Cancer Association of South Africa (CANSA)

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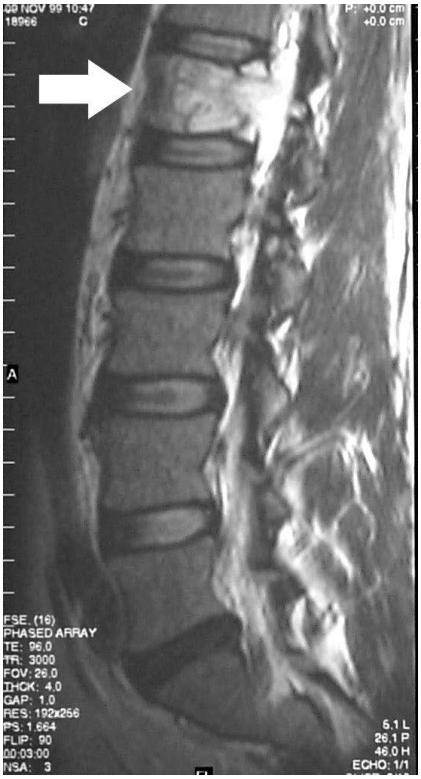
Fact Sheet
on
Chordoma

Introduction

Chordoma is a rare type of cancer that occurs in the bones of the skull and spine. It is part of a family of cancers called sarcoma, which include cancers of the bones, cartilage, muscles and other connective tissue.



Chordomas are thought to arise from remnants of the embryonic notochord, a rod-shaped, cartilage-like structure that serves as a scaffold for the formation of the spinal column. Notochord cells normally persist after birth lodged inside the spine and skull, and rarely these cells can undergo a malignant transformation that leads to the formation of a Chordoma.

Chordomas are generally slow growing, but are relentless and tend to recur after treatment. Because of their proximity to critical structures such as they spinal cord, brainstem, nerves and arteries, they are difficult to treat and require highly specialised care.

[Picture Credit: Chordoma of Lumbar Spine]

Chordomas can occur anywhere along the spine, from the head to the tailbone. The most common locations are in the clivus (a bone in the middle of the head - 32%) and sacrum or coccyx (vertebrae at the bottom of the spine - 29%). Less frequently, Chordomas can occur in the cervical (neck), thoracic (upper back), and lumbar (lower-back) vertebrae of the spine. Extremely rare cases of Chordoma occurring away from the spine have been reported in the ribs, legs and feet.

Chordomas occurring in the head are sometimes called brain tumours because they grow inside the skull toward the brain, however they do not actually develop from brain cells. Metastasis (spread of tumour to other body parts) occurs in 20-40% of patients with Chordomas of the spine and less than 10% of patients with skull-base tumours. The most common sites of distant metastasis are the lungs, liver, bones, and skin. Metastasis usually

only occurs when the primary tumour is advanced or uncontrolled and rarely is reported at the time of initial diagnosis.
(Chordoma Foundation).

Incidence of Chordoma in South Africa

The National Cancer Registry (2011) does not provide information about the diagnosis or incidence of Chordoma. The National Cancer Registry only provides information regarding Cancer of Bone.

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

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	100	1:2 864	0,27%
Asian males	2	1:4 817	0,26%
Black males	60	1:4 628	0,51%
Coloured males	10	1:1 761	0,23%
White males	28	1:1 002	0,14%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	79	1:4 050	0,21%
Asian females	0	-	-
Black females	48	1:6 457	0,29%
Coloured females	8	1:2 384	0,20%
White females	23	1:1 494	0,14%

The frequency of histologically diagnosed cases of bone cancer 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	31	35	6	9	10	2	6	0
Asian males	0	1	0	1	0	0	0	0
Black males	22	19	2	4	6	0	1	0
Coloured males	2	4	1	0	0	1	1	0
White males	3	5	1	2	9	3	1	0

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	24	13	10	11	9	6	3	2
Asian females	0	0	0	0	0	0	0	0
Black females	19	12	7	3	2	3	0	1
Coloured females	1	1	0	2	2	0	1	0
White females	4	0	2	5	5	3	1	1

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.

Frequently Asked Questions Concerning Chordoma
The following are questions that are frequently asked about this rare type of cancer called Chordoma:

Is Chordoma a type of cancer? - Cancer is a term for a disease in which abnormal cells divide without control and can invade other tissues. In cases of Chordomas, cells divide without control and can also invade other tissues – it is, therefore, classified as a type of cancer.

Is Chordoma a sarcoma? - Sarcomas are cancers of the connective tissue including bones, cartilage and muscles. Chordomas arise from the bones of the skull base and spine. Chordoma cells are derived from a tissue called the notochord which is an embryonic cartilage-like structure. During development, notochord cells get lodged inside the bones of the skull and spine.

Is Chordoma a brain tumour? - Chordomas of the skull base often involve the brainstem and can spread through the spinal fluid to the brain or elsewhere on the spinal cord. As such, Chordomas are sometimes considered brain tumours or central nervous system tumours, but they do not arise from brain cells and are, therefore, not true brain tumours.

Are Chordomas benign or malignant? - Chordomas are considered malignant because they can invade other tissues, frequently recur after removal, and have the potential to metastasise (spread to other parts of the body). Chordomas are considered a low grade malignancy because they are relatively slow growing and tend to recur locally rather than spreading throughout the body. Because Chordomas are low grade, they sometimes are mistakenly called benign. Benign tumours do not invade other tissue, do not metastasise, and usually do not return after being removed.

Are there different types of Chordoma? - Chordomas are most often classified based on their location in the body and their histology (appearance under a microscope). Locations that Chordomas can occur include the skull base (head), cervical spine (neck), thoracic spine (mid-back), lumbar spine (lower back), sacrum (pelvis area), and coccyx (tail bone). Extremely rarely Chordomas occur elsewhere in the body. Chordomas can be grouped into three different histologies: classic, chondroid, and dedifferentiated.
(Chordoma Foundation).

Classic Chordoma
Classic Chordoma has a lobular pattern with syncytial arrangements of neoplastic cells separated by fibrous septae and set in a bluish myxoid matrix. The tumour cells vary appreciably in cytology. Many have abundant, homogeneous and well-defined cytoplasm thought to represent early notochordal morphology. The majority of Chordomas also contain neoplastic cells with varying amounts of mucin and/or glycogen. The hallmark cell of Chordoma is the large phsaliphorous cell with a central nucleus and numerous clear cytoplasmic vacuoles. Signet ring type morphology is also common (Burger *et al*., 2002, Barnes *et al*., 1997). Presumably, the vacuole-laden cells develop from the eosinophilic cells in a recapitulation of notochordal embryology. Appreciable pleomorphism and mitoses are uncommon. The differential diagnosis of the histologic appearance of this tumour includes liposarcoma, metastatic carcinoma (particularly signet ring cell and renal carcinomas), chondrosarcoma (particularly the myxoid variant), and, intracranially, mixed tumour of the salivary gland (Mirra, 1989).

Chondroid Chordoma
In 1973, Heffelfinger and colleagues described a variant of Chordoma termed chondroChordoma which, in their series, comprised approximately 14% of all Chordomas. ChondroChordomas are biphasic, exhibiting both areas with classic morphology and others resembling hyaline cartilage. According to Heffelfinger *et al*., these areas represented chondroid differentiation and denoted a prognosis similar to that of low grade chondrosarcoma (considered better than conventional Chordoma). This assertion sparked a controversy that continues to this day and a number of studies have attempted to identify tumours with true biphasic differentiation both histomorphologically and immunohistochemically.

Brooks *et al*. (1987) found 100% (7/7) of lesions classified morphologically as chondroChordoma had immunological features of chondrosarcoma and concluded that tumours should be classified as either Chordoma or low grade chondrosarcoma. Conversely, Mitchell *et al*. (1993) and Ishida & Dorfman (1994) found that Chordomas in which there are even small areas of chondroid differentiation express epithelial markers throughout the tumour, which raises the possibility that the chondroChordomas of the previous study were misclassified chondrosarcomas, probably of the myxoid variety. It is now established that true Chordomas and cartilaginous tumours all express S100. Both foetal notochord and Chordoma are positive for cytokeratin and epithelial membrane antigen. Foetal cartilage, chondroma and chondrosarcoma are negative for cytokeratin and EMA and are positive for vimentin. Therefore the expression of cytokeratin diffusely in a morphologically heterogeneous tumour is central to the diagnosis of chondroid Chordoma (Radner et al., 2001).

In their immunohistologic analysis of 41 cases, Mitchell and Scheithauer (1993) found no difference in prognosis between classic Chordoma, chondroid Chordoma, and low grade chondrosarcoma when tumour site and patient age were taken into account. Probably more useful prognostic indicators are those related to tumour recurrence. Ishida and Dorfman (1994) found that increasing patient age, mitotic activity, Ki67 labelling index in excess of 6% were associated with faster growing tumours and therefore shorter disease free intervals.

Differentiated Chordoma
Dedifferentiated Chordoma is also a biphasic tumour exhibiting areas of conventional Chordoma morphology and areas of high grade spindle cell or pleomorphic sarcoma. They comprise approximately 1% to 8% of all Chordomas and may occur spontaneously or after radiation to a conventional Chordoma. Prognosis is exceedingly poor with most patients dying of tumour related complications within one year (Barnes *et al.* 1997).

Signs and Symptoms of Chordoma
It may take some time for a Chordoma to be diagnosed, as symptoms often develop gradually. The symptoms a person has will depend on where the tumour is. If the Chordoma starts in the spine, symptoms may include:

- pain
- changes in bowel habit - for example, constipation
- incontinence (poor bladder control)
- numbness

- changes in mobility - for example, weak legs
- impotence (problems with erections).

If the Chordoma starts in the base of the skull, symptoms may include:

- a headache
- double vision
- facial pain
- changes in hearing
- difficulty swallowing
- a feeling of dizziness (vertigo).

All of these symptoms are common to many other conditions and you will need further tests and investigations before an accurate diagnosis can be made.
(MacMillan Cancer Support).

Diagnosis of Chordoma
Usually the person begins by seeing a medical practitioner, who will examine him/her and may arrange any necessary tests or X-rays. For Chordomas in the spine, the doctor will probably refer the patient to a specialist surgeon called a spinal surgeon, who can carry out other investigations.

The doctor may also decide to refer the patient to a specialist hospital or bone tumour centre for further tests. This is because many of the tests for diagnosing bone tumours, such as biopsies, require experience and specialist techniques.

If someone has a Chordoma affecting the base of the skull, he/she may be referred to:

- a neurologist (a doctor who specialises in treating illnesses of the brain and nervous system) or
- a neurosurgeon (a doctor who specialises in operating on the brain).

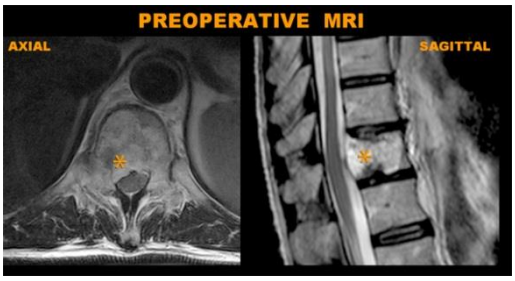
The doctors need to find out as much as possible about the type, position and size of the tumour so they can plan the treatment. The patient may have a number of tests and investigations done. The doctor will examine the patient thoroughly. They will test the reflexes and the power and feeling in the patient's arms and legs.

The patient will have a CT or MRI scan to find the exact position and size of the tumour.

CT (computerised tomography) scan - A CT scan takes a series of X-rays that build up a three-dimensional picture of the inside of the body. The scan is painless and takes 10-30 minutes. CT scans use small amounts of radiation, which are very unlikely to harm the patient or anyone he/she comes into contact with.

The patient may be given an injection of a dye, which allows particular areas of the inside of the body to be seen more clearly. For a few minutes, this may make the individual feel hot all over. If the patient is allergic to iodine or have asthma, he/she could have a more serious reaction to the injection, so it is important to let the doctor know about this beforehand.

MRI (magnetic resonance imaging) scan - This test is similar to a CT scan, but uses magnetism instead of X-rays to build up a detailed picture of areas of the body. Before the scan, the patient may be asked to complete and sign a checklist. This is to make sure it is safe for the individual to have an MRI scan.



[Picture Credit: MRI Scan Chordoma]

Before having the scan, the patient will be asked to remove any metal belongings including jewellery. Some people are given an injection of dye into a vein in their arm. This is called a contrast medium and can help the images from the scan to show up more clearly.

During the test the patient will be asked to lie very still on a couch inside a long cylinder (tube) for about 30 minutes. It is painless, but can be slightly uncomfortable, and some people feel a bit claustrophobic during the scan. It is also noisy, but the patient will be provided with earplugs or headphones.

Biopsy - To give an exact diagnosis, the patient may have a sample of cells taken from the tumour and examined under a microscope. This is called a biopsy. The biopsy involves an operation and the patient may have to stay in hospital for a few days. How it is done will depend on the position of the tumour in the spine. The doctor will discuss whether a biopsy is necessary in every case and exactly what the operation involves.

Staging of Chordoma

According to the AJCC 7th Edition Chordoma and other sarcomas are staged as follows:

Primary Tumour:

- T1 - 8 cm or less in greatest dimension
- T2 - >8 cm
- T3 - discontinuous tumours in the primary bone site

Regional Lymph Nodes:

- N0 - no
- N1 - yes

Distant Metastases:

- M0 - no
- M1a - lung
- M1b - other distant sites

Stage Grouping:

- IA - T1 N0, Low grade
- IB - T2 N0, Low grade; or T3 N0, Low grade
- IIA - T1 N0, High grade
- IIB - T2 N0, High grade
- III - T3 N0, High grade
- IVA - M1a
- IVB - N1, M1b

(Wikibooks).

Treatment of Chordoma
The treatment of Chordoma includes:

Chordoma Surgery - The primary treatment for Chordoma is the complete surgical removal of the tumour. To ensure the best outcome and prevent the spread of Chordoma , the surgeon(s) must remove the Chordoma and a margin of normal tissue surrounding it. The result of the first surgery is critical in determining the patient's prognosis (outcome). It is vital that an experienced, expert team of surgeons perform the initial operative procedure.

Skull based Chordoma are generally removed through minimally invasive surgery by highly trained, skilled surgeons. Patients with Chordoma at the base of the skull following this procedure usually require a brief hospital stay.

Chordomas that occur in the cervical, thoracic, lumbar or sacral spine have a larger area to grow requiring a more extensive operative procedure to remove them.

Sacral Chordomas, those in the lower spine, may involve nerves that control the bowel and/or bladder function. Most patients are able to manage control using a bowel regime and/or intermittent catherisation. A colostomy may be indicated if the size and location of the Chordoma requires the sacrifice of nerves that control bowel function.

The multidisciplinary approach continues throughout the patient admission including general surgical oncologists; thoracic surgeons; ear, nose and throat specialists (ENT); and reconstructive surgeons; neurological surgeons; orthopaedic oncology surgeons; radiation oncologists; orthopaedic pathologists; medical oncologists; and clinical nurse specialists; social workers; physical therapists; and occupational therapists working as a disciplined team to achieve the best possible outcome for the individual patient

Surgical intervention for the removal and treatment of cervical, thoracic, lumber or sacral Chordoma by and large requires a hospital admission of 3-10 days and likely follow-up rehabilitation in a hospital or specialty facility.

Radiation Therapy for Chordoma – Pre- and/or postoperative radiation therapy has improved local control of Chordoma. It can also slow the growth of the tumour if it has been incompletely resected or if it has recurred.

Proton beam therapy uses energy from protons of atoms to destroy cancer cells. It can be aimed at a tumour very precisely and can be concentrated on the tumour with little harm to the surrounding tissue.

For some patients for whom surgery is not a good option, high-dose radiation with a combination of X-rays and protons has been able to control tumours for over a decade and may be an important option for them.

Chemotherapy - Chemotherapy has not proved effective in the past, but there are a number of clinical trials with new agents currently underway.
(The Stephan L Harris Center for Chordoma Care).

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).

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