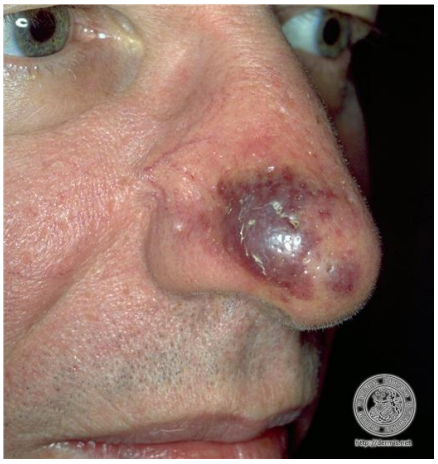
Cancer Association of South Africa (CANSA)

Research • Educate • Support

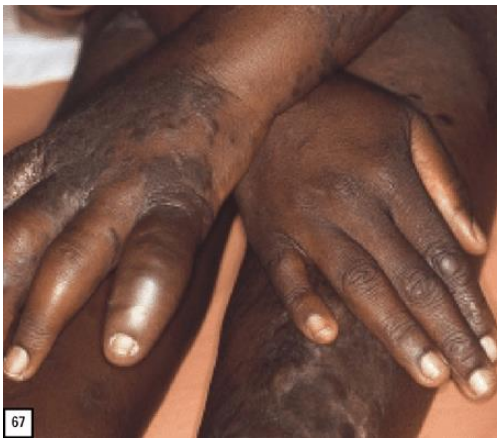
Fact Sheet on Kaposi Sarcoma

Introduction

Kaposi's sarcoma (KS) is a cancer that causes patches of abnormal tissue to grow under the skin, in the lining of the mouth, nose, and throat or in other organs. The patches are usually red or purple and are made of cancer cells and blood cells. The red and purple patches often cause no symptoms, though they may be painful. If the cancer spreads to the digestive tract or lungs, bleeding can result. Lung tumours can make breathing difficult.



[Picture Credit: Kaposi Sarcoma]



Before the HIV/AIDS epidemic, KS usually developed slowly. In HIV/AIDS patients, though, the disease moves quickly. Treatment depends on where the lesions are and how bad they are. Treatment for HIV itself can shrink the lesions. However, treating KS does not improve survival from HIV/AIDS itself (Medline Plus).

[Picture Credit: Kaposi Sarcoma 2]

Kaposi Sarcoma

Kaposi Sarcoma (KS) is a multicentric, malignant neoplastic vascular proliferation characterised by the development of bluish-red cutaneous (on the skin) nodules, usually on the lower extremities, most often on the toes or feet, and slowly increasing in size and number and spreading to more proximal areas. The tumours have endothelium-lined channels and vascular spaces admixed with variably sized aggregates of spindle-shaped cells, and often remain confined to the skin and subcutaneous tissue, but widespread visceral (body organ) involvement may occur.

Kaposi's sarcoma occurs spontaneously in Jewish and Italian males in Europe and the United States. An aggressive variant in young children is endemic in some areas of Africa. A

Researched and Authored by Prof Michael C Herbst
[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health]
Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

third form occurs in about 0.04% of kidney transplant patients. There is also a high incidence in AIDS patients. (From Dorland, 27th ed & Holland *et al*., Cancer Medicine, 3d ed, pp 2105-7) HHV-8 is the suspected cause.
(DermIS; HIV Insight).

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

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	1 225	1:227	3,32%
Asian males	12	1:896	1,43%
Black males	1 104	1:183	9,47%
Coloured males	53	1:484	1,23%
White males	55	1:567	0,28%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	885	1:382	2,35%
Asian females	6	1:1 454	0,55%
Black females	819	1:313	4,96%
Coloured females	32	1:1 063	0,77%
White females	28	1:1 087	0,18%

The frequency of histologically diagnosed cases of Kaposi Sarcoma 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	21	108	424	370	156	42	14	12
Asian males	0	1	4	5	0	0	0	0
Black males	21	98	381	327	140	37	11	10
Coloured males	0	3	20	15	8	4	1	1
White males	0	6	17	20	7	1	2	1

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	14	170	340	190	76	23	5	13
Asian females	0	1	2	1	0	1	0	0
Black females	14	155	313	173	69	22	5	12
Coloured females	0	9	8	8	6	0	0	1
White females	0	5	16	6	1	0	0	0

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.

Causes of Kaposi Sarcoma
Kaposi's sarcoma (KS) is a tumour caused by Human herpes virus 8 (HHV8), also known as Kaposi's sarcoma-associated herpes virus (KSHV). It differs from other cancers as it starts in several areas of the body at once, while other forms of cancer start in one place and then spread. This type of tumour was first described in 1872 by the dermatologist Moritz Kaposi

who died in 1902. Born in Austro-Hungary, Kaposi first identified this skin cancer in older Italian and Eastern European Jewish men.

Kaposi sarcoma is now far more common and spreads more aggressively through the body among patients with AIDS. Because of the AIDS epidemic, Kaposi sarcoma left its obscure oncologic niche and entered into daily usage during the 1990s.

With the rise of the AIDS epidemic, KS was researched more intensively in hopes that it might reveal the cause of AIDS. The disease was erroneously referred to as the 'AIDS rash'.

> According to Medilexicon's medical dictionary:
> *Kaposi's Sarcomas a multifocal malignant neoplasm of primitive vasoformative tissue, occurring in the skin and sometimes in the lymph nodes or viscera, consisting of spindle cells and irregular small vascular spaces frequently infiltrated by haemosiderin-pigmented macrophages and extravasated red blood cells. Clinically manifested by cutaneous lesions consisting of reddish-purple to dark-blue macules, plaques, or nodules; seen most commonly in men older than 60 years of age and in AIDS patients, as an opportunistic disease associated with human herpes virus-8 infection.*

(Medical News Today; Cancer Research UK).

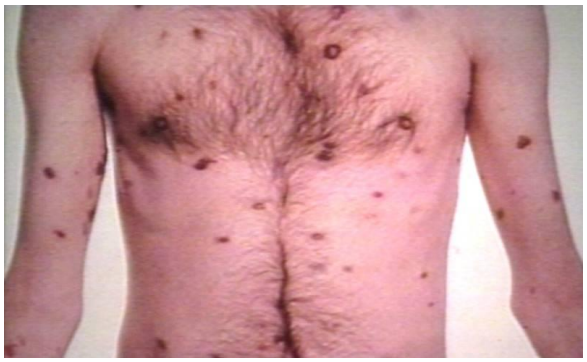
Risk Factors for Kaposi Sarcoma

The following factors can raise a person's risk of developing KS:

- Ethnicity - people of Jewish or Mediterranean descent, as well as equatorial Africans, have a higher risk of developing KS
- Gender – men, generally, have a higher risk of developing Kaposi sarcoma than women
- Human herpes virus 8 (HHV-8) - this virus may be the cause for Kaposi sarcoma to develop. It is also called the Kaposi sarcoma herpes virus (KSHV). Most people infected with HHV-8 do not get Kaposi sarcoma - the cancer appears most often when a person with HHV-8 also has a lowered immune system. Kaposi sarcoma-associated herpes virus (KSHV) is the eighth human herpes virus; its formal name according to the International Committee on Taxonomy of Viruses (ITCV) is HHV-8. Like other herpes viruses, its informal name (KSHV) is used interchangeably with its ITCV name. This virus causes Kaposi sarcoma, a cancer commonly occurring in Aids patients, as well as primary effusion lymphoma and some types of multicentric Castleman's disease. Castleman disease, also known as giant or angiofollicular lymph node hyperplasia, lymphoid hamartoma, angiofollicular lymph node hyperplasia, is a group of uncommon lymphoproliferative disorders that share common lymph node histological features that may be localised to a single lymph node (unicentric) or occur systemically (multicentric). It is named after Benjamin Castleman.
- Immune deficiency - people with HIV/Aids and people whose immune systems are suppressed because of organ transplantation have a higher risk of developing Kaposi Sarcoma.
- Sexual activity - homosexual (active) men tend to have a higher risk of HHV-8

(Cancer.Net; Wikipedia).

Signs and Symptoms of Kaposi Sarcoma (KS)
The first symptom of KS is usually skin lesions. Occasionally KS can also affect other parts of the body such as the lymph nodes, lungs, stomach or bowel. When this happens the symptoms will depend on the part of the body that is affected. Some people may have general symptoms such as fever, weight loss and loss of energy.



Skin lesions - these can range in colour from pink to brown, brown-red or reddish purple. KS can appear as a raised or slightly raised bump (nodule) or a flat area on the skin. The lesions can develop quickly. Although there may be a single area at first, it is possible for more than one to appear. Often the lesions merge to form a larger tumour. Any part of the skin can be affected, including the inside of the mouth.

[Picture Credit: Kaposi Sarcoma Picture]

Lymph nodes (glands) - if the lymph nodes are affected by KS, the nodes may become swollen but this generally causes few symptoms.

Swelling in the arms, legs and elsewhere - KS can cause damage to lymph vessels. These are part of the lymphatic system, which helps fight infection. When the lymph vessels are damaged this can lead to a build-up of fluid in the arms or legs. This is called lymphoedema. There can also be severe swelling of the face and scrotum (in males).

Lung problems - KS in the lungs can cause breathlessness and a cough which may be life threatening.

Digestive system (stomach and bowel) problems - KS may cause symptoms such as feeling nauseas and being sick (vomiting). The patient may also have trouble eating and/or swallowing

Anaemia - occasionally the lesions may bleed slowly, which over a period of time may cause anaemia (low numbers of red blood cells).
(McMillan Cancer Support; WebMD; University of California San Francisco; PubMed Health).

Types of Kaposi Sarcoma
There are five (5) main types of Kaposi Sarcoma (KS):

Classic KS - this type of KS is very rare and is usually only found on the skin, mainly on the lower legs and feet. It is most common in older men of Jewish or Mediterranean origin. It is a slow growing cancer and does not usually cause any problems. In the early stages, it does not usually need treatment. If the lesions are large, and in very visible areas on the body, the

patient may be given radiotherapy to get rid of it. The doctor may also suggest freezing it with liquid nitrogen or removing it with a small operation.

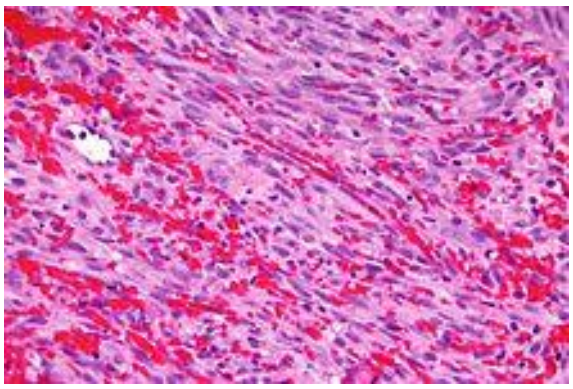
Endemic or African KS - as the name suggests, this type of KS is found in parts of Africa, where HHV-8 infection is common. It is faster growing than Classic KS. It is more common in men, but women and children of all ages may develop it. The doctor will treat this type of KS the same way as Classic KS but may use chemotherapy if the other treatments do not work.

Transplant KS found in people with weakened immune systems – People who have weakened or damaged immune systems are most likely to develop this type of KS, for example, people who have had an organ transplant operation. These people need to take drugs to stop their bodies rejecting the donated organ. These drugs suppress the immune system. This type of KS is also very rare. Reducing or changing the immunosuppressive drugs usually improves it. If that does not help, it may be necessary to treat the KS with radiotherapy or chemotherapy.

Aids related KS - this is the most common and fastest growing type of KS. If someone has Aids, the immune system is weakened. This increases the risk for developing KS. The treatment for this type of KS depends on how well the patient is and whether or not he/she is well enough to cope with the side effects of treatment. Chemotherapy is used for this type of KS. The patient may also be given interferon.

Non-epidemic Gay-Related Kaposi Sarcoma - there is a type of non-epidemic KS that develops in (active) homosexual men who have no signs or symptoms of HIV infection. This type of Kaposi sarcoma progresses slowly, with new lesions appearing every few years. The lesions are most common on the arms, legs, and genitals, but can develop anywhere on the skin. This type of Kaposi sarcoma is rare.
(Cancer Research UK; Fox chase Cancer Center; PubMed Health).

Diagnosis of Kaposi Sarcoma
To be sure that a lesion is caused by KS, the doctor will need to take a small sample of tissue from the lesion and send it to a laboratory to be analysed. This is called a *biopsy*. A specially trained doctor called a *pathologist* can often diagnose KS by looking at the cells in the biopsy sample under a microscope.



Micrograph of a Kaposi sarcoma showing the characteristic spindle cells, high vascularity and intracellular hyaline globs. H&E stain.

[Picture Credit: Kaposi Sarcoma Micrograph]

For skin lesions, the doctor will usually perform a *punch biopsy*, which removes a tiny round piece of tissue. If the entire lesion is removed, it is called an *excisional biopsy*. These procedures can often be done under local

anaesthesia. Lesions in other areas, such as the lungs or intestines, can be biopsied during other procedures such as bronchoscopy or endoscopy.

Other tests may include:

- an oral examination, to check for lesions on the palate, tongue, gums, or tonsils
- a rectal examination, to check for lesions in the anus
- *endoscopy - a* procedure to look at organs and tissues inside the body to check for abnormal areas. An endoscope is inserted through an incision (cut) in the skin or opening in the body, such as the mouth. An endoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue or lymph node samples, which are checked under a microscope for signs of disease. This is used to find Kaposi sarcoma lesions in the gastrointestinal tract.
- a *barium enema*, which allows doctors to track the progress of barium through the colon by using X-rays
- *sigmoidoscopy*, which involves using an endoscope or sigmoidoscope to view the lining of the rectum and colon
- chest X-rays, to check for lung lesions
- *computed tomography* (CT) imaging, which looks for lesions or other abnormalities
- *bronchoscopy - a* procedure to look inside the trachea and large airways in the lungs for abnormal areas. A bronchoscope is inserted through the nose or mouth into the trachea and lungs. A bronchoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue samples, which are checked under a microscope for signs of cancer.
- *lung biopsy* - if bronchoscopy shows lesions in the lungs, the doctor can take a sample for microscopic examination (American Cancer Society; CHealth; Fox Chase Cancer Center).

Staging of Kaposi Sarcoma

Staging is a way of describing where the cancer is located, if or where it has spread, and whether it is affecting the functions of other organs in the body. Doctors use diagnostic tests to determine the cancer's stage, so staging may not be complete until all the tests are finished. Knowing the stage helps the doctor to decide what kind of treatment is best and can help predict a patient's prognosis (chance of recovery). There are different stage descriptions for different types of cancer.

For epidemic Kaposi sarcoma, there is no official staging system; however, in 1988 the Aids Clinical Trials Group (ACTG) developed a staging system called the TIS system. The ACTG is the largest HIV clinical trials organisation in the world and is funded by the National Institutes of Health.

The TIS system evaluates:

- The size of the tumour (Tumour, **T**)
- The status of the immune system, which is measured by the number of a specific type of white blood cell, called CD4 cell, in the blood (Immune System, **I**)
- The spread of the disease or the presence of HIV/Aids-related systemic illness (Systemic Illness**, S**)

Within each of the three parts of the system, there are two subgroups: good risk (0, zero) or poor risk (1, one) (Cancer.Net).

Treatment of Kaposi Sarcoma
Treatment of Kaposi sarcoma can be difficult due to the immunosuppressed state of many of the people who are affected. These people are at a high risk of infections from procedures. The doctor will recommend treatment based on the patient's general health as well as on where the lesions are, how extensive they are, and how many there are.

Generally, most cancers are treated by physical removal of the tumour or lesion (*cryotherapy* in this case), chemotherapy, radiation, or a combination. For people with Aids, anti-HIV medications are used against the virus. This can improve the person's overall health and help treat Kaposi sarcoma.

For skin lesions, some possible treatments are:

- Cryotherapy - cryotherapy is a procedure that uses liquid nitrogen or other cryogens to freeze tissue. In cases of Kaposi's sarcoma, a doctor might freeze the lesions to destroy them.
- Locoregional therapy - locoregional therapy involves injecting chemotherapy agents directly into the Kaposi's sarcoma lesions.
- Radiation therapy - direct radiation therapy is another option to treat for the lesions. This involves aiming radiation directly at the spots. Some side effects associated with radiation include:
    - fatigue
- If the Kaposi's sarcoma has advanced and affects the internal organs, other therapies might include:
    - interferon: Some success has been found using high-dose interferon. Its use is limited to certain people, however, because it's a very toxic treatment.
- Chemotherapy: as with many cancers, chemotherapy is an option in treating Kaposi sarcoma. Because this treatment is *systemic* (i.e., it affects many systems in the body) or generalised, many side effects can occur. Most chemotherapy medications are given by intravenous drip (IV), but some can be taken by mouth. Some common side effects of chemotherapy include:
    - nausea and vomiting
    - hair loss
    - fatigue
    - diarrhoea
    - chills
    - shortness of breath
    - coughing
    - mouth sores

(CHealth; Fox chase Cancer Center; PubMed Health).

Prognosis (Outlook)
The outlook for Kaposi's sarcoma depends on the form of the disease. Milder forms are rare and develop slowly. People with classic KS usually die of other causes or develop a second type of cancer. About one-third of people with classic Kaposi's sarcoma develop another cancer.

Immunosuppression-related KS often improves by changing the drug(s) or its dose.

The most important factor in the prognosis for Aids-related KS is how well the immune system functions. Developing KS suggests that the immune system is highly impaired.

People with this disease usually die of a different HIV-related infection. People who take highly active antiretroviral therapy (HAART) have a better prognosis
(InteliHealth).

Reducing the Risk for Kaposi Sarcoma
While it is not possible to completely prevent Kaposi sarcoma, a person can significantly reduce his or her risk by avoiding the known risk factors that raises the risk of HIV/Aids infection, especially by avoiding risky sexual practices, such as having unprotected sex and using intravenous (IV) needles that have been used by someone else.

Because Kaposi's sarcoma is likely caused by an interaction between immune suppression and exposure to the sexually transmitted infection of HHV8, the precautions taken against other sexually transmitted infections should also be taken to try to prevent Kaposi's sarcoma. Practicing safer sex can also protect one from becoming infected with HIV, the virus that causes Aids. Since Aids increases the risk of KS, practicing safer sex can help reduce the risk for this cancer.
(CHealth; Cancer.Net).

Lifestyle Changes Following Kaposi Sarcoma Diagnosis
Lifestyle changes following Kaposi sarcoma diagnosis can be helpful in a variety of important ways:

- Strengthening the body so that one can withstand some of the rigors of treatment
- Optimising the function of the immune system to aid in the fight against cancer
- Improving one's emotional outlook, so one can enjoy life to the fullest, even during treatment
- Making healthful choices that will help to avoid other medical problems that could complicate health

General Guidelines
Stop smoking - Smoking is a known risk factor for many cancers. It is never too late to stop smoking.

Reduce the risk of infection - To decrease the risk of infection, avoid exposure to bacteria and viruses:

- try to avoid crowds, especially during cold and flu season
- ask a doctor about immunisation against the flu and pneumonia
- wash hands thoroughly and often. Hand washing is the most effective method of decreasing the chance of catching colds and flu. One may wish to carry hand sanitiser for occasions when washing is not convenient.

Follow a Nutritious Diet - Eating a healthful diet may help avoid other medical conditions linked to poor nutrition. Because cancer itself and some cancer treatment may have a dulling effect on one's appetite, it is important that one makes the most of the kilojoules taken in. Strongly consider consulting a registered dietician (RD) to help learn more about the best kinds of foods to eat and how to eat other less healthful foods in moderation.

Rest when tired - The treatments for cancer can add to the fatigue patients may experience. Fatigue is the most frequently experienced symptom of cancer and cancer treatments. The fatigue can range from 'just feeling tired' to complete and utter exhaustion. It is important to allow the body time to rest. This will help the body have the strength to heal itself. Studies have shown a relationship between fatigue and an increased morbidity of cancer and cancer treatments as a result of fatigue's adverse effect on appetite, diminished quality of life, and loss of hope.

Seek support - The diagnosis of cancer is a life-defining event that is difficult to handle for anyone. Facing the uncertainty of a serious disease, feeling anxious about how one will feel during treatment, and worrying about the impact of both the diagnosis and treatment can take a devastating toll that no one should have to tackle on their own. Try to have access to the following:

- family
- friends
- religious community
- empathetic support groups for people with your type of cancer
- professional support (social workers, psychologists, and/or psychiatrists who are trained to help support cancer patients and their families)

People who allow themselves to seek help while they are recovering from cancer can often maintain better emotional equilibrium, which will help them face the challenges of cancer and its treatment.
(Winchester Hospital).

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

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.

Whilst the Cancer Association of South Africa (CANSA) has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.

References and Sources

American Cancer Society
http://www.cancer.org/cancer/kaposisarcoma/detailedguide/kaposi-sarcoma-diagnosis

Cancer.Net
http://www.cancer.net/cancer-types/sarcoma-kaposi/risk-factors-and-prevention
http://www.cancer.net/cancer-types/sarcoma-kaposi/staging

Cancer Research UK
http://www.cancerresearchuk.org/cancer-help/about-cancer/cancer-questions/kaposis-sarcoma

CHealth
http://chealth.canoe.ca/channel_condition_info_details.asp?channel_id=12&relation_id=1619&disease_id=275&page_no=2

DermIS
http://www.dermis.net/dermisroot/en/17313/diagnose.htm

Dermnet NZ
http://www.dermnetnz.org/lesions/kaposi-sarcoma.html

Fox Chase Cancer Center
http://www.fccc.edu/cancer/pdq/English/Patients/KaposiSarcomaTreatment.html

HIV Insight
http://hivinsite.ucsf.edu/InSite?page=kb-06-02-03#S3X

InteliHealth
http://www.intelihealth.com/IH/ihtIH/WSIHW000/9339/11078.html

Kaposi Sarcoma
http://www.dermis.net/dermisroot/en/11060/image.htm

Kaposi Sarcoma 2
http://www.google.co.za/search?q=kaposi+sarcoma+black+patients&source=lnms&tbm=isch&sa=X&ei=8bfvUaiqHIjOhAf97oHgDA&ved=0CAcQ_AUoAQ&biw=1366&bih=614#facrc=_&imgdii=_&imgrc=BLbtinsuPO2v_M%3A%3BTxRIV5ePCDWZ-M%3Bhttp%253A%252F%252Fweb.squ.edu.om%252Fmed-Lib%252FMED_CD%252FE_CDs%252Fhealth%252520development%252Fhtml%252Fclients%252Fskin%252Fhtml%252Fskin_067.gif%3Bhttp%253A%252F%252Fweb.squ.edu.om%252Fmed-Lib%252FMED_CD%252FE_CDs%252Fhealth%252520development%252Fhtml%252Fclients%252Fskin%252Fhtml%252Fskin_06.htm%3B450%3B394

Kaposi Sarcoma Micrograph
https://en.wikipedia.org/wiki/Kaposi%27s_sarcoma

Kaposi Sarcoma Picture
http://wwideco.com/tag/sarcoma/

MacMillan Cancer Support
http://www.macmillan.org.uk/Cancerinformation/Cancertypes/Kaposissarcoma/Symptomsdiagnosis/Signssymptoms.aspx

Medical News Today
http://www.medicalnewstoday.com/articles/173259.php

Medline Plus
http://www.nlm.nih.gov/medlineplus/kaposissarcoma.html

National Cancer Institute
http://www.cancer.gov/clinicaltrials/learningabout/what-are-clinical-trials
http://www.cancer.gov/about-cancer/treatment/clinical-trials

PubMed Health
http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001682/

University of California San Francisco
http://www.ucsfhealth.org/conditions/kaposis_sarcoma/index.html

WebMD
http://www.webmd.com/hiv-aids/guide/aids-hiv-opportunistic-infections-kaposis-sarcoma

Wikipedia
https://en.wikipedia.org/wiki/Castleman%27s_disease

Winchester Hospital
http://www.winchesterhospital.org/health-library/article?id=32653