for symptoms and side effects, an important part of any patient's care. Patients should take time to learn about treatment options and must be sure to ask questions about things that are unclear. Also, they should talk about the goals of each treatment with their doctor and what they can expect while receiving treatment.

Surgery

Surgery is the removal of the tumour and surrounding tissue during an operation.

For patients with a localised GIST, surgery is the standard treatment and should be performed whenever possible. A surgical oncologist is a doctor who specialises in treating cancer using surgery.

Sometimes, the tumour may be large, or it has spread into nearby organs. In many of these instances, a drug called imatinib (see Kinase inhibitors below) will be given before surgery. The surgeon will most likely still try to remove the entire tumour in an effort to reduce the risk that the tumour will recur or block the gastrointestinal tract. In order to remove the entire tumour, it is possible that the surgeon may have to remove parts of nearby organs, depending on the tumour's location.

The removal of lymph nodes is not generally needed because GISTs do not often spread to the lymph nodes. A tumour that cannot be removed using surgery is called unresectable.

The doctor will then recommend a different type of treatment.
After surgery, patients who may have a high risk of recurrence often receive imatinib for at least three years. This type of post-surgical treatment is called adjuvant therapy.

Kinase inhibitors

Kinase inhibitors are drugs that target specific proteins that contribute to the tumour's growth and survival. This type of targeted treatment blocks the growth and spread of tumour cells while limiting damage to healthy cells.

Recent studies show that not all tumours have the same kinases. To find the most effective treatment, the doctor may run tests to identify the genes, proteins, and other factors in the tumour. As a result, doctors can better match each patient with the most effective treatment whenever possible. In addition, many research studies are taking place now to find out more about specific molecular targets and new treatments directed at them.

In 2002, the U.S. Food and Drug Administration (FDA) approved imatinib for the treatment of GISTs. Imatinib is a kinase inhibitor, and it is often the first drug used to treat GISTs. Since this drug has become available, the prognosis for patients with a GIST has improved considerably. It is usually given alone or either before or after surgery, as described above under 'Surgery'.

Imatinib is usually given for a long time. Research has been conducted to find out how long imatinib should be given after surgery to help delay or prevent a recurrence. If a GIST has spread to other parts of the body, imatinib is taken for the rest of the patient's life to help control the tumour.

The usual dose of imatinib is 400 milligrams (mg) daily. For some patients, the dose may be raised to 800 mg daily, especially for those who have an exon 9 genetic mutation in the *KIT* gene. This mutation may occur when the tumour starts in the small bowel or colon.

The most common side effects of imatinib are fluid accumlulation, rash, nausea, and minor muscle aches. Serious but relatively rare side effects include bleeding and inflammation of the liver. Some side effects from imatinib get better over time, so a decision to stop treatment because of side effects should be considered carefully. People who have serious side effects may take a reduced dose of imatinib and still benefit from it.

Sunitinib (Sutent) is a kinase inhibitor that stops angiogenesis, which is the process of making new blood vessels. Because a tumour needs the nutrients delivered by these blood vessels to grow and spread, the goal of anti-angiogenesis therapies is to 'starve' the tumour. Sunitinib was approved in 2006 by the FDA for treating GISTs when the tumour continues to grow even after treatment with imatinib. Sunitinib may also be used when the side effects of imatinib are too serious despite taking a lower dose. Patients should talk with their doctor about the possible side effects for a specific medication and how they can be managed.

Regorafenib (Stivarga) is a tyrosine kinase inhibitor that works in many different ways to slow tumour growth. It was approved in 2013 for people with later stage GIST that cannot be surgically removed and when both imatinib and sunitinib did not work or caused severe side effects.

Radiation therapy

Radiation therapy is the use of high-energy X-rays or other particles to destroy cancer cells. A doctor who specialises in giving radiation therapy to treat cancer is called a radiation oncologist. The most common type of radiation treatment is called external-beam radiation therapy, which is radiation given from a machine outside the body. A radiation therapy regimen (schedule) usually consists of a specific number of treatments given over a set period of time.

[Picture Credit: Radiation Therapy]

Radiation therapy is not often used for GISTs; however, it may be used as a palliative treatment to relieve pain or stop bleeding. Radiation therapy may damage healthy cells as well as tumour cells. Side effects from radiation therapy include tiredness, mild skin reactions, upset stomach, and loose bowel movements. Most side effects go away soon after treatment is finished.

Chemotherapy

Traditional chemotherapy is the use of drugs to destroy cancer cells by damaging the tumour's DNA. However, standard chemotherapy is not effective for treating GISTs; therefore, it should not be used.
(Cancer.Net; American Cancer Society).

Follow-up Care

Comprehensive follow-up is extremely important in all but the smallest and lowest-grade tumours.

A follow-up plan should include these measures:

- Periodic office visits and physical examinations are crucial in the follow-up of patients with GISTs.
- Periodic CT scanning can be ordered to aid in the detection of locally recurrent disease or distant metastasis. The optimal frequency for CT scan follow-up is not known. This is left to the discretion of the attending physician.

Positron emission tomography scanning may be indicated in the follow-up of patients with GISTs, especially those receiving imatinib mesylate for incompletely resected, recurrent, or metastatic disease.

PET scans help differentiate active tumour from necrotic or inactive scar tissue and malignant from benign tissue.
(MedScape).

About Clinical Trials

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials

have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

Types of Clinical Trials

Cancer clinical trials differ according to their primary purpose. They include the following types:

Treatment - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

Prevention - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer.
Screening - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

Diagnostic - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

Quality of life or supportive care - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different “phase” in the clinical research process. The following phases are used for cancer treatment trials:

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers

can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.
Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

Use of Placebos

The use of placebos as comparison or “control” interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

Possible benefits of taking part in a clinical trial

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

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.

(National Cancer Institute).

Medical Disclaimer

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