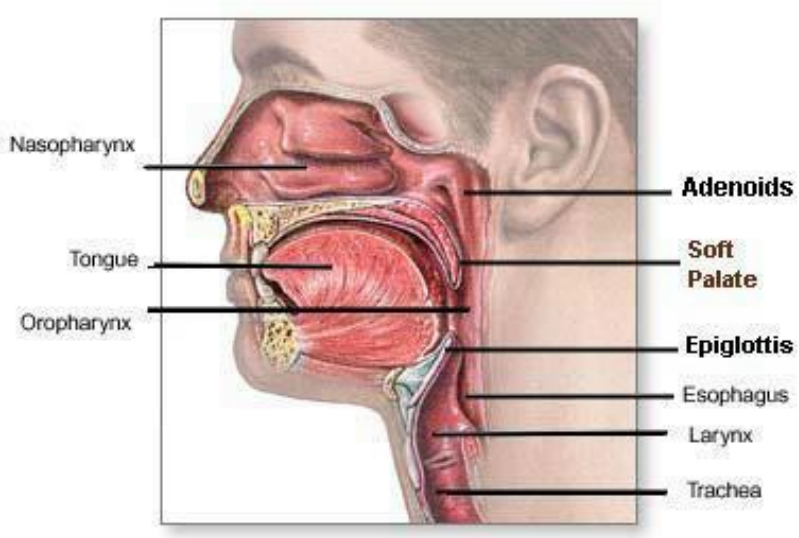
Cancer Association of South Africa (CANSA)

Research • Educate • Support

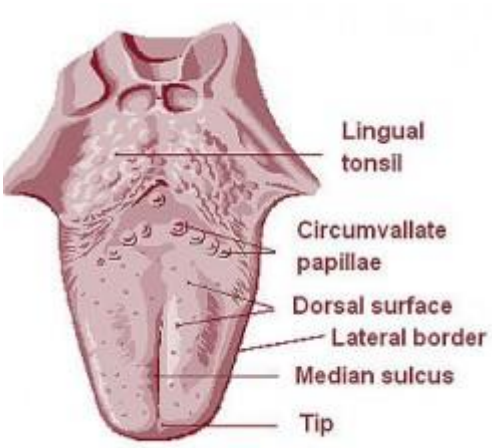
Fact Sheet on Cancer of the Tongue

Introduction

The tongue is a muscular organ on the floor of the mouth of most vertebrates which manipulates food for mastication (chewing). It is the primary organ of taste (gustation), as much of the upper surface of the tongue is covered in papillae and taste buds. The tongue is very sensitive and is kept moist by saliva. It is richly supplied with nerves and blood vessels. In humans an additional function of the tongue is phonetic articulation (speech). The tongue also serves as a natural means of cleaning one's teeth.



[Picture Credit: Tongue]



While the tongue's muscles guide food between the teeth and shape it so that it is digestible, the peripheral sense organ is perhaps better known for its role in the perception of taste. The tongue not only detects gustatory (taste) sensations, but also helps sense the tactile, thermal and even painful stimuli that give food its flavour.

[Picture Credit: Tongue 2]

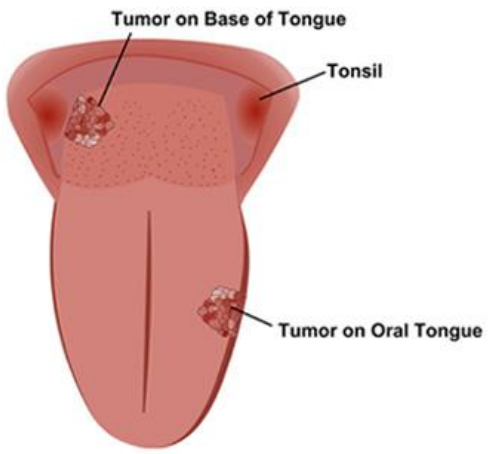
Many people mistake the bumpy structures that cover the tongue's surface for taste buds. These are actually papillae: goblet-shaped elevations that sometimes contain taste buds and help create friction between the tongue and food. Taste buds are

smaller structures, tucked away in the folds between papillae. Every taste bud is made up of basal and supporting cells that help maintain about 50 gustatory receptor cells. These specialised receptors are stimulated by the chemical makeup of solutions. They respond to several primary tastes: sweet, salty, bitter, sour, umami (savory) and fat, which some scientists claim might be a sixth taste. When a stimulus activates a gustatory cell, the receptor will synapse with neurons and send an electrical impulse to the gustatory region of the cerebral cortex. The brain interprets the sensation as taste (HowStuffWorks).

Cancer of the Tongue

Cancer of the tongue is cancer that develops in or on the tongue. Cancer occurs when cell growth becomes erratic and abnormal; specifically, it tends to grow much too quickly. Many factors can cause or increase the risk of developing cancer.

Tongue cancer is classed as a mouth or oropharyngeal cancer. There are two parts to the tongue, the oral tongue and the base of the tongue. Cancer can develop in either part of the tongue. The oral tongue is the part one can see when the tongue is poked out. This is the front two thirds of your tongue. Cancers that develop in this part of the tongue come under a group of cancers called mouth (oral) cancers.



[Picture Credit: Areas of Tongue]

The base of the tongue is the back third of the tongue. This part is very near the throat (pharynx). Cancers that develop in this part of the tongue are called oropharyngeal cancers.

Tumours on the base of the tongue are usually larger when diagnosed because in the early stages the tumour is difficult to see. The only early symptom is ear pain. Voice changes and difficult swallowing occur later.

Because bases of the tongue cancer is diagnosed later, the cancer may have already spread to the neck. A neck dissection is frequently needed to remove the affected lymph nodes.
(Cancer Research UK; About.Com; Cedars-Sinai).

Incidence of Cancer of the Tongue in South Africa

According to the National Cancer Registry (2012) the following number of cases of cancer of the tongue was histologically diagnosed in South Africa during 2012

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	330	1:399	0,89%
Asian males	11	1:318	1,25%
Black males	153	1:573	1,32%
Coloured males	65	1:176	1,50%
White males	101	1:291	0,50%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	168	1:1 190	0,45%
Asian females	10	1:571	0,88%
Black females	54	1:2 323	0,33%
Coloured females	31	1:558	0,74%
White females	73	1:544	0,46%

The frequency of histologically diagnosed cases of cancer of the tongue in South Africa for 2012 was as follows (National Cancer Registry, 2012):

Group - Males 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	1	0	2	35	104	118	50	12
Asian males	1	0	0	0	2	3	3	0
Black males	0	0	1	17	53	50	18	2
Coloured males	0	0	0	6	25	20	8	2
White males	0	0	1	12	22	34	18	8

Group - Females 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	1	2	6	9	49	47	35	16
Asian females	0	1	0	0	4	2	2	0
Black females	1	1	2	3	14	14	10	3
Coloured females	0	0	0	0	9	9	8	3
White females	0	0	4	4	17	21	14	9

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Risk Factors for Cancer of the Tongue

The exact causes of most head and neck cancers are not known, however several risk factors have been identified. Smoking tobacco (cigarettes, cigars and pipes) and drinking a lot of alcohol are the main risk factors for cancers of the head and neck in the western world.

Main causes for cancer of the tongue include:

- tobacco use
- alcohol use
- human papillomavirus (HPV) infection
- male gender
- certain genetic forms of anaemia - Fanconi Anaemia has been diagnosed at ages ranging from birth to >50 years of age; males and females are equally affected and it has been linked to cancer of the tongue
- a condition called Graft Versus Host Disease, which occurs in *some* patients who undergo stem cell transplants

(Cancer Research UK; About.Com; National Cancer Institute).

Signs and Symptoms of Cancer of the Tongue

While an annual screening for oral cancer is important, it is possible that one will notice some change in one's mouth or throat that needs examination between ordinary annual

screenings. A doctor or dentist should be contacted immediately when noticing any of the following symptoms:

- a sore or lesion in the mouth that does not heal within two weeks
- a lump or thickening in the cheek
- a white or red patch on the gums, tongue, tonsil, or lining of the mouth
- a sore throat or a feeling that something is caught in the throat
- difficulty chewing or swallowing
- difficulty moving the jaw or tongue
- numbness of the tongue or other area of the mouth
- swelling of the jaw that causes dentures to fit poorly or become uncomfortable
- chronic hoarseness
- pain in the ear (rare)

These symptoms may be caused by other, less serious problems, but it may also indicate the possible presence of oral cancer. Many people would think that a medical doctor is the appropriate person to visit, but dentists are trained in this simple, quick screening, which involves the examination of the oral cavity as a whole and not just teeth.
(Oral Cancer Foundation; Cancer Research UK).

Diagnosis of Cancer of the Tongue
Besides a visual examination of all the tissues in the mouth, the doctor or dentist will feel the floor of the mouth and portions of the back of the throat with his/her fingers, in the search for abnormalities. A thorough oral screening also includes indirect examination of the nasopharynx and larynx, and involves manually feeling the neck for swollen lymph nodes and other abnormalities such as hardened masses.

The mouth will also be checked for white patches, red patches, ulcerations, lumps, loose teeth, as well as review of dental x-rays for abnormalities. Tobacco use in any form should be reported as tobacco use is implicated in many cases of oral cancer.

If any suspicious area is identified, a biopsy may be recommended. This is simply taking a small portion of the suspicious tissue for examination under a microscope.

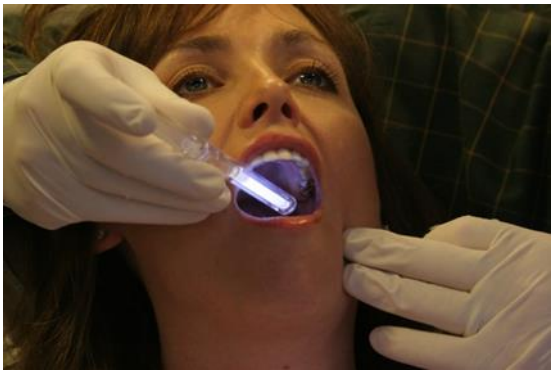
Incisional biopsy -The most traditional type of biopsy is incisional. It may be done by the doctor who did the examination, or the patient may be referred to another doctor for the procedure. In an incisional biopsy, the doctor will remove part or all of the lesion depending on its size and the ability to define the extent of the lesion at this early stage. The sample of tissue is then sent to a pathologist who examines the tissue under a microscope to check for abnormal, or malignant cells.

Fine-needle-aspiration biopsy (FNA) - When dealing with an area of significant mass, such as an enlarged lymph node, fine needle aspiration cytology (fine needle biopsy or FNB) has found an increasing role in diagnosis. The technique is reliable and relatively inexpensive. In it, a small needle attached to a syringe is inserted into the questionable mass and cells are aspirated, or pulled out into the syringe as the doctor draws back the piston of the syringe. The success of this method depends on how accurately the needle is placed, as well as the skill and experience of the tissue pathologist who will be examining the cells. It is likely that the doctor will insert the needle and draw out cellular material from several different locations in the mass to ensure that a thorough and representative sample has been taken.

Brush biopsy or exfoliative cytology **-** some dental offices are doing a 'brush biopsy' where a sampling of cells is collected by aggressively rubbing a brush against the suspect area. While this has some usefulness in preliminary evaluation of a suspect area, it is not a stand-alone procedure. If a positive find returns, this must be confirmed by a conventional incisional biopsy.

Mucosal staining - a blue dye called toluidine blue is applied to the area where cancer is suspected. If any blue areas remain after rinsing, it probably will be investigated with a biopsy.

Chemiluminescent light - after the rinsing of the mouth with a mild acid solution, the mouth will be examined with a special light. Healthy cells do not reflect the light; cancerous cells do.



[Picture Credit: Chemiluminescence]

Imaging tests, which may include:

- Computed axial tomography (CAT) scans
- Positron emission tomography (PET) scans
- Magnetic resonance imaging (MRI) scans
- Chest and dental X-rays
- Barium swallow: Also called an upper gastrointestinal (GI) series, this set of X-rays of the esophagus and stomach may be used to look for other cancers and determine how well you swallow.
- Endoscopy – where the doctor uses a laryngoscope to look into the back of the throat to examine the base of the tongue

(Oral Cancer Foundation; MD Anderson Cancer Center).

Types of Cancers of the Tongue

The most common type of tongue cancer is squamous cell carcinoma (SCCA). Squamous cells are the flat, skin like cells that cover the lining of the mouth, nose, larynx, thyroid and throat. SCCA is the name given to a cancer that starts in these cells.

Cancer of the tongue occurs in two different anatomical sites, namely:

Oral Tongue Cancer

- a lump on the side of the tongue that touches the teeth (lateral side)
- the lump often looks like an ulcer and is grayish-pink to red in colour
- the lump bleeds easily if bitten or touched

Base of the Tongue Cancer

- the tumour is often difficult to see in the early stages so it is usually diagnosed when it is larger
- there are few symptoms in the early stages
- in later stages, the cancer may cause pain, a sense of fullness in the throat, difficulty swallowing, the feeling of a lump in the neck or throat, voice changes or ear pain

(Cancer Research UK; Cedars-Senai).

Lowering the Risk for Cancer of the Tongue
Scientists look at risk factors and protective factors. Anything that increases one's chance of developing cancer is called a cancer risk factor, whilst anything that decreases one's chance of developing cancer is called a cancer protective factor.

Some risk factors for cancer can be avoided. For example, both smoking and inheriting certain genes are risk factors for some types of cancer, but only smoking can be avoided. Regular exercise and a healthy diet may be protective factors for many types of cancer.

Avoiding risk factors and increasing protective factors may lower your risk for cancer but it does not mean that cancer will never recur.

Reducing the cancer risk includes:

- a balanced lifestyle and healthy eating habits
- avoiding carcinogens (substances known to cause cancer)
- treating of precancerous conditions like chronic inflammation

Staging Cancer of the Tongue
The terms TNM stand for Tumour, Node and Metastasis of the cancer. It helps to explain the size of primary tumour (**T**), if the cancer has spread to the lymph nodes (**N**) and if the cancer has spread to other parts of the body (**M**).

Tumour Stage
The tumour stage is divided into 4 stages:

T1 stage the tumour is still present in the tongue tissues and is about 2 cm in size.
T2 stage the tumour is larger than 2 cm in size, but it is smaller than 4 cm
T3 stage the tumour is larger than 4 cm in size
T4a tumour it has spread from the tongue to the nearby tissues of the sinuses and skin. As well as the spaces behind the jaws, upper jaw muscles and base of the skull

Node Stage
The node stage is also broken down into 4 stages:

N0 stage there are no cancer cells present in the lymph nodes
N1 stage there are cancer cells present in one lymph node on the same side of the cancer. However, the lymph node is no more than 3 cm away from the cancer
N2a stage one **(**1) lymph node on the same side of the cancer is affected, but is more than 3 cm away, but less than 6 cm across
N2b stage there is more than just one lymph node affected by the cancer, but these lymph nodes are not more than 6cm away. Also, these lymph nodes are present on the same side of the neck
N2c stage cancer has spread to lymph nodes on both sides of the cancer, but are not more than 6 cm away
N3 stage there is at least one lymph node affected by the cancer and present more than 6 cm away from the site of cancer

Metastasise Stage
The **'M'** stage is divided into just two parts:

M0 stage the cancer has not spread to any other part of the body
M1 stage the cancer has spread to other distant parts of the body, like the lungs

Number Staging
Stage 0
Cancer is 'in situ', meaning it is isolated and has not traveled into a deeper layer of tissue or the lymph nodes, small almond-shape glands that help fight infection or trap tumour cells.

Stage I
- tumour is 2 centimetres or smaller
- tumour has not spread to lymph nodes or other parts of the body

Stage II
- tumour is between 2 and 4 centimetres
- tumour has not spread to lymph nodes or other parts of the body

Stage III
Tumour is either:
- larger than 4 centimeters or
- any size and has traveled to one lymph node on the same side of the head or neck. The lymph node with cancer measures 3 centimeters or less
- tumour has not spread to other parts of the body

Stage IV
Tumour is any size and has invaded deeply into muscle or facial skin or the jaws and has spread to:
- other parts of the body
- more than one lymph node on the same side of the head or neck as the main tumour
- lymph nodes on one or both sides of the neck
- any lymph node that measures more than 6 centimeters

Recurrent
The oral cancer has reappeared after treatment in the oral cavity or other part of the body. (MD Anderson Cancer Center; Buzzle).

Prognosis (Outlook)
Rates for individual mouth cancers include:
- lip cancer – 89% of patients will live for 5 years or more
- tongue cancer – 55% of women and 44% of men will live for 5 years or more
- oral cavity – this includes all other mouth cancers (not lip or tongue) - nearly 55% of women and 48% of men will be alive 5 years later

(Cancer Research UK).

Treatment of Cancer of the Tongue
As with many types of cancer, diagnosing your cancer early means it will be easier to control and possibly cure it. The treatment for tongue cancer depends on the size of the cancer and whether or not it has spread to the lymph nodes in the neck.

- Surgery - If the cancer has grown quite big, the patient may need to have an operation to remove part or all of the tongue (a glossectomy). This is a major operation and the doctor may suggest that the patient first try radiotherapy and chemotherapy to shrink the cancer. If this works, the patient may not need the surgery.

  If a person has a partial or complete removal of the tongue, it will permanently change that person's ability to speak and swallow – this will severely affect eating and drinking. This can be very hard to cope with and the person is likely to need a lot of support and help following the operation. It is important to talk to a doctor or specialist nurse before the operation.

- Radiotherapy - Intensity-Modulated Radiation Therapy (IMRT)
  Radiation therapy may be prescribed before surgery, after surgery, or sometimes as the only treatment. Radiation uses high-energy X-rays, electron beams, or radioactive isotopes to destroy cancer cells.

  IMRT uses a computer to help calculate the precise dose of radiation needed for the tumour. This minimizes radiation exposure to the surrounding normal tissue. IMRT uses a more effective radiation dose with fewer side effects than conventional radiotherapy techniques.
  Radiation therapy, including IMRT, stops cancer cells from dividing. The dose of radiation is calculated to damage only the rapidly dividing cancer cells. It causes only minimal damage to the normal tissues in the path of the radiation beam. Radiation therapy usually involves 5-6 weeks of daily treatments.

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- Chemotherapy - Although chemotherapy alone will not cure this type of cancer, it helps control growth of the tumour when used in combination with surgery or radiation therapy.

Chemotherapy is prescribed in different ways:

- together with radiation as an alternative to surgery (called chemoradiation)
- after surgery to decrease the risk of the cancer returning
- to slow the growth of a tumour and control symptoms if the cancer cannot be cured (palliative treatment)

A patient may have one of the above treatments or a combination of treatments. The best treatment for very small tongue cancers is surgery. For larger tumours that have spread to the lymph nodes in the neck, the person will most likely have a combination of surgery and radiotherapy. This means having an operation to remove the cancer from the tongue and the lymph nodes in the neck. The person may need to have all the nodes on one or both sides of the neck removed. The operation is called a neck dissection. It lowers the risk of the cancer coming back in the future. Surgery will then be followed by a course of radiotherapy to help get rid of any cancer cells left behind.
(Cancer Research UK; About.Com; Cedars-Sinai).

Lifestyle Changes After a Diagnosis of Cancer of the Tongue
After treatment, the treating doctor will usually recommend:

- therapy to improve tongue movement, chewing, and swallowing
- speech therapy, if use of the tongue is affected
- close monitoring of the patient's mouth, throat, oesophagus and lungs to see if the cancer has come back or spread

(NYU Langone Medical Center).

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.

<u>Types of Clinical Trials</u>
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

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

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