

Soft Tissue Sarcoma

What is
soft tissue sarcoma?

Let us explain
it to you.

www.anticancerfund.org

www.esmo.org

SOFT TISSUE SARCOMAS: A GUIDE FOR PATIENTS

PATIENT INFORMATION BASED ON ESMO CLINICAL PRACTICE GUIDELINES

This guide for patients has been prepared by the Anticancer Fund as a service to patients, to help patients and their relatives better understand the nature of soft tissue sarcomas and appreciate the best treatment choices available according to the subtype of soft tissue sarcomas. We recommend that patients ask their doctors about what tests or types of treatments are needed for their type and stage of disease. The medical information described in this document is based on the clinical practice guidelines of the European Society for Medical Oncology (ESMO) for the management of soft tissue sarcomas. This guide for patients has been produced in collaboration with ESMO and is disseminated with the permission of ESMO. It has been written by a medical doctor and reviewed by two oncologists from ESMO including the leading author of the clinical practice guidelines for professionals. It has also been reviewed by patient representatives from ESMO's Cancer Patient Working Group.

More information about the Anticancer Fund: www.anticancerfund.org

More information about the European Society for Medical Oncology: www.esmo.org

For words marked with an asterisk, a definition is provided at the end of the document.

Table of contents

Factsheet about Soft Tissue Sarcomas	3
Definition of Soft Tissue Sarcomas	4
Are Soft Tissue Sarcomas frequent?	5
What causes Soft Tissue Sarcomas?	6
How are Soft Tissue Sarcomas diagnosed?.....	8
What is important to know to get the optimal treatment?.....	10
What are the treatment options?.....	13
What are the possible side effects of the treatments?	19
How can Patient Support Groups help?.....	24
What happens after the treatment?	26
Definitions of medical terms.....	28

This text was written by Dr. Vittoria Colia (for the Anticancer Fund) with the help of Dr. Paolo Casali (ESMO), Dr. Silvia Stacchiotti (Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy) and Dr. Salvatore Provenzano (Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy). It was reviewed by Dr. Gauthier Bouche (Anticancer Fund), Dr. Svetlana Jezdic (ESMO), Jorge Freitas RN, MSc (EONS), Jane Beveridge BSc Hons, MSc, Nurse Consultant (EONS), Anita Margulies BSN RN (EONS), Markus Wartenberg (Sarcoma Patients EuroNet Association - SPAEN), Roger Wilson (SPAEN) and Prof. Jean-Yves Blay (ESMO).

FACTSHEET ABOUT SOFT TISSUE SARCOMAS

Definition of soft tissue sarcomas

- It describes a group of malignant tumours that originate in “soft tissues”. Soft tissues include muscles, tendons, fat, blood and lymph vessels, nerves and joint linings (synovial tissue*).
- As soft tissues are found everywhere in the body, soft tissue sarcomas may arise in any part of the body.

Diagnosis

- Unfortunately, sarcomas* can be asymptomatic for a long time and the symptoms will depend on the part of the body which is affected. Sarcomas can be suspected when a lump appears on a leg, an arm or the trunk.
- Radiological examinations* are mandatory to determine the extent of a soft tissue sarcoma and to establish the presence or absence of distant metastasis*.
- A sample of the tumour (biopsy*) must be obtained for analysis in the laboratory to confirm the diagnosis and get more details about the type of sarcoma*.

Treatment

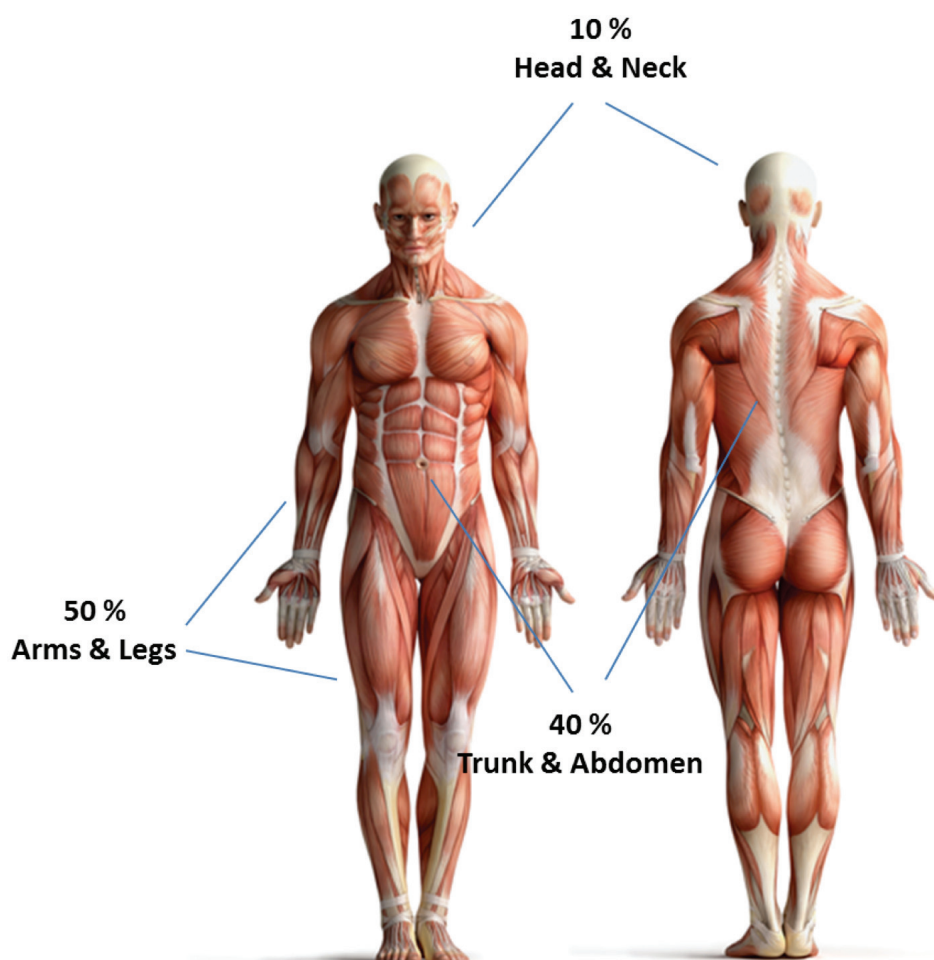
- Localised sarcomas are confined to the primary site and have not spread to nearby tissues or to other areas of the body.
 - Removal of the tumour by surgery is the standard treatment
 - Radiotherapy* and chemotherapy*, either alone or in combination after surgery, can sometimes be used to increase the chance of definitive cure or reduce the risk that the tumour comes back.
 - Radiotherapy* can be used before surgery to shrink the size of the tumour and allow it to be removed completely
- Advanced sarcomas* have spread from where they started to other parts of the body. This is known as metastatic or advanced cancer.
 - The main treatment approach is the use of chemotherapy* and molecularly targeted therapy*. The choice of the drugs will mainly depend on the clinical conditions of the patient and on the type of sarcomas*.
 - Radiotherapy* either during or after chemotherapy* could be used to relieve symptoms and control metastases*.
 - Surgery may be used to relieve symptoms or to cure the cancer in some specific cases.

Follow-up

- Follow-up appointments include physical examination, blood tests and radiological examination; they will be done for several years.
- The optimal time schedule for follow-up for soft tissue sarcomas is unknown and depends on the location, the size and the aggressiveness (grade) of the tumour. Follow-up after treatment for high or intermediate grade soft tissue sarcoma is more intensive than for low grade sarcoma*.

DEFINITION OF SOFT TISSUE SARCOMAS

Soft tissue sarcomas are a diverse group of malignant tumours that originate when abnormal cells grow out of control in “soft tissues” and “connective tissues”. Soft tissues can be found in any part of the body and include muscles, tendons, fat, blood and lymph vessels, nerves and joint linings (synovial tissue*). The type of sarcoma* depends on the kind of cells it arises from. Connective tissues include all tissues that support, connect or separate different tissues in the body. Therefore it can be found in the structure of organs in the body (e.g., the uterus). Soft tissue sarcomas, therefore, can grow almost anywhere, but are most common in arms and legs (50%), followed by trunk and abdomen (40%), and head and neck (10%).



Important note regarding other types of sarcomas

Kaposi sarcomas* and gastrointestinal stromal tumours* (GIST) are soft tissue sarcomas which are treated differently than the other soft tissue sarcomas and therefore are not covered in this guide. Bone sarcomas arise from cells making the bones and are also called osteosarcomas*. Ewing’s sarcoma is a rare type of sarcoma* usually also arising in the bone. Bone and Ewing’s sarcomas are treated differently than soft tissue sarcomas and therefore are not covered in this guide.

ARE SOFT TISSUE SARCOMAS FREQUENT?

Soft Tissue Sarcomas are rare tumours. In Europe, 4 to 5 cases will be diagnosed among 100,000 people every year, with no major difference between countries. The lifetime risk of developing a soft tissue sarcoma is about 0.15-0.50%. Soft tissue sarcomas are more common in adults than in children and the peak incidence is around the age of 50-60, but the tumour can occur at any age.

Because of their rarity and the frequent need of multimodal treatment*, management of soft tissue sarcomas should be carried out in reference centres with expertise in the treatment of this cancer, involving dedicated pathologists*, radiologists*, surgeons, orthopaedists*, radiation oncologists*, medical oncologists* and paediatric oncologists*.

WHAT CAUSES SOFT TISSUE SARCOMAS?

It is not clear why soft tissue sarcomas occur. However, some risk factors have been identified. A risk factor increases the risk of cancer occurring, but it is neither necessary nor sufficient to cause cancer. A risk factor is not a cause in itself.

Some people with these risk factors will never develop a soft tissue sarcoma and some people without any of these risk factors may nonetheless develop this cancer.

The main risk factors for soft tissue sarcoma are the following.

- Genetic predispositions: both inherited and acquired conditions may be associated to a soft tissue sarcoma.
 - *Li-Fraumeni syndrome* is an inherited genetic condition due to the mutation* of a tumour suppressor gene* (p53), i.e., a gene which helps protect cells from cancer. Patients with this rare syndrome are more prone to develop several type of cancers, including soft tissue sarcomas.
 - *Familial Adenomatous Polyposis* is a condition characterised by mutations* in the APC (adenomatous polyposis coli) gene*, which is a tumour suppressor gene*. Families affected by familial adenomatous polyposis develop hundreds to thousands of colonic polyps that most often arise from the second decade of life. Colonic polyps are benign* tumours which can evolve to colon cancer. There is also a high frequency of intra-abdominal desmoid tumours (a type of soft tissue tumours) among patients with familial adenomatous polyposis.
 - *Gardner's syndrome* is a type of familial adenomatous polyposis associated with the development of other benign* tumours such as osteomas*, epidermal cysts*, and fibromas*. There is a high frequency of intra-abdominal desmoid tumours (a type of soft tissue tumours) among patients with Gardner's syndrome.
 - *RB (retinoblastoma) syndrome* is a familial syndrome characterised by an alteration of the RB gene*, which is a tumour suppressor gene*. Patients usually develop malignant tumours of the retina in both eyes during infancy. Sarcomas of soft tissue and bone may develop later in life.
 - *Neurofibromatosis I (von Recklinghausen's disease*)*: this inherited disease is genetically characterised by a mutation* in the NF1 gene*, which is a tumour suppressor gene*. Clinical features include the presence on the skin of multiple, widespread benign* tumours known as neurofibromas*, and of café-au-lait spots*. Patients with Von Recklinghausen's disease* have an increased risk of developing malignant peripheral nerve sheath tumours (MPNST)* and, to a lesser extent, gastro-intestinal stromal tumours (GISTs)* and rhabdomyosarcomas*.
 - *Neurofibromatosis II*: this syndrome is caused by mutations* to the tumour suppressor gene NF2. It is typically associated with schwannomas* of the acoustic nerve* in ear(s) or other nerves. There is a predisposition to meningiomas* and gliomas*, two types of tumour developing from cells of the nervous system.
 - Other genetic conditions such as *Basal cell nevus syndrome**, *Tuberous sclerosis**, and *Werner's syndrome** are associated with an increased risk of developing a soft tissue sarcoma.



- Ionizing radiations*: exposure to ionizing radiations can increase the risk of soft tissue sarcomas even in the absence of other risk factors. Sarcomas* can rarely arise following exposure to radiation given to treat other cancers, like breast cancer or lymphoma*. In these cases the sarcoma* mostly starts in the area of the body that had been treated with radiation. The frequency increases with the treatment dose and decreases with age. The average time between radiation exposure and diagnosis of a sarcoma* is about 10 years. Radiation exposure is, however, a very rare cause of soft tissue sarcomas.
- Chemical agents: many chemical carcinogens* have been put forward as risk factors of soft tissue sarcoma, though few of these associations have been clearly established. There is an association between exposure to vinyl chloride* or arsenic and hepatic* angiosarcoma* (a type of soft tissue sarcoma) and between exposure to phenoxy herbicides* or dioxins* and soft tissue sarcoma in general. Occupational exposure carries the highest risk.

HOW ARE SOFT TISSUE SARCOMAS DIAGNOSED?

Sarcomas* often do not cause symptoms for a long time, until they become quite large and press on an organ, a nerve or a muscle. They may arise in any part of the body and the symptoms will depend on the part of the body that is affected. The main circumstance is when a lump appears on the leg, arm or trunk. They may also be found during an investigation of other symptoms or during a routine operation.

The diagnosis of sarcoma* is based on the following examinations:

- 1. Medical History and Clinical Examination.** Your doctor will begin by taking your complete medical history, asking when the symptoms began and how they have changed over time and check for risk factors. Your doctor will then perform a complete physical examination, including the area where there is the lump and/or pain. If the sarcoma* is in any part of arm or leg, the most common symptom is an uncomfortable swelling. Occasionally, this swelling may be painful or tender, but it may also be painless. If the sarcoma* is in the central part of the body (the trunk), the symptoms will depend on which organ is affected. For example a sarcoma* in lung may cause breathlessness and cough; a lump in abdomen could cause abdominal pain, vomiting and constipation; a sarcoma* affecting the womb could cause uterine bleeding and pain in the lower part of the abdomen, occurring outside of menstrual periods or after menopause*.



- 2. Blood Test.** A blood sample is performed to check your general health status, and to explore the function of the liver, kidneys and blood cells.
- 3. Radiological examination*.** A wide range of imaging techniques is used to look inside the body to determine the extent of a soft tissue sarcoma and establish the presence or absence of distant metastatic disease.



- **Chest X-ray*:** a plain chest X-ray could be done to determine whether the sarcoma* has spread to the lungs, as this is one of the most common sites it may spread to.
- **Ultrasonography:** a type of examination that uses sound waves and their echoes to create images from within the body. There are different kinds of ultrasound* scans depending on which part of the body is being examined and why. An external ultrasound* may be used to examine the liver, kidneys, and other organs in the abdomen and pelvis, or heart function. An ultrasound* probe* placed into vagina allows a doctor to look at the womb. Endoscopic Ultrasound Scan (EUS) uses a tube-like instrument called endoscope with an ultrasound scanner attached; it uses sound waves to produce pictures of abdominal organs.
- **CT scan*:** a Computerised Tomography scan is an X-ray* technique that produces detailed pictures of the inside of the body. You may be asked to drink a liquid called oral contrast and you may also receive an intravenous contrast dye to help the organs or tissues show up more clearly.



- **PET scan:** Positron Emission Tomography is mainly used to find out if the sarcoma* has spread to other parts of the body. It uses a substance that contains glucose*, which is injected into the patient. This radiolabeled* glucose-based substance is absorbed by cancerous cells which are less able to eliminate it than normal tissues so that it remains “trapped” in cancerous tissues. PET scans can also be used to examine the effect of the treatment on tumours.
- **MRI:** Magnetic Resonance Imaging uses magnetic fields and radio waves to create a series of detailed pictures of the tissue of the body. MRI is able to show more clearly soft tissues than other types of scan. It is often used for tumours of the limbs.
- **Bone scintigraphy:** a type of scan using a radiolabelled* substance to find out whether the sarcoma* has spread to the bones. The radiolabelled* substance travels to areas of bone changes, which appear brighter and indicates possible spread of the tumour.

4. Histopathological examination. Histopathologic* exam is made on a biopsy* or a piece of tissue after excision of the whole tumour by surgery. Only the histopathologic* assessment of the tumour will disclose whether the tumour is a soft tissue sarcoma, and the type of sarcoma*. It will also provide the “malignancy grade”*, i.e., a score of the aggressiveness of the cells making the tumour. Grades are explained in more details further in the text.

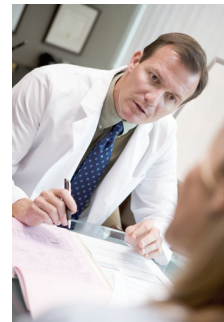
A biopsy* takes a sample of the tumour, which will be examined under a microscope to look for cancer cells. Different types of biopsies may be used: core needle biopsy, excisional biopsy and open biopsy.



- **Core needle biopsy:** a sample of cells or part of a lump is removed using a needle. Before the biopsy* is taken, a local anaesthetic* is injected to numb the area and several samples may be taken. If the lump is deep within the body the doctor may use an ultrasound* or a CT scan* to guide the needle into the right place.
- **Incisional / Excisional biopsy:** under anaesthesia*, a surgical knife is used to remove a tissue sample from the lump (“incisional”), or the entire tumour (“excisional”). This is the most practical option for rather small sarcomas* near the surface of the body (<5cm superficial lesions).
- **Open biopsy:** a surgical knife is used to open the area and remove a tissue sample from the lump or the entire tumour; it may be done under a local or general anaesthesia*, depending on the position and depth of the tumour.

WHAT IS IMPORTANT TO KNOW TO GET THE OPTIMAL TREATMENT?

Doctors will need to consider many aspects of both the patient and the cancer in order to decide on the best treatment.



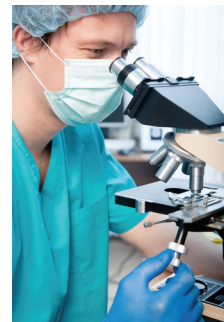
Relevant information about the patient

- General well-being
- Personal medical history
- History of cancer in relatives
- For women, status regarding menopause*, which in some cases requires taking a blood sample to measure the level of some hormones in the blood
- Results from the clinical examination by the doctor
- Results from blood tests performed to assess the white blood cells*, the red blood cells* and the platelets*, and tests performed to exclude any problems in the heart, liver, and kidneys.

Relevant information about the cancer

- **Results of the biopsy***

The sample of tumour obtained through biopsy* will be examined in the laboratory. This examination is called histopathology*. The second histopathological* examination involves the examination of the whole tumour after surgical removal. It is very important to confirm the results of the biopsy* and to provide more information on the cancer. Results of the examination of the biopsy* should include:



- **Histological type:** Soft tissue sarcomas include several dozen different histologic subtypes. It is strongly recommended that the examination of the biopsy* and of the tumour is done by an expert pathologist* from a reference centre. The most common sub-types of soft tissue sarcoma in adults include:
 - **Undifferentiated (or unclassified) pleomorphic soft tissue sarcoma***, although rare, it is the most frequent sarcoma* in adult life. It can arise in any part of the body but most commonly in the leg, especially in the thigh.
 - **Liposarcoma*** arises from cells storing the fat in deep soft tissue. It can occur in almost any part of the body, but more than half of liposarcoma* cases involve the thigh, and up to a third involve tissue in the abdomen.
 - **Leiomyosarcoma*** arises from cells in a type of muscle tissue called smooth muscle. Smooth muscles are found in the walls of organs like the heart and stomach, as well as in the walls of blood vessels. This means it can develop anywhere in the body, but most common places are the walls of the womb (uterus), the limbs, and the stomach.
 - **Synovial sarcoma*** usually occurs near to the main joints of the arms, legs, and neck.
 - **Malignant peripheral nerve sheath tumour (MPNST)*** arises from connective tissue surrounding the nerve. They are also called neurofibrosarcoma or malignant schwannoma*.

- **Angiosarcoma*** arises in the structures of the inner lining of blood vessels and can occur in any area of the body. Most commonly, it occurs in the skin, breast, liver, spleen, and deep tissue.
- **Solitary fibrous tumour (SFT)*** mostly involves the pleura*.
- **Dermatofibrosarcoma Protuberans (DFSP) *** develops in the deep layers of skin and is most commonly found on the torso, but also on the arms, legs, head and neck areas.
- **Desmoplastic small round cell tumour (DSRCT)*** occurs in adolescents and young adults and generally has an aggressive course. Clinical manifestations are often related to widespread abdominal disease.
- **Rhabdomyosarcoma*** arises from cells making the skeletal muscles, the muscles one can voluntarily control. However, rhabdomyosarcoma* can also start from cells making the muscles nearly anywhere in the body, even in parts/organs that normally lack skeletal muscles. The most common places for rhabdomyosarcoma* include the head, neck, bladder, vagina, arms, legs, and trunk of the body. Very rarely, rhabdomyosarcoma* develops in the prostate gland, in the middle ear, or in the bile ducts.

Desmoid tumours, also called deep or aggressive fibromatosis, are rare tumours which are not formally sarcomas*. They are usually grouped together with soft tissue sarcomas because they arise from fibroblasts, which are cells found throughout the body providing support and protection to organs such as lung, liver, blood vessels, heart, kidneys, skin, bowels etc. Desmoid tumours can arise in virtually any part of the body. Treatment principles for desmoid tumours are described in this guide for patients.*

- **Grade:** The grade of a tumour indicates how “aggressive” the tumour looks when analysed under a microscope by a doctor called a pathologist*. In soft tissue sarcomas, it considers how closely the tumour resembles normal tissue (differentiation), how many of the cells appear to be dividing (mitotic count*), and how much of the tumour is made up of dying tissue (necrosis*). The Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system is generally used, which distinguishes three malignancy grades based on differentiation, necrosis*, and mitotic rate*. Based on these 3 characteristics, tumours are classified into grade 1 (low), grade 2 (intermediate) and grade 3 (high) tumours. The lower the grade, the better the prognosis*.
- **Molecular profiling:** Additional information about the characteristics of the tumour may be asked. This relies on examination of structures (such as chromosomes or genes) and molecules (such as proteins) of the cells. These analyses may be performed either to confirm or clarify the histological type of soft tissue sarcoma, to provide additional information about the prognosis* of the disease, or to help making decision about the treatment, especially with regard to the use of targeted therapies*, therapies that work by binding to a specific protein or structure of the cells and thereby inhibiting their function.

- **Staging**

Doctors use staging to assess the extension of the cancer in the body, which is an important determinant of prognosis*. The most widely used staging system for soft tissue sarcomas is the TNM system. The combination of T, size of the tumour and invasion of nearby tissue, N, involvement of lymph nodes*, and M, metastasis* or spread of the cancer to other organ of the body, will classify the cancer into one of the following stages. For soft tissue sarcomas, the TNM staging takes also into account the malignancy grade (G), which in soft tissue sarcomas is a very important prognostic factor.

The stage is fundamental in order to make the right decision about the treatment. The lower the stage, the better the prognosis*.

The table below presents the different stages for soft tissue sarcomas. The definitions are somewhat technical, so that it is highly recommended to ask doctors for more detailed explanations.

Stage	Definition
Stage IA	<i>The tumour</i> <ul style="list-style-type: none"> - is categorised as grade 1; - is no more than 5 cm in its greatest dimension; - has not spread to lymph nodes* or to other parts of the body.
Stage IB	<i>The tumour</i> <ul style="list-style-type: none"> - is categorised as grade 1 - is more than 5 cm in its greatest dimension - has not spread to lymph nodes* or to other parts of the body.
Stage IIA	<i>The tumour</i> <ul style="list-style-type: none"> - is categorised as grade 2 or grade 3; - is no more than 5 cm in its greatest dimension; - has not spread to lymph nodes* or to other parts of the body.
Stage IIB	<i>The tumour</i> <ul style="list-style-type: none"> - is categorised as grade 2; - is more than 5 cm in its greatest dimension; - has not spread to lymph nodes* or to other parts of the body.
Stage III	<i>The tumour</i> <ul style="list-style-type: none"> - either is categorised as grade 3 and more than 5 cm in its greatest dimension but has not spread to lymph nodes* or to other parts of the body; - or has spread to lymph nodes*, irrespective of its size and grade.
Stage IV	<i>Irrespective of its size and grade, the tumour has spread to other part(s) of the body (metastasis*).</i>

WHAT ARE THE TREATMENT OPTIONS?

Planning of the treatment involves a multidisciplinary team* of medical professionals with a high level of experience in the management of these tumours (usually called reference or expert centres). This usually implies a meeting of different specialists, called multidisciplinary opinion* or tumour board review. In this meeting, the planning of treatment will be discussed according to the relevant information mentioned before.



The treatment will usually combine therapies that:

- Act on the cancer locally, such as surgery or radiotherapy*.
- Act on the cancer cells all over the body by systemic therapy*, such as chemotherapy*.

The extent of the treatment will depend on the stage of the sarcoma*, on the characteristics of the tumour and on the risks for the patient.

Treatments have their benefits, their risks and their contraindications*. It is recommended that patients ask their doctors about the expected benefits and risks of every treatment in order to be informed about the consequences of the treatment. For some treatments, several possibilities are available and the choice should be discussed according to the balance between benefits and risks.

Treatment plan for localised disease

Soft tissue sarcomas are localised when they are still confined to the primary site and have not spread to nearby tissues or to other areas of the body. At this stage, the main therapeutic goal is to remove the whole tumour by surgery whenever possible. Radiotherapy and chemotherapy* can also be used to increase the chance of definitive cure or to reduce the risk that the tumour comes back.*

Treatment for localised form of soft-tissue sarcomas includes therapy options that aim to act locally in the region affected by disease.

Surgery

Most frequently, surgery is the standard treatment method used for localised sarcoma*. As soft tissue sarcomas are rare, surgery should be performed by a surgeon who specialises in treating them. The goal of most sarcoma surgery is complete resection without leaving anything behind (microscopically negative margins*), thereby reducing the risk of local recurrence*.

The completeness of the surgical resection can be defined by several terms:

- "R0" resection means complete removal of all tumour according to the analysis of the tissue margins by microscope done by the pathologist*;
- "R1" resection indicates that the margins of the resected parts show presence of tumour cells when viewed microscopically;
- "R2" resection indicates a macroscopical residual disease (a portion of tumour visible to the naked eye).



Small sarcomas* can usually be effectively removed by surgery alone. R1 and R2 margins may need additional treatment by surgery; other options are to treat the resected margin containing tumour cells with radiation and possibly chemotherapy*.

Radiotherapy

High grade, deep seated tumours larger than 5 cm are often treated with a combination of surgery and radiation therapy; radiation therapy may be used before (neo-adjuvant) surgery (to shrink the tumour size and allow it to be removed completely) or after (adjuvant) surgery (to kill any remaining cancer cells); re-operation may be considered in case of positive margins*.



Chemotherapy

There is no consensus over the current role of chemotherapy* for patients who have a localised disease. Chemotherapy* may be considered alone or in combination with radiotherapy* before or after surgery in selected cases. It may especially be considered in these 2 situations:

- When the disease is considered to be at high risk of recurrence* (i.e. high grade, deep seated, > 5 cm). In this case, the goal is to reduce the risk of distant recurrence*, while possibly exerting a local benefit as well. In these cases, using regional hyperthermia together with chemotherapy* has been shown to extend survival without the disease coming back. Regional hyperthermia uses a machine placed around the area to be treated. The machine will heat the area for 60 minutes at a temperature of around 42°C. Heat kills tumour cells directly, increases efficacy of the chemotherapy drugs, and induces an immune response towards the tumour.
- When the disease is localised but cannot be resected at all or when the resection is incomplete because part of the tumour could not be removed (positive margins*). It may indeed not be possible to remove a tumour completely for several reasons, including its size or its location in an area considered as too risky for surgical removal (involvement of major blood vessels, nerves, etc.). It could also be because of other health conditions that could increase the risk of surgery

Today, it is rare to resort to amputations for limb sarcomas* because currently it is often possible to remove just the cancer and some of the tissues around it using a conservative approach, known as “limb-sparing” surgery, possibly with the contribution of other treatment modalities, including radiotherapy* and chemotherapy*.

In a few selected cases, a procedure known as isolated hyperthermic limb perfusion* can be proposed. It is a surgical technique aiming at injecting high-dose of chemotherapy* in the affected arm or leg, which has been previously heated to a temperature of about 41°C to make cancer cells more sensible to the effect of chemotherapy*. This technique requires temporary deviation of the blood circulation to and from the limb using surgery. With this technique, a high concentration of chemotherapy* can be obtained in the limb with very limited diffusion to the rest of the body. This model of therapy is complicated and is restricted to centres experienced in this technique.

Treatment plan for advanced disease

Soft tissue sarcomas are advanced when they have spread from where they started to other parts of the body. This is known as metastatic cancer. At this stage, the main therapeutic goal is to control it, leading to a better quality of life by improving symptoms.

There is no “one” advanced disease and deciding about the best treatment strategy requires careful consideration of the different options by a multidisciplinary team.

Occasionally, surgery may be considered in metastatic disease to relieve symptoms and to cure the cancer in some specific cases, mainly when lung metastases* are relatively few, slowly growing, and are not accompanied by extra-pulmonary lesions.

Radiotherapy* may also be given to relieve symptoms and control metastases*, in particular bone metastases.

However, the main treatment approach in case of advanced disease is the use of systemic therapy*, which includes both chemotherapy* and molecularly targeted therapy*. Each type of drug works differently, but all alter the way a cancer cell grows, divides and repairs itself.

Chemotherapy

Chemotherapy* is the mainstay of the treatment of advanced disease, as the drugs administered enter the bloodstream and reach cancer cells throughout the body. The most commonly chemotherapeutic drugs used in soft tissue sarcomas are doxorubicin* and other anthracyclines*, ifosfamide*, trabectedin*, gemcitabine*, docetaxel* and paclitaxel*.

These drugs can be given alone or in combination, and may be given as an outpatient* or as an inpatient* with admission to hospital for a few days. Chemotherapy* is given in cycles of treatment and the chemotherapy regimen usually consists of a number of cycles given over a set period of time: the number of cycles depend on the type, site and size of sarcoma* and how it is responding to the drugs.

Chemotherapy* in patients with advanced disease should be based on doxorubicin* or epirubicin* (both drugs belonging to the same ‘family’ and called anthracyclines*). In patients with angiosarcoma*, paclitaxel* (or docetaxel*) can be proposed in place of doxorubicin*.

Adding other drug(s) to doxorubicin* or epirubicin* can allow a greater shrinkage of the tumour in some patients. This choice primarily depends on the histological type of the cancer, as types known to be sensitive to chemotherapy will shrink more when a combination of drugs is used. In the majority of cases, ifosfamide* is preferred to be used in combination with doxorubicin or epirubicin*. Dacarbazine* combined with doxorubicin* is however preferred for patients with leiomyosarcoma* or solitary fibrous tumour*.



If the first chemotherapy* administered did not help, another chemotherapy* may be proposed even though the evidence for a benefit remains limited. The choice of the drug(s) will depend on the drug(s) already received as well as on the tumour histological type. Drugs that can be considered includes ifosfamide*, trabectedin*, gemcitabine*, docetaxel* and paclitaxel*.

Targeted therapy

Targeted therapy* may also be used. These therapies work by binding to a specific protein or structure involved in tumour growth and progression. Side effects are different from the side effects of the traditional chemotherapy*, and depend on the mechanism of action of the drug. The targeted drugs approved for the use in soft tissue sarcomas in Europe are:

- Pazopanib (in soft tissue sarcomas other than liposarcomas*)
- Imatinib* (in dermatofibrosarcoma, when it requires a systemic therapy*)

There is anecdotal evidence in favour of the use of other targeted therapies* for patients with some rare specific tumour types. It is recommended to ask doctors about these options.

Radiation therapy

Radiation therapy may be considered to relieve symptoms or prevent complications, for example in the case of bone metastases*.

Surgery

Surgery of metastases* may be considered depending on their location and on the history of the disease. For example, this would be the case when lung metastasis* appears a long time after initial treatment and when, the surgeon considers it can be completely removed.

Why are clinical trials important?

Clinical trials* try to find new treatments for cancer and find out if new cancer treatments are safe and effective or better than the standard treatment. Patients who take part in a clinical trial* may receive the standard treatment or be among the first to receive new therapy options. The purpose of clinical trials* also includes testing new ways to stop cancer from recurring, reducing the side effects of cancer treatment, and looking for better ways to prevent, screen or diagnose a tumour. Trials help to extend knowledge about cancer, improve current treatment and develop new treatments, now and for future patients. You are encouraged to ask whether there are any clinical trials* in which you could be enrolled.

Special clinical presentations and soft tissue sarcoma entities

The management of some very rare sarcomas* varies from the general management of the soft tissue sarcomas described until now. These differences are explained below.

Retroperitoneal sarcoma

Some sarcomas* arise in the retroperitoneum*, which is the space between the abdominal wall and the peritoneum - a membrane* that forms the lining of the abdominal cavity and covers most of the intra-abdominal organs. Retroperitoneal sarcomas* most commonly present as an abdominal mass and can grow very large without causing symptoms. The most common early symptoms leading to a discovery of a retroperitoneal sarcoma* are feeling full quicker than usual when eating, pain in the abdomen, bleeding, gastrointestinal obstruction*, or oedema* of the legs.

Special care should be taken for the diagnosis of retroperitoneal sarcomas*, especially in terms of imaging and ways of obtaining a sample of the tumour (biopsy*). For these reasons, it is crucial that these steps are undertaken in a centre with experience in soft tissue sarcomas and that results of the imaging and biopsy* are discussed by a multidisciplinary team.

Surgery is the standard treatment of a retroperitoneal sarcoma*. Resection of organs in the abdomen is often required and complete resection margins may be difficult to achieve due to the complexity of the anatomy in this part of the body. Administering chemotherapy*, radiotherapy*, regional hyperthermia or combinations before surgery may be considered after careful discussion, especially when it is expected that the treatment will reduce the size of the tumour and therefore allow a complete surgical resection.

Although not standard, chemotherapy* and radiotherapy* may also be considered after the operation but seems however of limited benefit in most patients.

Uterine sarcoma

Uterine sarcoma is a tumour in which malignant cells form in the muscles of the uterus or other connective tissues that support the uterus. Types of tumours include leiomyosarcomas*, endometrial stromal sarcomas* and undifferentiated* sarcoma, based on the type of cell from which they originally developed. Carcinosarcomas (also called malignant müllerian mixed tumours) are currently considered as cancer originating from epithelial tissue and are treated as endometrial cancers. Common symptoms are pain or feeling of pressure in the pelvis, and unusual or postmenopausal bleeding. Standard treatment for localised uterine sarcoma is surgery, which can include removal of the uterus and the cervix. It is not clear if removing both ovaries and both fallopian tubes* has any benefit. Other approaches may include radiotherapy*, chemotherapy*, hormonal therapy*, and simple observation with no additional intervention. The choice of the best approach depends on the specific subtype of uterine sarcoma, on the grade and on the extent of the disease.

Desmoid-type fibromatosis

Desmoid tumour (also called deep or aggressive fibromatosis*) arises from fibroblasts*, a type of cells that play a critical role in wound healing and in the structure of vital organs. Desmoid tumours can develop in any part of the body. Superficial desmoid tumours usually present as a painless or slightly painful lump whereas desmoid tumours inside the abdomen can cause severe pain, rupture or compression of organs, or bleeding.

Desmoid tumours can be indolent* and have periods of stability and temporary regression or can be extremely aggressive. They never metastasise* and if slow growing they need to be carefully watched by a medical oncologist*.

Given the very slow growth of these tumours, a watchful waiting* strategy may be the best option. In case of progression of the tumour, optimal treatment may consist of surgery, radiation therapy, chemotherapy*, or hormonal therapy*.

Breast sarcoma

Breast sarcomas arise from the connective tissue* within the breast. They can be primary or secondary tumours. Primary tumours develop with no clear cause whereas secondary tumours develop after radiotherapy* or as a consequence of chronic lymphoedema* of the arm or of the breast after treatment for another malignancy. A specific type of breast sarcoma is angiosarcoma*, which develops in the blood vessels or lymph vessels. Angiosarcomas* are usually more aggressive than the other types of breast sarcomas such as phyllodes tumours and carcinosarcomas.

Patients with breast sarcoma should be treated in centres with experience in breast sarcomas. Surgery is the most important treatment option for breast sarcomas. The type of surgery may include wide local excision* or mastectomy (surgery to remove the whole breast). The wide excision, which may be considered for smaller, low-grade breast sarcomas, removes the tumour and extra tissues to help reduce the chance of recurrence*. Radiation therapy or chemotherapy* may be recommended if the tumour is very large or is known to have spread outside of the breast or to reduce the risk of spreading.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF THE TREATMENTS?

Risks and side effects of surgery

General risk of surgery

Minor surgery and biopsies usually pose less risk than major surgery: pain, infections at the site of surgery and reaction to the local anaesthesia* are possible.

Risks in major surgical interventions are shared by all surgical interventions performed under general anaesthesia*. These complications are infrequent and include deep vein thrombosis, heart or breathing problems, bleeding, infection, or reaction to the anaesthesia*. Although there are risks, doctors will take the most appropriate steps to minimise them. Before any surgery, you should be clearly and carefully informed by the hospital about the risks.



Resection* of a tumour in the arm or leg

After your operation you may have a tube in the wound to remove any fluid that collects in the area of the operation; the drainage tube will be removed once fluid has stopped draining. Immediately after surgery, your pain will usually be controlled either by an epidural or an intravenous* continuous dose of painkillers administered with the aid of an electronic pump.

The consequences of the surgical resection depend on the extent of the resection. It is not always possible to preserve the entire limb and occasionally amputation of a part of the limb may be necessary.

- Some people have a pain that appears to come from the part of the limb that has been amputated, known as phantom pain. It can be difficult to treat phantom limb pain* and several types of treatment may be needed: anticonvulsants*, antidepressants* and opioids* can help relieve pain from nerve damage or to attempt to block pain signals.
- Rehabilitation begins shortly after surgery. The goal of rehabilitation is to help the patient return to the maximum level of function and independence possible, while improving the overall quality of life, physically, emotionally, and socially. The physiotherapist* will show you how to do exercises to strengthen the trunk, arm, and leg muscles in order to prepare the remaining part of the limb for use of an artificial limb, called a prosthesis.



Resection* of a tumour in the abdomen

Surgery of soft tissue sarcomas located within the abdomen may involve the removal of other organs or tissues (i.e. the kidney, the spleen, the pancreas, or part of the bowel). Your doctor should help you to find out how the treatment will influence daily life.

Risks and side effects of radiotherapy

During radiotherapy*, side effects may occur in organs that are directly targeted, but also in healthy organs that lie close to the region irradiated. Side effects may be more intense when radiotherapy* is administered together with chemotherapy*. Radiotherapy* in addition to surgery may also increase the risk of surgical complications and may cause problems with wound healing. Major improvements in radiotherapy* techniques and machines have been made during the last decades and severe side effects are now very rare.

Most side effects of radiotherapy* disappear gradually once the course of treatment has ended. For some people, however, they may continue for weeks or even longer. The radiotherapist team will support you during this treatment period.



Immediate side effects

Since radiotherapy* is a local treatment, its side effects are local too. The most frequent general side effects of radiotherapy* are:

- Skin reaction (redness, soreness or/and itchiness) after three to four weeks of having external radiotherapy, but they usually settle down two to four weeks after the treatment has finished. However, the treated area may remain slightly more pigmented than the surrounding skin.
- Dysphagia or difficulty to swallow due to inflammation of the oesophagus is frequent during radiotherapy* directed to the neck or chest areas.
- Nausea and vomiting, diarrhoea: some people find that their treatment makes them feel sick; this is most common when the treatment area is near the stomach or bowel.
- Hair loss can occur when the head is irradiated.
- Fatigue: this is a common side effect and may continue for some time after treatment finishes.
- Sore mouth and oral mucositis*: your mouth may become sore or dry, or you may notice small ulcers during this treatment; this is common when the treatment area is near the oral cavity. It's very important to keep the oral mucosa* well hydrated and your teeth clean during the course of the entire treatment.

Long-term side effects

It is rare to develop severe, long-term side effects after radiotherapy*. However, long-term side effects can greatly affect the quality of life in some patients. Some possible long-term side effects are:

- Long-term changes to the skin;
- Occurrence of lymphoedema*, a swelling that occurs when the lymph nodes* and vessels are damaged by the radiotherapy*;
- Bowel incontinence*, bladder incontinence*, infertility* and early menopause* in women when pelvis is irradiated. If there is a risk of infertility following radiotherapy*, your doctor will discuss all the options with you and suggest available support before your treatment. It may be possible for men to store sperm and women to store eggs for use in the future;
- Neuropathic pain when major nerves are present in the radiated field.

Radiotherapy* is associated with a slightly increased risk of developing a second tumour many years after the treatment. To reduce the risk, the type and the dose of the radiation therapy will be carefully planned.

Risks and side effects of chemotherapy

Side effects of chemotherapy* are frequent, even if progress has been made in managing them using adequate supportive measures. They will depend on the drugs administered, on the doses, and on individual factors. If a patient has suffered from other medical problems in the past, some precautions should be taken and/or adaptation of the treatment should be made. Please tell your health care team about your previous experiences.

Listed below are the side effects that are known to occur with one or several of the chemotherapy drugs currently used for sarcomas*. The nature, frequency and severity of the side effects vary for every chemotherapeutic drug combination used.

The most frequent general side effects of chemotherapy* are:

- Risk of infection: chemotherapy* works by interfering with the cell's ability to grow or reproduce and can reduce the number of white blood cells*, which help fight infection, a condition known as neutropenia*. A blood test will be performed before having chemotherapy* to check the number of white blood cells*.
- Bleeding: chemotherapy* can reduce the number of platelets*, which helps the blood to clot. Sometimes a platelet transfusion is needed if your platelet* count is low.
- Anaemia*: chemotherapy* can reduce the number of red blood cells*, this may make you feel tired and breathless. A blood transfusion may be needed if your red blood cells count is low.
- Nausea and vomiting: effective antiemetic drugs* can be used to prevent, or reduce them.
- Sore mouth: your mouth may become sore or dry, or you may notice small ulcers during treatment. Drinking plenty of fluids and cleaning your teeth regularly can help to reduce the risk of ulcers or mucositis*.
- Hair loss: not all chemotherapy drugs cause hair loss; hair may be lost completely or may just thin. If your hair does fall out, it will almost always grow back over a period of 3-6 months once the chemotherapy* has finished.
- Fatigue: feeling tired is a common side effect of chemotherapy*.
- Fertility: as there is a risk of infertility, your doctor will discuss with you all the options and available support before your treatment.

A local reaction may happen at place of insertion into the vein but also the local tissue might be damaged if drug leaks from the vein.

More specific side effects may occur depending on the specific chemotherapy* drugs used. Not all available chemotherapy drugs will be used during the course of your disease. The choice will depend on the type of soft-tissue sarcoma and therefore, a profile of side effects will depend on specific drug(s) used. It is important that the health care team inform you upfront about the specific side effects that could be expected from the drugs you will receive.

- For instance, with doxorubicin* and epirubicin*, urine may turn red or orange for a few days after treatment. It is important to know as this is not blood and is only due to the colour of the medication and should therefore not worry you.
- Doxorubicin* and epirubicin* can cause damage to the heart muscle, therefore the assessment of heart function is important before therapy with these two drugs; the chance of heart problems depends on the dose of this drug and the patient's condition. Heart problems may happen even if the patient does not have any risk factors. These drugs can make the skin more sensitive to sunlight and cause redness in areas where the patient has had radiotherapy* in the past. The urine may turn red or orange for a few days after treatment. This is not blood and is only due to the colour of the medication.
- Ifosfamide* may cause kidney problems in some patients with blood in the urine and bladder pain. In some cases, it may also cause neurotoxicity* with sleepiness, hallucinations, and confusion.
- Docetaxel* may cause swelling or fluid retention. It can sometimes cause temporary nail discoloration and an itchy skin rash. Severe allergic reactions are possible with docetaxel* during the first or second infusion.
- Gemcitabine* may cause lung problems with trouble breathing, which can happen up to two weeks after discontinuation of the drug. Gemcitabine* may cause flu-like symptoms such as feeling hot or cold and/or shivery and having a headache.
- Vinorelbine* may cause numbness or tingling in the fingers or toes, a condition known as peripheral neuropathy.
- Vincristine* may cause constipation or abdominal cramping, numbness or tingling in the fingers or toes.
- Dacarbazine* may cause an alteration of liver function. Dacarbazine* may irritate the vein and may burn the skin if the drug leaks from the vein when it is given; tell your doctor if you have any redness, burning, pain, swelling, or leaking of fluid where the drug is going into your body.
- Cisplatin* can cause damage to the kidneys. Therefore, blood tests will be done before and during treatment to check renal function. Extra fluids through a drip before and after chemotherapy* will be given intravenously* to help protect your kidneys.
- Cyclophosphamide* may cause bladder damage with bladder irritation causing discomfort when passing urine. Treatment can affect kidneys and liver functions but this is usually mild and goes back to normal after treatment. At high doses, cyclophosphamide* can cause damage to the lungs or the heart. Development of a second cancer is a rare side effect.
- Trabectedin* may cause tissue damage if the drug leaks from the vein. It may also affect liver and kidneys functions and sometimes cause pain in the joints or muscles for a few days after chemotherapy*. Another potential side effect is deep vein thrombosis*.

Tell your doctor about the symptoms you experienced, like rash, itching, shortness of breath, wheezing, cough, swelling of face, lips, tongue, throat, or any other signs.

Risks and side effects of targeted therapy

Pazopanib* and imatinib* are the only targeted therapies* approved for the medical treatment of soft tissue sarcomas.

The main side effects of pazopanib* include oedema* (legs, arms, and face), wound healing problems, high blood pressure, diarrhoea, fatigue, abnormal liver function (often noticed by elevation of liver enzymes measured on blood tests), coagulation disorders (bleeding and clotting) and hair modification.

Imatinib* may cause dizziness, diarrhoea, nausea and vomiting, muscle cramps, bleeding problems, blurred vision, oedema*, most frequently around the eyes or in the legs and numbness or tingling in the hands, feet, or lips. Imatinib* can also cause neutropenia*, reducing the number of white blood cells*, which help to fight infections.

Most of these side effects can be treated with appropriate medications or dose adjustments; therefore it is very important to tell your doctor about any discomfort you feel.

HOW CAN PATIENT SUPPORT GROUPS HELP?

By Markus Wartenberg of the Sarcoma Patients EuroNet Association (www.sarcoma-patients.eu)

The day of the diagnosis. Whether it is a patient in the doctor's office, or a carer to hold a family member's hand or comfort a friend, a sarcoma diagnosis is a new, unplanned, and scary experience. Suddenly, there is a great deal to learn, understand, and cope with. But fortunately patients and caregivers are often not alone. There are people in the same situation who have never heard the word "sarcoma" before, who know what it's like to seek answers, to wait for results, to finally find THE right sarcoma expert, or to have to decide between therapy options.



In some European countries, patients with Sarcomas came together and founded patient support and advocacy groups. Mostly these are not-for-profit organisations founded by patients and their relatives - for patients. Their mission is to work together with leading sarcoma experts, the research industry, health insurance, other patient groups and other representatives of the healthcare system to optimize information, treatment and research situations for patients with a sarcoma, a GIST, a desmoid tumour or a specific type of bone cancer. The most important areas of their work are:

- Improving the patient's level of information and competence (help them to help themselves)
- Securing access to innovative therapies and improving the quality of treatment
- Supporting sarcoma research
- Advocating in the national health policy environment

Meanwhile, numerous studies show that timely treatment in interdisciplinary sarcoma centres significantly improves the results and prognoses among many patients. Hence, the international treatment guidelines (ESMO and NCCN) and the European sarcoma patients' organisations, which maintain that sarcoma - on account of its rarity - should be treated by experienced doctors and centres.

Unfortunately many patients with soft tissue sarcoma, spend a lot of time lost in the health-care system before getting in contact with experienced sarcoma experts. This much is painfully clear: had they been informed earlier of the existence of sarcoma centres, or if their doctors had referred them to these experts, their disease would have been diagnosed earlier, and they would have received better treatment. Several patients would have better prognoses today.

If a soft tissue sarcoma is suspected or concretely diagnosed, it may be useful to get a second opinion from another doctor before embarking on surgery or long-term, extensive treatment. In addition, it never hurts to seek independent, secondary findings, such as in an experienced sarcoma centre, if the patient has reasonable doubts about the initial diagnosis and/or does not feel well-advised. A second opinion can exclude the possibility of misdiagnoses, check over therapy options, and possibly introduce new/different treatment methods. Sarcoma patient support groups are very experienced when it comes to the national sarcoma expert landscape. They know very well where the sarcoma experts/centres are located in a country and they can help patients to find the best support for a second opinion, a very rare sarcoma subtype, for a special treatment option or a clinical study.

If a patient would like more information about her/his situation, or just needs someone to talk to, it could be extremely valuable to get in touch with a national sarcoma patient support group.

For a list of sarcoma support groups and charities in different countries, visit the Sarcoma Patients EuroNet Association's group locator page at <http://www.sarcoma-patients.eu>.

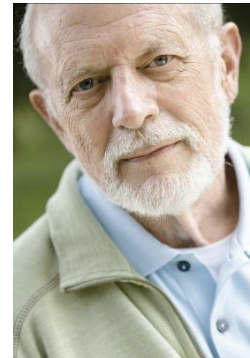
WHAT HAPPENS AFTER THE TREATMENT?

Follow-up with doctors

Regardless of the goal of the therapy, after treatment, you will have regular follow-up appointments for several years. The usual practice will include a physical examination to look for any signs of cancer recurrence*, and blood tests to check your general conditions and possible treatment side effects. Depending on primary localisation and sarcoma* type, your doctor may ask for radiological examination* of that area, as well as of areas where it can come back. This appointment is an important moment for you to talk about any new symptoms or changes you notice and any questions or problems you have.

At first, the appointments will be every few months. They will gradually become less frequent and the gap between them will get longer because the risk of the cancer coming back gets steadily lower over time. Generally, in high-risk soft tissue sarcomas it is expected that the recurrence* appear in the first two to three years after treatment; low-risk sarcomas may relapse later, with lower odds.

The routine follow up depends on tumour grade, tumour size and tumour site. The optimal time schedule for routine follow-up is unknown, however the routine follow up after treatment for intermediate or high grade soft tissue sarcoma is more intensive than for low grade sarcoma*.



Returning to normal life

Returning back to normal life is one of the main objectives in the treatment of soft tissue sarcomas. You are encouraged to tell your doctor about any worries, troubles or feelings about going home, or back to work or school. Make sure you discuss them with the health care team in advance so that help can be organised. Some patients may also find support from ex-patient groups or patient-targeted information media; additional expert psychological advice may be very useful.

What if the cancer comes back?

Soft tissue sarcomas can come back in the same area as the initial tumour. This is called a local recurrence*. Patients with an isolated local recurrence* may be offered surgery again to resect the tumour, but may also receive additional treatment.

Soft tissue sarcomas can also come back in organs and parts of the body other than the initial site. This process is called metastasis*. In sarcoma* patients, metastases mainly occur in the lungs, bone and liver. Since metastases*, especially at early stage when they can be resected, may not cause any symptom, your doctor will pay specific attention to these sites during the follow-up. In patients previously treated with systemic drugs*, further treatment lines with chemotherapy* or targeted therapy* may be considered.

Radiotherapy* may be applied to relieve symptoms or prevent complications related to the tumour. It is important that every tumour recurrence* is evaluated by a multidisciplinary expert team*, to select the most appropriate treatment modality or the most appropriate combination of treatments.

It may also happen, as a late effect of some therapies used for soft tissue sarcomas, that a new – secondary cancer appears. In case of suspicion for secondary cancer, your doctor will order a set of examinations to analyse the type of secondary cancer and its extent. Most appropriate options for management should be discussed within a multidisciplinary team*, taking into consideration the previous treatments applied for soft tissue sarcoma.

DEFINITIONS OF MEDICAL TERMS

Acoustic nerve

A nerve involved in hearing, balance, and head position. It has two branches, a cochlear branch that transmits sounds for hearing and a vestibular branch that senses balance and head position. Also known as the vestibulocochlear nerve.

Anaemia

Condition characterized by the shortage of red blood cells* or haemoglobin, the iron that carries oxygen from the lungs to the whole body; this process is diminished in this condition

Anaesthesia

Reversible state of loss of awareness in which the patient feels no pain, has no normal reflexes, and responds less to stress, induced artificially by the employment of certain substances known as anaesthetics. It can be complete or partial and allows patients to undergo surgery or other invasive procedures.

Angiosarcoma

A type of cancer that begins in the cells that line blood vessels or lymph vessels. Cancer that begins in blood vessels is called hemangiosarcoma. Cancer that begins in lymph vessels is called lymphangiosarcoma.

Anthracyclines

Antibiotic drug used in chemotherapy* to treat a wide range of cancers.

Anticonvulsant

A drug or other substance used to prevent or stop seizures or convulsions. Also called antiepileptic.

Antidepressant

A drug used to treat depression.

Antiemetic drug

An agent that prevents or reduces nausea and vomiting that may be associated with anticancer therapies. Antiemetic drugs include granisetron, metoclopramide, and ondansetron.

APC (adenomatous polyposis coli) gene

It is a tumour suppressor gene. Mutation in that gene may result in colorectal cancer.

Basal cell nevus syndrome

A genetic condition that causes unusual facial features and disorders of the skin, bones, nervous system, eyes, and endocrine glands. People with this syndrome have a higher risk of basal cell carcinoma of the skin. Also called Gorlin syndrome and nevoid basal cell carcinoma syndrome.

Benign tumour

Not cancerous. Benign tumours may grow larger, but do not spread to other parts of the body. Also called non-malignant.

Biopsy

The removal of cells or tissues for examination by a pathologist*. The pathologist* may study the tissue under a microscope or perform other tests on the cells or tissue. There are many different types of biopsy procedures. The most common types include: (1) incisional biopsy, in which only a sample of tissue is removed; (2) excisional biopsy, in which an entire lump or suspicious area is removed; and (3) needle biopsy, in which a sample of tissue or fluid is removed with a needle. When a wide needle is used, the procedure is called a core biopsy. When a thin needle is used, the procedure is called a fine-needle aspiration biopsy.

Bladder incontinence

Inability to control the flow of urine from the bladder (also called urinary incontinence).

Bowel incontinence

Inability to control the escape of stool from the rectum (fecal incontinence).

Café-au-lait spot

A flat light-brown color spot on the skin. Café au lait is French for "coffee with milk" and refers to the color of the spot.

Carcinogen

A substance that can cause cancer.

Chemotherapy

A type of cancer treatment using drugs that kill cancer cells and/or limit their growth. These drugs are usually administered to the patient by slow infusion into a vein but can also be administered orally, by direct infusion to the limb or by infusion to the liver, according to cancer location.

Cisplatin

A drug used to treat many types of cancer. Cisplatin contains the metal platinum. It kills cancer cells by damaging their DNA and stopping them from dividing. Cisplatin is a type of alkylating agent.

Clinical trial

A research study conducted with patients to evaluate whether a new treatment is safe (safety) and whether it works (efficacy). Clinical trials are performed to test the efficacy of drugs but also non-drug treatments such as radiotherapy* or surgery and combinations of different treatments.

Contraindication

Condition or symptom that prevents the administration of a given treatment or procedure to the patient. Contraindications are either absolute, meaning the treatment should never be given to patients with this condition or symptom, or relative, meaning that the risk can be outweighed by the benefits in some patients with this condition or symptom.

CT scan/ Computed Tomography scan

A form of radiography in which body organs are scanned with X-rays* and the results are synthesized by a computer to generate images of parts of the body.

Cyclophosphamide

A drug that is used to treat many types of cancer and is being studied in the treatment of other types of cancer. It is also used to treat some types of kidney disease in children. Cyclophosphamide attaches to DNA in cells and may kill cancer cells. It is a type of alkylating agent.

Dacarbazine

A drug that is used to treat Hodgkin lymphoma* and malignant melanoma and is being studied in the treatment of other types of cancer. It attaches to DNA in cells and may kill cancer cells. It is a type of alkylating agent.

Deep vein thrombosis

The formation of a blood clot in a deep vein of the leg or lower pelvis or upper extremity. Symptoms may include pain, swelling, warmth, and redness in the affected area. Also called DVT.

Dioxin

By-products of various industrial processes known to be highly toxic.

Docetaxel

Docetaxel belongs to the group of anticancer medicines known as the taxanes*. Docetaxel prevents cells from destroying the internal 'skeleton' that allows them to divide and multiply. With the skeleton still in place, the cells cannot divide and they eventually die. Docetaxel also affects non-cancer cells such as blood cells, which can cause side-effects.

Doxorubicin

A drug that is used to treat many types of cancer and is being studied in the treatment of other types of cancer. Doxorubicin comes from the bacterium *Streptomyces peucetius*. It damages DNA and may kill cancer cells. It is a type of anthracycline antitumour antibiotic. Also called doxorubicin hydrochloride and hydroxydaunorubicin.

Endometrial stromal sarcoma

A type of sarcoma arising from tissue in the uterus

Epidermal cyst

A closed, sac-like pocket of tissue that formed in the epidermis, the outer layer of the two main layers of the skin. It may be filled with fluid, air, pus, or other material. Most cysts are benign (not cancer).

Epirubicin

A drug used together with other drugs to treat early breast cancer that has spread to lymph nodes*. It is also being studied in the treatment of other types of cancer. Epirubicin is a type of anthracycline antibiotic.

Fallopian tubes

A slender tube through which eggs pass from an ovary to the uterus. In the female reproductive tract, there is one ovary and one fallopian tube on each side of the uterus.

Fibroblast

A connective tissue cell that makes and secretes collagen proteins.

Fibroma

A benign tumour*, usually in the uterus or gastrointestinal tract.

Fibromatosis

A condition in which multiple fibromas develop. Fibromas are benign tumours that affect connective tissue.

Gastrointestinal obstruction

Blockage in the stomach or intestines.

Gastrointestinal stromal tumours (GIST)

A type of tumour that usually begins in cells in the wall of the gastrointestinal tract. It can be benign or malignant.

Gemcitabine

The active ingredient in a drug that is used to treat pancreatic cancer that is advanced or has spread. It is also used with other drugs to treat breast cancer that has spread, advanced ovarian cancer, and non-small cell lung cancer that is advanced or has spread. It is also being studied in the treatment of other types of cancer. Gemcitabine blocks the cell from making DNA and may kill cancer cells. It is a type of antimetabolite.

Glioma

A cancer of the brain that begins in glial cells (cells that surround and support nerve cells).

Glucose

Glucose is a monosaccharide sugar that occurs widely in plant and animal tissue. It is the major energy source of the body.

Hepatic

Hepatic refers to the liver. A hepatic vein is a vein that drains blood away from the liver; a hepatic disease is a disease that affects the liver.

Histopathologic/histopathology

The examination and study of tissue and cells using a microscope. Tissue obtained from the body by biopsy or surgery is placed in a fixative and transported to the laboratory. Here, it is cut into thin sections, stained with various dyes and then studied under the microscope.

Hormonal therapy

The use of hormones as medical treatment.

Ifosfamide

A drug that is used with other drugs to treat germ cell testicular cancer that did not respond to previous treatment with other drugs. It is also being studied in the treatment of other types of cancer. Ifosfamide attaches to DNA in cells and may kill cancer cells. It is a type of alkylating agent and a type of antimetabolite.

Imatinib

Imatinib is a protein-tyrosine kinase inhibitor. This means that it blocks some specific enzymes known as tyrosine kinases. These enzymes can be found in some receptors on the surface of cancer cells, including the receptors that are involved in stimulating the cells to divide uncontrollably. By blocking these receptors, imatinib helps to control cell division.

Indolent (tumour)

A type of cancer that grows slowly.

Inpatient

A patient whose care requires a stay in a hospital. As opposed to an outpatient*.

Intravenous(ly)

Into or within a vein. Intravenous usually refers to a way of giving a drug or other substance through a needle or tube inserted into a vein. Also called IV.

Ionizing radiation

A type of radiation made (or given off) by x-ray* procedures, radioactive substances, rays that enter the Earth's atmosphere from outer space, and other sources. At high doses, ionizing radiation increases chemical activity inside cells and can lead to health risks, including cancer.

Isolated hyperthermic limb perfusion*

A procedure that may be used to deliver a warmed solution containing anticancer drugs directly to an arm or leg. The flow of blood to and from the limb is temporarily stopped with a tourniquet (a tight band around the limb), and anticancer drugs are put directly into the blood of the limb. This allows the person to receive a high dose of drugs in the area where the cancer occurred. Also called limb perfusion.

Kaposi sarcoma

A type of cancer in which lesions (abnormal areas) grow in the skin, lymph nodes*, lining of the mouth, nose, throat, and other tissues of the body. The lesions are usually purple and are made of cancer cells, new blood vessels, and blood cells. They may begin in more than one place in the body at the same time. Kaposi sarcoma is caused by Kaposi sarcoma-associated herpesvirus (KSHV). In Western countries, it usually occurs in people who have a weak immune system caused by AIDS or by drugs used in organ transplants. It is also seen in older men of Jewish or Mediterranean descent, or in young men in Africa.

Leiomyosarcoma

A malignant (cancer) tumour of smooth muscle cells that can arise almost anywhere in the body, but is most common in the uterus, abdomen, or pelvis.

Liposarcoma

A rare cancer of the fat cells.

Local excision

A surgical procedure to remove a small area of diseased or problematic tissue with a margin of normal tissue. This procedure is commonly performed on the breast and to skin lesions, but can be used on any area of the body.

Lymph nodes

A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph and they store lymphocytes. They are located along lymphatic vessels. Also called lymph gland.

Lymphoedema

A condition in which extra lymph fluid builds up in tissues and causes swelling. It may occur in an arm or leg if lymph vessels are blocked, damaged, or removed by surgery.

Lymphoma

Cancer that begins in cells of the immune system. There are two basic categories of lymphomas. One kind is Hodgkin lymphoma, which is marked by the presence of a type of cell called Reed-Sternberg cell. The other category is non-Hodgkin lymphomas, which includes a large, diverse group of cancers of immune system cells. Non-Hodgkin lymphomas can be further divided into cancers that have an indolent (slow-growing) course and those that have an aggressive (fast-growing) course. These subtypes behave and respond to treatment differently. Both Hodgkin and non-Hodgkin lymphomas can occur in children and adults, and prognosis* and treatment depend on the stage and the type of cancer.

Medical oncologist

A doctor who specializes in diagnosing and treating cancer using chemotherapy*, hormonal therapy, biological therapy, and targeted therapy. A medical oncologist often is the main health care provider for someone who has cancer. A medical oncologist also gives supportive care and may coordinate treatment given by other specialists

Membrane

In biology, a membrane can define (1) a layer within a cell that encloses different internal structures, (2) a layer around a cell that separates the cell from its surrounding, (3) a layer of cells that separate one tissue from another (like basement membrane and mucosa).

Meningioma

A type of slow-growing tumour that forms in the meninges (thin layers of tissue that cover and protect the brain and spinal cord). Meningiomas usually occur in adults.

Menopause

The time of life when a woman's ovaries stop producing hormones and menstrual periods stop. Natural menopause usually occurs around age 50. A woman is said to be in menopause when she hasn't had a period for 12 months in a row. Symptoms of menopause include hot flashes, mood swings, night sweats, vaginal dryness, trouble concentrating, and infertility.

Metastasis

The spread of cancer from one part of the body to another. A tumour formed by cells that have spread is called a metastatic tumour or a metastasis. The metastatic tumour contains cells that are like those in the original tumour.

Mitotic count/rate

A measure of how fast cancer cells are dividing and growing. To find the mitotic rate, the number of cells dividing in a certain amount of cancer tissue is counted. Mitotic rate is used to help find the stage of melanoma (a type of skin cancer) and other types of cancer. Higher mitotic rates are linked with lower survival rates.

Mucositis

A complication of some cancer therapies in which the lining of the digestive system becomes inflamed. Often seen as sores in the mouth.

Multimodal treatment

Therapy that combines more than one method of treatment. Also called combination therapy and multimodality therapy.

Mutation

A change in the sequence of base pairs in the DNA that makes up a gene. Mutations in a gene do not necessarily change the gene permanently.

Necrosis

Refers to the death of living tissues.

Negative margin

The edge or border of the tissue removed in cancer surgery. The margin is described as negative or clean when the pathologist* finds no cancer cells at the edge of the tissue, suggesting that all of the cancer has been removed. The margin is described as positive or involved when the pathologist finds cancer cells at the edge of the tissue, suggesting that all of the cancer has not been removed.

Neurofibroma

A benign tumour that develops from the cells and tissues that cover nerves.

Neurotoxicity

The tendency of some treatments to cause damage to the nervous system.

Neutropenia

A condition in which there is a lower-than-normal number of neutrophils, a type of white blood cell*. It may be seen with viral infections and after radiation and chemotherapy*. It lowers the immunologic barrier to bacterial and fungal infections.

NF1 gene

A gene responsible for making a protein called neurofibromin. This protein is produced in many types of cells, including nerve cells and specialized cells called oligodendrocytes and Schwann cells that surround nerves.

Oedema

An abnormal collection of fluid beneath the skin or in a body cavity.

Opioid

A substance used to treat moderate to severe pain. Opioids are like opiates, such as morphine and codeine, but are not made from opium. Opioids bind to opioid receptors in the central nervous system. Opioids used to be called narcotics. An opioid is a type of alkaloid.

Oral mucosa

The moist, inner lining of the mouth. Glands in the mucosa make mucus (a thick, slippery fluid). Also called mucous membrane.

Oral mucositis

A complication of some cancer therapies in which the lining of the digestive system becomes inflamed. Often seen as sores in the mouth.

Orthopaedists

A surgeon who specializes in diagnosing and treating injuries and diseases of the musculoskeletal system. This includes the bones, joints, tendons, ligaments, and muscles.

Osteoma

An osteoma is a new piece of bone usually growing on another piece of bone, typically the skull. It is a benign tumour.

Osteosarcoma

A cancer of the bone that usually affects the large bones of the arm or leg. It occurs most commonly in young people and affects more males than females. Also called osteogenic sarcoma.

Outpatient

A patient who visits a health care facility for diagnosis or treatment without spending the night. Sometimes called a day patient.

Paclitaxel

A drug used to treat breast cancer, ovarian cancer, and AIDS-related Kaposi sarcoma*. It is also used together with another drug to treat non-small cell lung cancer. Paclitaxel is also being studied in the treatment of other types of cancer. It blocks cell growth by stopping cell division and may kill cancer cells. It is a type of antimitotic agent.

Paediatric oncologist

A doctor who specializes in treating children with cancer.

Pathologist

A doctor specialized in histopathology* which is the study of diseased cells and tissues using a microscope.

Pazopanib

A drug used to treat advanced renal cell carcinoma, which is the most common type of kidney cancer. It is also used to treat advanced soft tissue sarcoma that has been treated with other anticancer drugs. It is being studied in the treatment of other types of cancer. Pazopanib hydrochloride may prevent the growth of new blood vessels that tumours need to grow. It is a type of protein tyrosine kinase inhibitor and a type of antiangiogenesis agent.

Peripheral nerve sheath tumours (MPNST)

A type of soft tissue sarcoma that develops in cells that form a protective sheath (covering) around peripheral nerves, which are nerves that are outside of the central nervous system (brain and spinal cord). Also called malignant peripheral nerve sheath tumour.

Phantom limb pain

The sensation of pain or other unpleasant feelings in the place of a missing (phantom) limb.

Phenoxy herbicides

A phenoxy herbicide is any member of a family of chemicals related to the growth hormone indoleacetic acid (IAA). When sprayed on broad-leaf plants they induce rapid, uncontrolled growth, eventually killing them.

Physiotherapist

A health professional trained to evaluate and treat people who have conditions or injuries that limit their ability to move and do physical activities. Physical therapists use methods such as exercise, massage, hot packs, ice, and electrical stimulation to help strengthen muscles, relieve pain, and improve movement. They also teach exercises to help prevent injury and loss of motion.

Pleura

A thin layer of tissue that covers the lungs and lines the interior wall of the chest cavity. It protects and cushions the lungs. This tissue secretes a small amount of fluid that acts as a lubricant, allowing the lungs to move smoothly in the chest cavity while breathing.

Platelet

Small cell fragments that play a fundamental role in the formation of blood clots. Patients with a low platelet count are at risk of severe bleeding. Patients with a high count are at risk of thrombosis, the formation of blood clots that can block blood vessels and result in stroke or other severe conditions and can also be at risk of severe bleeding because of platelet dysfunction.

Positive margin

The edge or border of the tissue removed in cancer surgery. The margin is described as positive or involved when the pathologist finds cancer cells at the edge of the tissue, suggesting that all of the cancer has not been removed.

Probe

It is a long and thin instrument used to explore wounds, cavities or body passages.

Prognosis

The likely outcome or course of a disease; the chance of recovery or recurrence*.

Radiation oncologist

A specialist treating cancer with radiation. He or she is different from a radiologist* - another specialist who performs imaging tests to diagnose and follow up on different conditions.

Radiolabelled

Tagged with a radioactive substance. Once injected in the body, the progress of the substance can be followed through the body with a detector.

Radiological examination

Test that uses imaging technology (such as radiography, ultrasound*, computed tomography* and nuclear medicine) to visualize organs, structures and tissues within the body to both diagnose and treat diseases.

Radiologist

A doctor who specializes in the diagnosis of disease and injury with the use of imaging devices such as those used for X-rays*, CT scans* or MRIs* (magnetic resonance imaging).

Radiotherapy

A therapy in which radiation is used in the treatment of cancer always oriented to the specific area of the cancer.

RB gene

A tumour suppressor gene.

Recurrence

Cancer or disease that has come back, usually after a period of time during which the cancer or disease was not present or could not be detected. This may happen at the same location as the original (primary) tumour or in another area of the body. Also called recurrent cancer or disease.

Red blood cell

The most common type of blood cell. It is the substance that makes the blood appear red. The main function is the transport of oxygen.

Retroperitoneal sarcoma

A type of cancer that begins in bone or in the soft tissues of the body, including cartilage, fat, muscle, blood vessels, fibrous tissue, or other connective or supportive tissue. Different types of sarcoma are based on where the cancer forms. In this case the cancers forms in the retroperitoneum, the area behind the peritoneum.

Retroperitoneum

A space located in the back part of the abdominal cavity, behind (retro) a tissue layer known as peritoneum and ahead of the muscles and bones that form the lower back (also known as posterior wall of the abdominal cavity). All organs behind the peritoneum, hence within the retroperitoneum are retroperitoneal organs. The kidneys, part of the pancreas and part of the colon, amongst others, are retroperitoneal organs.

Rhabdomyosarcoma

Cancer that forms in the soft tissues in a type of muscle called striated muscle. Rhabdomyosarcoma can occur anywhere in the body.

Sarcoma

A cancer of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.

Schwannoma

A tumour of the peripheral nervous system that arises in the nerve sheath (protective covering). It is almost always benign, but rare malignant schwannomas have been reported.

Solitary fibrous tumour (SFT)

A rare tumour that can originate in the pleura* or at virtually any site in the soft tissue. It can be benign or malignant.

Synovial sarcoma

A malignant tumour that develops in the synovial membrane of the joints.

Synovial tissue

Thin, loose vascular connective tissue that makes up the membranes surrounding joints and the sheaths protecting tendons where they pass over bony prominences. Synovial cells secrete a liquid called synovial fluid which serves as a lubricant and nutrient for the joint cartilage surfaces.

Systemic therapy/drugs

Treatment using substances that travel through the bloodstream, reaching and affecting cells all over the body. Chemotherapy* and immunotherapy are examples of systemic therapy.

Targeted therapies

A type of treatment that uses drugs or other substances, such as monoclonal antibodies, to identify and attack specific cancer cells. Targeted therapy may have fewer side effects than other types of cancer treatments.

Taxane

A type of drug that blocks cell growth by stopping mitosis (cell division). Taxanes interfere with microtubules (cellular structures that help move chromosomes during mitosis). They are used to treat cancer. A taxane is a type of mitotic inhibitor and a type of antimicrotubule agent.

Trabectedin

A substance that comes from a type of sea squirt and is being studied in the treatment of cancer. It binds to DNA and causes breaks in the DNA. It also blocks the ability of the cell to repair the DNA damage, and may cause cancer cells to die. Trabectedin is also made in the laboratory. It is a type of DNA excision repair inhibitor.

Tuberous sclerosis

A genetic disorder in which benign (not cancer) tumours form in the kidneys, brain, eyes, heart, lungs, and skin. This disease can cause seizures, mental disabilities, and different types of skin lesions.

Tumour suppressor gene

A type of gene that makes a protein called a tumour suppressor protein that helps control cell growth. Mutations (changes in DNA) in tumour suppressor genes may lead to cancer. Also called antioncogene.

Ultrasound

A procedure in which high-energy sound waves are bounced off internal tissues or organs and make echoes. The echo patterns are shown on the screen of an ultrasound machine, forming a picture of body tissues called a sonogram. Also called ultrasonography.

Undifferentiated/unclassified pleomorphic soft tissue sarcoma*

A cancer that begins in the muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body.

Vincristine

The active ingredient in a drug used to treat acute leukemia. It is used in combination with other drugs to treat Hodgkin disease, non-Hodgkin lymphoma*, rhabdomyosarcoma*, neuroblastoma, and Wilms tumour. Vincristine is also being studied in the treatment of other types of cancer. It blocks cell growth by stopping cell division. It is a type of vinca alkaloid and a type of antimetabolic agent.

Vinorelbine

An anticancer drug that belongs to the family of plant drugs called vinca alkaloids.

Vinyl chloride

A substance used to make plastics. Exposure to vinyl chloride may increase the risk of developing liver tumours, brain tumours, lung cancers, lymphoma* and leukaemia.

Von Recklinghausen's disease

A disease known as neurofibromatosis 1, see previously.

Watchful waiting*

Closely watching a patient's condition but not giving treatment unless symptoms appear or change. Watchful waiting is sometimes used in conditions that progress slowly. It is also used when the risks of treatment are greater than the possible benefits. During watchful waiting, patients may be given certain tests and exams. Watchful waiting is sometimes used in prostate cancer. It is a type of expectant management.

Werner's syndrome

An inherited disorder marked by rapid aging that begins in early adolescence. Patients may be shorter than average, and have health problems such as loss and graying of hair, hardening of the arteries, thinning of the bones, diabetes, and thin, hardened skin. They also have an increased risk of cancer, especially osteosarcoma (a type of bone cancer). Werner syndrome is caused by a mutation (change) in a gene involved in cell division. It is a type of autosomal recessive gene disease. Also called adult progeria and WS.

White blood cell

Cells of the immune system that are involved in the body's defence against infections.

X-ray

X-rays are a form of radiation used to take images of the inside of objects. In medicine, X-rays are commonly used to take images of the inside of the body.

The **ESMO / Anticancer Fund Guides for Patients** are designed to assist patients, their relatives and caregivers to understand the nature of different types of cancer and evaluate the best available treatment choices. The medical information described in the Guides for Patients is based on the ESMO Clinical Practice Guidelines, which are designed to guide medical oncologists in the diagnosis, follow-up and treatment in different cancer types. These guides are produced by the Anticancer Fund in close collaboration with the ESMO Guidelines Working Group and the ESMO Cancer Patient Working Group.

For more information please visit www.esmo.org and www.anticancerfund.org

