Soft tissue sarcomas and rare soft tissue tumours – Brief information

Author: Maria Yiallouros, created 2026/01/07, Editor: Maria Yiallouros, Release: PD Dr. med. Monika Sparber-Sauer, English Translation: ['Dr. med. Gesche Riabowol (nee Tallen)'], Last modified: 2026/06/23

Kinderkrebsinfo is sponsored by Deutsche Kinderkrebsstiftung

KINDER KREBS STIFTUNG

Table of Content

Soft tissue sarcomas and rare soft tissue tumours – Brief information

1. General information on the disease

The term soft tissue tumours includes a variety of very different diseases that all share having developed due to a malignant transformation (degeneration) of immature precursor cells of *soft tissue*s.

Soft tissues, however, include different tissue types such as muscles, fatty and connective tissues as well as blood vessels and tissue of the *peripheral nervous system*. Therefore, different types of soft tissue tumours exist. They differ with regard to their *histological* structure and the type of *cell*s they arise from, and they also have different frequencies and biological behaviour. This means, for example, that they present with different growth rates and spread patterns (metastasis), or respond to treatment, such as *chemotherapy*, differently.

Soft tissue tumours can be benign, malignant or medium-grade (intermediate-grade) malignant. Usually, malignant soft tissue tumours are called soft tissue sarcomas; the term “soft tissue tumour” is rather neutral and refers to any type of tumour behaviour. “Soft tissue tumours“ and "soft tissue sarcomas“ summarize at least 150 different histological tumour types (entities).

Most soft tissue sarcomas are highly malignant; they grow and spread rapidly and, hence, are lethal within a few weeks or months, if not treated appropriately. The majority of the less frequent soft tissue tumours, however, is of intermediate malignancy or partially even benign. The growth pattern of these tumours varies; they can do both, spontaneously regress or locally grow very aggressively.

2. Incidence

Soft tissue tumours account for about 5.4 % of all malignant diseases in childhood and adolescence, thereby representing one of the most frequent *solid tumour* types in this age group, following tumours of the *central nervous system* (CNS tumours, brain tumours). According to the German Childhood Cancer Registry (Mainz), about 10 out of 1,000,000 (a total of approximately 125) children and adolescents between 0 and 17 years are diagnosed with a soft tissue tumour each year. More than half of these patients present with *rhabdomyosarcoma*, the most frequent soft tissue sarcoma in childhood and adolescence.

Soft tissue tumours are most frequent in children younger than five or six years of age. The average age at diagnosis is 8.5 years. Boys are slightly more affected than girls (gender ratio: 1.2:1). However, both age distribution and gender ratio differ very much depending on the type of soft tissue tumour.

The most frequent soft tissue sarcomas – that is to say, malignant soft tissue tumours – in children and adolecents under 18 years of age are:

- rhabdomyosarcoma (RMS): 61 %
- extraosseal tumours of the Ewing-group: 16 %
- synovial sarcoma (SySa): 7 %
- fibrosarcoma (FS): etwa 3 %
- leiomyosarcoma (LMS): etwa 2 %
- undifferenciated sarcomas (UDS): 2 %

All other soft tissue sarcomas are rather rare in childhood and adolescence.

3. Tumour types

There are multiple variants of soft tissue tumours, including more than 20 different types of soft tissue sarcomas.

As per currently valid clinical classification, soft tissue tumours are divided into three large groups:

1. rhabdomyosarcomas (RMS)
2. non-rhabdomyosarcoma soft tissue sarcomas (NRSTS)
3. rare soft tissue tumours

In addition, there are also soft-tissue *Ewing sarcoma*s – that is, Ewing sarcomas that arise outside the bone (extraosseous). According to the *WHO*, these “extraosseous tumors of the Ewing group” belong to the overall group of Ewing sarcomas and are now generally treated according to the treatment protocols of the Ewing Study Group.

The following paragraphs will provide more information on the three groups of soft tissue sarcomas.

3.1. 1. Rhabdomyosarcoma (RMS)

For a long time, *rhabdomyosarcoma*s (RMS) have been divided into two major groups based on their microscopic (histological) appearance: embryonal RMS (ERMS) and alveolar RMS (ARMS). Aside from their different *histological* features, the two RMS types usually also show different characteristics regarding their growth pattern (localisation, extent, spread) as well as regarding age distribution and prognosis: embryonal RMS particularly affect children under 10 years of age and are mostly associated with a favourable outcome when compared to alveolar RMS, the incidence of which increases in children older than 10 years.

It is well-known by now that the course of the disease is mainly impacted by the *molecular genetic* characteristics of the tumour cells. Hence, there are genetic alterations, so-called fusion genes,

whose presence is associated with an unfavourable *prognosis*. This is, for example, the case for a typical fusion in the *PAX-FOXO* gene, which can be found in the majority of alveolar RMS (but not in embryonal RMS); the affected ARMS are also called fusion-positive RMS, whereas RMS lacking this specific *PAX-FOXO* gene fusion are called fusion-negative. However, in the meantime, additional alterations have been identified that can cause high malignancy in fusion-negative RMS, too.

Important to know: Today, RMS are not primarily assessed based on their histological features, but rather on the presence or lack of *genetic* alterations. Genetic characterization of the tumours therefore plays a major role when assessing the probability of survival and choosing the appropriate treatment approach.

3.2. 2. Non-rhabdomyosarcoma soft tissue sarcomas (NRSTS)

The non-rhabdomyosarcoma soft tissue sarcomas (NRSTS) represent a rather heterogenous group of soft tissue sarcomas, which differ regarding multiple aspects, such as their growth behaviour, sensitivity to chemotherapy (chemosensitivity) and outcomes.

For example, alveolar soft tissue sarcoma, epitheloid sarcoma, malignant peripheral nerve sheath tumour, fibrosarcoma and leiomyosarcoma all belong to the group of NRSTS. Since these tumours may develop in adults, too, they are also known as "adult type NRSTS“. NRSTS meanwhile also include synovial sarcomas and undifferentiated sarcomas; previously, due to their sensitivity to chemotherapy and treatment similar to that of rhabdomyosarcomas, they were classified as “RMS-like” (rhabdomyosarcoma-like) and assigned to a separate group.

3.3. 3. Rare tumours

The group of the "rare soft tissue tumours” includes tumour types with malignant, medium-grade (intermediate) malignant or benign biological behaviour. Due to their extreme rarity, they are summarized, despite of their different growth patterns and degrees of malignancies. Rare soft tissue tumours are myofibromatosis, desmoid-type fibromatosis (DTF), inflammatory myofibroblastic tumour (IMT), gastrointestinal stromal tumour (GIST) and many more. Based on the tumour type, there are individual treatment concepts for each of these rare diseases.

4. Location and spread

Soft tissue tumours may generally develop anywhere in the human body, since there is soft tissue everywhere. The tumours usually spread along certain anatomical structures, for example along muscle sheaths, ligaments or blood vessels. In the course of this, single cells may detach from the *primary tumour* and spread to other body sites via the blood and/or lymph stream. They can settle there and start multiplying again; daughter tumours are developing (*metastasis*). Metastases of soft tissue sarcomas particularly occur in the lungs, in adjacent *lymph nodes* and in the bones. Other organs can be affected as well.

Origin and growth behaviour of soft tissue tumours are strongly associated with the tumour type.

Rhabdomyosarcomas, for example, can generally develop in almost every organ, however, most frequently, they are found in the head-and-neck area, the urinary tract and reproductive organs as well as the extremities. Usually, fusion-positive alveolar rhabdomyosarcomas (ARMS) show a more aggressive behaviour compared to embryonal rhabdomyosarcomas (ERMS), meaning that they frequently grow and spread faster via the blood and/or lymph stream. Also, fusion-positive ARMS are associated with a higher risk of recurrent disease than most ERMS.

Synovial sarcomas occur most frequently close to joints in the extremities as well as in the head-and-neck area. All these tumour types tend to metastasize early. About 20 % of patients with a soft tissue sarcoma present with distant metastases already at the time of diagnosis.

5. Causes

The causes for the development of soft tissue tumours are not completely understood as of today. The assumption is that they originate from precursor cells of the connective tissue (soft tissue). In medical jargon, these cells are called "*mesenchymal stem cells*“. The malignant transformation is most certainly initiated by *genetic* and/or chromosomal aberrations in these cells.

Different genetic and chromosomal aberrations have already been identified in the malignantly transformed cells, however, these happen to be quite heterogenous, do vary depending on the type of soft tissue tumour and are not regularly found in all tumours after all. Overall, multiple genetic alterations are most certainly responsible for the development of a soft tissue tumour. According to current research, most patients do not have any hereditary predisposition.

However, there are families presenting with high incidences of rhabdomyosarcoma in multiple generations. Also, children present with rhabdomyosarcoma more frequently in families with a frequent history of *carcinoma*. These observations indicate that those patients have a genetic predisposition to develop this disease, a so-called *cancer predisposition syndrome* (CPS). These are complex diseases which are characterized by various kinds of developmental abnormalities and an elevated inherited risk to develop cancer. Cancer predisposition syndromes that are known to play a role in the development of a soft tissue tumour are, for example, *neurofibromatosis*, the *Beckwith-Wiedemann syndrome*, the *Li-Fraumeni syndrome*, the *Gorlin-Goltz syndrome*, the *DICER1 syndrome*, and the *Werner`s syndrome*.

Also, there are indications that certain external factors increase the risk to develop soft tissue tumour. These include *radiation exposure* of the unborn (for example by *X-rays* or *radiation therapy* received by the mother), alcohol or other parental drug abuse prior to or during pregnancy, respectively, as well as early radiotherapy of the child. Associations with viral *infection*s have been reported as well. Hence, *HIV*-positive, thus immunosuppressed children have an increased risk of developing leiomyosarcoma following an infection with the *Epstein-Barr virus* (EBV).

All patients with rhabdomyosarcoma should nowadays be tested for a genetic predisposition syndrome.

6. Symptoms

The symptoms of patients with soft tissue tumour depend on the site and the extent of the tumour and are therefore quite diverse. To name only a few of the frequent, representative symptoms here:

- **Soft tissue tumours developing close to the surface** often cause a continuously increasing swelling and/or pain. Both are not infrequently wrongly referred to as, for example, exercise-induced trauma. Also, they may cause a dysfunction of the affected organ, such as limited range of motion in arms and legs.

- **A soft tissue tumour of the orbita** may initially present with a painless bulging of the eye anteriorly out of the orbit (*exophthalmus*) and a swelling of the eyelid; later it usually causes pain because of the increased local pressure. Vision impairment is also possible.

- **Soft tissue tumours of the nose** are often associated with a long history of congestion or sniffle at the timepoint of diagnosis.

- **In case the skull base is involved**, cranial nerve impairments may occur, which present as facial nerve palsy or double vision.

- **Tumours of the urinary tract and reproductive organs** may present with general malaise, constipation and/or impaired urination, vaginal bleeds, blood in the urine and pain, however, usually once the tumour is already quite large

As for other parts of the body, soft tissue tumours are often getting noticed only because of their palpable or visible tumour mass, for example during a routine physical exam at the paediatrician or by *imaging* diagnostics such as an *ultrasound*. They often do not cause any complaints, meaning that the patients feel good.

Children and adolescents with complaints as described above do, of course, not always necessarily have soft tissue tumour or any other malignant tumour. Nevertheless, it is strongly recommended to have the cause of such *symptom*s be evaluated by an experienced paediatrician.

Good to know: in case of suspected soft tissue tumour, the paediatrician should refer the patient to a treatment centre that is specialized on cancer in children and adolescents (paediatric oncology / haematology program). Initial diagnostic tests (imaging procedures or biopsy, respectively) that are done elsewhere often turn out insufficient and, thus, may negatively impact appropriate treatment and also the patient's prognosis (chance of cure).

7. Diagnosis

If the doctor thinks that the young patient's history and physical exam are suspicious of a soft tissue tumour, the child should immediately be referred to a hospital with a childhood cancer program (paediatric oncology unit), where further diagnostics can be initiated and performed by childhood cancer professionals. Very close collaboration between various specialists (such as *paediatric oncologist*s, paediatric surgeons, paediatric *radiologist*s, to name a few) is required both to find out

whether the patient really suffers from a soft tissue tumour and, if so, to determine the tumour type and the extension of the disease.

Knowing these details is absolutely essential for optimal treatment planning and *prognosis*. Diagnostic management follows the European guidelines as well as the trial recommendations of the “Soft Tissue Sarcoma Study Group" of the Society of Paediatric Oncology and Haematology (*GPOH* STS Study Group) and the "European pediatric Soft tissue Sarcoma Study Group“ (EpSSG), the latter of which is the merger of the European study groups.

7.1. Diagnostic imaging

Apart from comprehensive medical history taking (*anamnesis*) and *physical examination*, *imaging* procedures – preferably a *magnetic resonance imaging* (MRI) with and without *contrast agent* – play a major role in soft tissue tumour diagnostics. First of all, they serve to assess or rule out a tumour. Also, the localization, size and volume of a tumour as well as its demarcation with regard to adjacent tissue (such as organs, blood vessels and nerves) or any tumour-induced changes of the bone system can be diagnosed by such imaging techniques very well.

7.2. Tissue extraction (biopsy) to confirm diagnosis

For final confirmation of the diagnosis, tumour tissue is required to be removed (biopsy), even if the tumour may be benign (as is the case with a *lipoma* or *haemangioma*, for example). The *biopsy* should only be performed by doctors who are specialized in surgery of sarcomas.

The obtained samples are subsequently analysed *histological*ly, *immunohistochemical*ly and *genetic*ally by specialists, with *molecular genetic* tests becoming more and more important. The analyses serve to confirm the diagnosis of a soft tissue tumour and, once confirmed, to determine the subtype. For this, a very comprehensive characterization of soft tissue tumours will be available soon, which will make individualized (meaning tailored) therapies for single patients possible. Hence, analysis and research on tumour tissue is crucial.

Since the disease is overall rare, the obtained tissue samples should not only be studied by the local *pathologist*, but should also be sent to a reference centre for paediatric pathology – such as the reference pathologist of the Soft Tissue Sarcoma Study Group of the *GPOH* (GPOH-STS-Study Group) in Bonn. Such a centre receives tissue samples of a certain tumours from all over Germany and therefore provides special experience with the assessment. The diagnosis is further confirmed by an additional molecular genetic analysis promoting superior tumour characterization, thereby providing relevant directions for the treatment. In many cases, however, research into unknown factors is still needed to gain a better understanding of these tumours.

Note: For molecular genetic analysis, fresh frozen tumour tissue is implicitly required. Therefore, it is crucial that the biopsy is taken in a centre that is specialized in paediatric oncology, where both the expertise and the facilities to process the tumour samples are adequately given. Remaining samples will be stored in the tumour bank (now biobank) and may be used for research aiming at treatment optimisation of these tumours. *For more information on tumour banking see additional page on registries and studies of the GPOH-STS Study Center.*

7.3. Tests to assess spread of disease (staging)

Once the diagnosis of "soft tissue sarcoma" or "(intermediate) malignant soft tissue tumour" has been confirmed, further tests are required to find out if and to which extent the cancer has spread and which organs are involved. Since especially soft tissue sarcomas predominantly develop metastases in the lungs [see *metastasis*], a chest *X-ray examination* as well as a *computed tomography* (CT) of the chest are indispensable.

In addition, a *magnetic resonance imaging* (MRI) and also a *positron emission tomography* with 18-fluorodeoxyglucose (FDG-PET) are performed to assess or, respectively, rule out metastases in the abdominal and pelvic region or the brain. PET is always combined with a MRI (PET-MRI) or CT (PET-CT) scan and, in accordance with ESCP guidelines (ESCP stands for 'European Standard Clinical Practice') and radiology guidelines, is currently being used increasingly in children and adolescents where metastases are suspected. The advantage is that it can detect not only soft-tissue metastases but also bone metastases.

For all high-grade malignant soft tissue sarcomas (G3 sarcomas), a *bone marrow puncture* is done as a standard to rule out *bone marrow* involvement. According to current data, a bone marrow aspiration is not necessary if the PET scan clearly shows bone or bone marrow involvement. This is taken into account in clinical trials (in particular the FaR-RMS trial, *see chapter "Trials and registries"*).

Depending on the disease and treatment situation, additional tests to diagnose and/or further assess metastases may be done, such as an *ultrasoun*d or a *lumbar puncture* (to analyze the *Ultraschall*cerebrospinal fluid when dealing with skull base or spinal tumours), and/or a total body *MRI*.

7.4. Tests before treatment begins

Before treatment begins, further tests are needed in order to assess the condition of different organs. Therefore, the doctors will recommend an *electrocardiography* (ECG) as well as an ultrasound of the heart (*echocardiography*), an *electroencephalography* (EEC), a hearing test (such as *audiometry*, *BERA hearing test* and/or *otoacoustic emissions*), special diagnostics for determining kidney and lung functions as well as various blood tests. Any changes occurring during the course of treatment can be assessed and managed better based on the results of those initial tests, which thus help to keep the risk of certain treatment-related side effects as low as possible.

Good to know: Not all the tests listed above need to be done for every patient. Contrariwise, the patient's individual situation may require additional diagnostic procedures that have not been mentioned in this chapter. Therefore, you should always ask your doctor, based on the information above, which test your child needs and why.

Psychosocial Care

A child's cancer is a stressful situation for the whole family. The psychosocial team of the clinic or later the aftercare facility provides advice and support to patients and their relatives from diagnosis to completion of treatment as well as during aftercare. Don't hesitate to take advantage of this offer.

It is an integral part of the treatment concept of all paediatric oncology centres in many countries. Here you will find comprehensive information on this.

8. Treatment planning

After the diagnosis has been confirmed and the spread of the disease has been assessed, therapy is planned. In order to design a highly individual, risk-adapted treatment regimen for the patient, certain individual factors influencing the patient's *prognosis* (called risk factors or *prognostic factors*) are being considered before and during treatment (risk-adapted treatment strategy).

Important prognostic factors are, for example, the type, the localisation, size and spread of the tumour. In addition, the patient's age has an impact on treatment planning.

- The type of the tumour (meaning its fine tissue features (*histology*) and *genetic* characteristics) impacts, amongst other factors, how fast the tumour grows and how the disease will respond to *chemotherapy* or another kind of *systemic* therapy (such as "new agent therapies"): there are, for example, chemosensitive and chemoinsensitive soft tissue sarcomas. The tumour type also impacts the risk of *metastasis* and the probability of relapse. Experts accordingly differentiate between soft tissue sarcomas with favourable and with unfavourable histology or genetics, respectively (*see also chapter "Tumour types"*).
- The site, size and extent of the tumour (including potential lymph node involvement and metastases) determine the options of surgical tumour removal and *radiation therapy* (radiotherapy).
- The patient's age is also considered for the decision with regard to systemic and/or radiotherapy. Hence, younger patients usually tolerate chemotherapy better than older children. For children under the age of three years (in particular under one year), radiotherapy is only rarely given, but still an option in individual cases.

All these factors are included in treatment planning in order to achieve the best outcome possible for each patient, while keeping the risks of side effects and long-term sequelae as low as possible.

Good to know: As a rule, patients are assigned to different risk groups depending on their prognosis and are treated according to different treatment plans (*see also chapter "Treatment of patients with rhabdomyosarcoma"*). In Germany and other European countries, the classification into risk groups, each with its own associated treatment plan, is carried out in accordance with the recommendations of the "European Paediatric Soft Tissue Sarcoma Study Group" (EpSSG) and the "Soft Tissue Sarcoma Study Group" of the GPOH (GPOH-STS).

9. Treatment

Treatment of children and adolescents with soft tissue tumour should take place in a children's hospital with a paediatric oncology program. Only such a childhood cancer centre provides highly experienced and qualified staff (doctors, nurses and many more), since they are specialised and focussed on the diagnostics and treatment of children and teenagers with cancer according to

the most advanced treatment concepts. The doctors in these centres collaborate closely with each other. Together, they treat their patients according to treatment plans (protocols) that are continuously optimised.

The **goal of treatment** is to eliminate the cancer while keeping the risk of side effects and late sequelae as low as possible.

9.1. Treatment methods

Treatment options for children and adolescents with soft tissue sarcomas or rare soft tissue tumours include **surgery**, **radiotherapy**, systemic therapy (such as **chemotherapy** or a so-called **“new agent” therapy**) or a combination of those, respectively.

Individual treatment (meaning which types of therapy to be applied and in which order) depends in particular on the microscopical and *molecular genetic* tumour type, the localisation of the tumour, as well as on the patient’s age. Treatment is also adapted to the extent of the tumour as well as to its surgical accessibility and sensitivity to chemotherapy or any other systemic therapy (*see chapter "Treatment planning“ above*).

Since the treatment of soft tissue tumours can be associated with side effects, supportive treatment measures (*supportive therapy*) are also applied to prevent and/or treat these side effects. Here your will find further information on *supportive care* as well as on *recommendations for home*, the latter of which may be helpful during or after chemo- and radiotherapy.

The following information outlines the standard treatment options recommended in accordance with guidelines and international consensus recommendations (*see also the chapters on diagnosis and treatment planning*).

9.1.1. Chemotherapy

Chemotherapy includes treatment with agents (so-called cytostatic agents or *cytostatics*), which inhibit cell growth, thereby contributing to eliminating the tumour and potentially existent metastases. In order to eliminate as many of the cancer cells as possible (even those that cannot be detected by diagnostic imaging techniques such as *magnetic resonance imaging*), a combination of cell and, thus, tumour growth inhibiting agents that have proven to be efficient in treating soft tissue sarcomas/tumours are used.

Frequently-used agents are, for example, vincristine, actinomycin D (also known as dactinomycin), cyclophosphamide and ifosfamide, in case of insufficient treatment response or in high-risk patients often doxorubicin (= adriamycin) and, if necessary, other agents as well. The combination of agents as well as their dosages and the duration of treatment vary depending on treatment or risk group. The cytostatic agents are given in multiple *chemotherapy* cycles with treatment pauses in between, which serve the patient’s recovery.

9.1.2. Local therapy

In addition to chemotherapy and/or other systemic treatment (*see “New-agent therapy” below*), local tumour control is provided by *surgery* and sometimes *radiotherapy*. Surgical tumour removal

may be performed both prior and after chemotherapy (primary or late resection, respectively), a potentially necessary radiotherapy either prior or after surgery (pre- or postoperative radiation). The GPOH-STS study centre and their reference experts will help the local caregiver team with decision-making regarding the treatment approaches for individual patients (where possible, the patient should be treated as part of a GPOH-STS study or registered in the registry).

Note regarding trial FaR-RMS: The study is currently investigating, amongst other things, the optimal se-quence of local treatment measures for patients with rhabdomyosarcoma (*see chapters on the treatment of RMS patients as well as on trials and registries*).

9.1.2.1. Surgery

Surgery aims at complete tumour removal. Hence, it is frequently scheduled later in the treatment plan, in fact, after the tumour volume has been decreased by chemotherapy (experts call this "late resection“). This particularly applies to soft tissue sarcomas that are known to be very responsive to chemotherapy, which hence allows to expect tumour shrinkage. These tumours include rhabdomyosarcomas and some other tumours behaving like RMS (such as synovial sarcomas and undifferentiated sarcomas).

Surgery as the first treatment choice (primary tumour resection) is usually per-formed only when, based on diagnostic imaging results, total gross tumour resection is possible without damaging healthy tissue. This is limited to very small tumours with favourable location. For patients with tumours less responsive to chemotherapy, primary surgery may also be an option as long as it is doable.

Surgery is carefully planned in the local treatment centre by representatives of all participating disciplines (*paediatric oncologist*s, surgeons, radiotherapists, *radiologist*s). The CWS study centre and the CWS reference expert group are standing by for advice. Since soft tissue sarcomas are rare, surgical treatments should only be performed in a centre with long-standing sarcoma experience.

9.1.2.2. Radiotherapy

Radiation therapy is done using energy-rich, *electromagnetic* radiation, given through the skin to the tumour region. Radiation causes *DNA* damage in tumour cells, thereby leading to cell death.

Radiotherapy is a very efficient treatment method for patients with eventually remaining soft tissue tumour tissue following surgery. It is a particularly favourable approach when surgery is not an option, for example for patients with rabdomyosarcoma in the head and neck area. Also, patients with a site-associated high risk of tumour spread (for example patients with rhabdomyosarcoma close to the *meninges* or inside the orbita) should receive *radiation therapy*. Patients with rhabdomyosarcoma (RMS) or a non-RMS-like soft tissue sarcoma (NRSTS) whose tumour could be resected completely by primary surgery do not require radiotherapy.

The radiation dose is calculated based on the tumour type, its localisation and extent, its response to chemotherapy as well as its surgical resectability. Conventional treatment uses total radiation doses of about 40-50 *gray* (Gy), given in single daily doses of 1.8-2 Gy. For individual cases,

modern radiation techniques such as the so-called *intensity-modulated radiotherapy* (IMRT) may be favourable. For certain tumour sites or age groups, *proton therapy* is increasingly used.

9.1.3. New therapy options – "new agent“ therapies

The term “new-agent“ therapy summarizes new types of *systemic* therapies (system therapies). These include targeted treatments with new agents that work in a different way compared to chemotherapy. These include substances which, in the presence of very specific *genetic* alterations in tumour cells (such as an *NRTK* or *ALK* genetic alteration), can be used as *inhibitor*s. NRTK and ALK inhibitors are now approved for use in children and adolescents with certain conditions. However, there are a number of promising agents which, in children and adolescents, can so far only be used as part of individual treatment approaches or within clinical trials (*see note on this below*).

Example: An already licensed targeted therapy for soft tissue tumours is the use of the NTRK-inhibitor Larotrectinib for patients with a so-called NTRK-positive infantile fibrosarcoma (a non-rhabdomyosarcoma-like soft tissue sarcoma, NRSTS). These patients have a NTRK gene fusion (NTRK is the abbreviation for neurotrophic tyrosine receptor kinase), which can be inhibited by Larotrectinib. The agent is the treatment of choice for metastatic disease and is even an option for tumours that are not surgically resectable. However, since data regarding length of treatment, development of *resistance* and long-term sequelae are still limited, the use of this agent versus the option of chemotherapy requires careful consideration. Children with this disease have been treated with chemotherapy and surgery for many years and show excellent prognosis.

Note: Future studies using these kinds of agents are being planned. Participation in clinical trials enables the effects and side effects of these medicines to be accurately recorded. For this reason, children and adolescents should, wherever possible, always receive such new active substances within the framework of clinical trials. In general, treatment within the context of clinical trials should always be given preference over any individualized treatment regimen. Only in this way can valid data be acquired that will serve to optimise future therapies.

9.2. Treatment of patients with rhabdomyosarcoma (RMS)

In Germany and other European countries, patients with rhabdomyosarcoma (RMS) are treated according to international guidelines for RMS (ESCP / ERN guideline / AWMF guideline), provided that no other treatment is planned as part of a study (currently FaR-RMS).

Depending on the patient’s risk factors, rhabdomyosarcoma are divided into four different risk groups: one low-risk group, one standard-risk group and two high-risk groups (“high-risk“ and “very high risk“, or HR and VHR for short). The intensity of treatment varies accordingly and also differs to some extent even within a single risk group.

Treatment for the different risk groups is as follows:

- **Low-risk group:** For patients with a low risk of relapse, treatment consists of total gross tumour resection and a chemotherapy with the agents vincristine and actinomycin D (dactinomycin) for about 22 weeks.

- **Standard-risk group:** For standard-risk patients, surgery and chemotherapy are also done. However, in addition to vincristine and actinomycin D (VA), this regimen also includes ifosfamide (IVA) in varying combinations. A total of nine cycles of chemotherapy are administered. Patients with residual tumour receive more intensive treatment than those without residual tumour, either in the form of higher-dose chemotherapy or adjuvant radiotherapy (treatment duration approximately 25 weeks). .
- **High-risk groups:** In both high-risk groups, surgical tumour removal is planned either prior to chemotherapy or later, depending on the site and extent of the tumour. All patients in these groups receive radiotherapy.
- a) **Group "high risk":** For patients at high risk of relapse, chemotherapy consists of at least nine cycles of ifosfamide, vincristine and actinomycin (IVA) over a period of approximately 25 weeks. This is followed by approximately six months of maintenance therapy with vinorelbine and cyclophosphamide; this therapy phase consists of six chemotherapy cycles, each lasting four weeks.
- b) **Group "very high risk"**: In patients at very high risk of relapse, with lymph node or distant metastases, chemotherapy (total duration 25 weeks) is further intensified with an additional drug: doxorubicin is administered (IVADo) in addition to ifosfamide, vincristine and actinomycin. This is followed by twelve cycles of maintenance therapy. The highest-risk group also includes patients whose disease has relapsed (*see chapter "Treatment of patients with recurrent diseases" below*).
- **Low-risk group:** For patients with a low risk of relapse, treatment consists of total gross tumour resection and a chemotherapy with the agents vincristine and actinomycin D (abbreviated to VA) for about 22 weeks.
- **Standard-risk group:** For standard-risk patients, surgery and chemotherapy are also done. However, in addition to vincristine and actinomycin D (VA), this regimen also includes ifosfamide (IVA) in varying combinations. A total of nine cycles of chemotherapy are administered. Patients with residual tumour receive more intensive treatment than those without residual tumour, either in the form of higher-dose chemotherapy or adjuvant radiotherapy (treatment duration approximately 25 weeks).
- **High-risk groups:** In both high-risk groups, surgical tumour removal is planned either prior to chemotherapy or later, depending on the site and extent of the tumour. All patients in these groups receive radiotherapy.
- a) **Group "high risk":** For patients at high risk of relapse, chemotherapy consists of at least nine cycles of ifosfamide, vincristine and actinomycin (IVA) over a period of approximately 25 weeks. This is followed by approximately six months of maintenance therapy with vinorelbine and cyclophosphamide; this therapy phase consists of six chemotherapy cycles, each lasting four weeks.
- b) **Group "very high risk":** In patients at very high risk of relapse, with lymph node or distant metastases, chemotherapy (total duration 25 weeks) is further intensified with an additional drug:

doxorubicin is administered (IVADo) in addition to ifosfamide, vincristine and actinomycin. This is followed by twelve cycles of maintenance therapy. The highest-risk group also includes patients whose disease has relapsed (*see chapter "Treatment of patients with re-current diseases" below*).

Note on the high-risk groups in the FaR-RMS trial: Within the framework of the FaR-RMS study, the respective standard treatment is being compared with a new treatment option in both high-risk groups:
"High-risk" group: Here, standard chemotherapy (IVA) is being compared with a treatment comprising IVA plus irinotecan. The study is also investigating whether extending maintenance therapy by a further six cycles (to twelve cycles) can improve patients' prognosis.
"Very high-risk" group: The study is investigating whether standard therapy with doxorubicin (IVADo) can be replaced by a regimen consisting of IVA plus irinotecan. The use of doxorubicin is controversial, as it can have serious long-term effects. Furthermore, the study is investigating whether extending the current maintenance therapy from twelve cycles to a total of 24 cycles leads to better outcomes.

9.3. Treatment of patients with non-RMS soft tissue sarcoma (NRSTS)

The wide variety of tumours in the group of non-rhabdomyosarcoma soft tissue sarcomas (NRSTS) is not only mirrored by their growth pattern, malignancy, operability and chemosensitivity; it also impacts the type of treatment to be considered for the individual patient:

There are NRSTS that are about as chemosensitive as rhabdomyosarcomas, for example the synovial sarcomas and the undifferentiated sarcomas. Patients with these tumour types are treated in accordance with the current ESCP/ERN guidelines. The current standard treatment involves ifosfamide and doxorubicin and lasts approximately 25 weeks, depending on the therapy group.

A large group of the rare NRSTS, the so-called "adult-type" NRSTS (named that way because they also appear in adults) are often not chemosensitive. For patients with these tumours, new, personalised treatment options may in some cases (depending on the type of tumour) be used and/or tested in the framework of clinical trials (*see chapter "New agent therapy" above*). Some other of these rare NRSTS are rather benign; treatment in this case involves mainly a so-called extended resection, which is defined by surgical removal of the tumour with a certain safety distance, meaning removal of adjacent tissue surrounding the tumour. For some patients with NRSTS, the type of treatment also depends on the size of the tumour and the success of surgery.

Important to know: the treatment spectrum for this inhomogenous disease group is quite large, and new treatment options are being tested. Your caregiver team will explain to you, which therapy options exist for you/your child.

9.4. Treatment of patients with rare soft tissue tumours

Treatment of patients with a rare (frequently intermediate malignant or benign) soft tissue tumour mainly depends on its growth pattern. For tumours growing locally very aggressively (this can be the case for both benign and intermediate malignant tumours), surgery aiming at tumour removal is not always the first choice of treatment. For most of these tumours, the doctors will wait and see whether growth is ongoing, since spontaneous tumour regression is possible as well. If this does not happen or if the localisation of the tumour jeopardizes adjacent organs, a low-dose chemotherapy, depending on the tumor type, is indicated. By now, even newer, so-called targeted therapies (that consider the individual genetic alterations) are an option as well.

9.5. Treatment of RMS patients with recurrent disease

Patients who experience a relapse (*recurrence*) or progression of the disease during treatment have a particularly poor *prognosis*. The standard chemotherapy regimen for recurrent RMS involves the administration of the *cytostatics* vincristine, irinotecan and temozolomide. (Replacing temozolomide with regorafenib did not show any improvement in prognosis in the FaR-RMS trial.) Due to the generally very poor prognosis, affected patients may take part in clinical trials (so-called phase I/II trials). If such experimental treatment approaches are an option for your child, your treatment team will inform you accordingly.

For example, there is a phase I/II vaccine trial (PerVision) for patients with fusion-positive *sarcoma*. The trial is investigating whether targeted *vaccination* can prevent a recurrence of the sarcoma. The treating doctor will assess whether a patient is eligible for inclusion in the PerVision vaccine trial.

10. Therapy trials and registries

In the large paediatriac treatment centres, children and adolescents with a soft tissue tumour receive therapy according to standardised treatment plans (protocols). These protocols are designed by experts and aim at steadily improving the patients' survival rates while also reducing the risk of therapy-related late effects. Therapy according to such treatment protocols is usually carried out within controlled clinical trials, which are developed, monitored and regularly updated in line with the current state of scientific knowledge, either within the framework of the Society of Paediatric Oncology and Haematology ("Gesellschaft für Pädiatrische Onkologie und Hämatologie", *GPOH*) or at European level.

For patients who are not being treated as part of a clinical trial – either because no trial was available at the time of their diagnosis or because they do not meet the inclusion criteria for an existing trial – a **registry** is available for recording all relevant patient data. However, these days, even patients receiving treatment within the framework of clinical trials are recorded in the registry with a limited set of data and, particularly at the end of a trial, are transferred to a registry wherever possible so that long-term effects and late complications can be recorded. To ensure the best possible treatment, the study group (with international participation) draws up detailed recommendations and advises treating doctors on selecting the most appropriate treatment for each individual patient.

In Germany, the following trials and registries are currently available for patients with soft tissue tumours:

- **Trial FaR-RMS:** In April 2025, the international, multicentre FaR-RMS trial (phases I and III) for children, adolescents and young adults with a first-time diagnosis or relapse of rhabdomyosarcoma (RMS) was launched at the first centre in Germany. Among other things, the trial is investigating whether new chemotherapy regimens and an extension of maintenance therapy can improve the chances of cure in high-risk patients. Various radiotherapy options are also to be compared with one another. Numerous treatment centres in Europe and beyond are participating in the trial. The national study coordination is based at the University Children's Hospital in Tübingen, under the direction of Prof. Dr. med. Monika Sparber-Sauer.

- **Registry SoTiSaR 2.0-NIS:** Since the end of 2024, the registry has been recording all children, adolescents and young adults with soft tissue sarcomas and other soft tissue tumours; it replaces the CWS-SoTiSaR registry, which was closed at the end of 2025. Patients included in the SoTiSaR 2.0-NIS registry who are not being treated as part of a clinical trial receive, depending on the type of soft tissue tumour (RMS, NRSTS, rare soft tissue tumour), the respective standard treatment based on European guidelines / consensus recommendations (ESCP guidelines for patients with rhabdomyosarcoma or NRSTS). The registry is headed by Prof. Dr Monika Sparber-Sauer (Olgahospital, Stuttgart) and Prof. Dr Martin Ebinger (University Children's Hospital, Tübingen).

For further information on above-mentioned registries and guidelines, please see here. Details are available on the website of the CWS Study Group: *https://www.klinikum-stuttgart.de/cws/home*

11. Prognosis

Prognosis for children and adolescents with a soft tissue tumour depends on multiple factors. Most relevant are the type, localisation and size of the tumour, its spread, operability (resectability) and the patient's age.

Over the past four decades, *prognosis* for patients with soft tissue tumour has improved drastically due to standardised treatment based on *therapy optimising trial*s. At the end of the 70s, still only 30 to 40 % of all children survived, while the 10-year survival rate is now around 70 % due to continuous treatment optimisation (*see note below*).

In favourable constellations, long-term survival can be observed in over 80 % of patients, while the chance of long-term cure decreases for patients with large, inoperable tumours at diagnosis. Similar, even more unfavourable outcomes have been reported for patients presenting with *lymph node* involvement and/or spread into other body sites at the time of diagnosis. For example, for patients with a *metastasis*ed RMS-like soft tissue sarcoma, the 5-year-survival rate is currently 30 %. Various studies aim at improving the prognosis for these patients as well.

Important note: The above-mentioned numbers are statistical values. Therefore, they only provide information on the total cohort of patients with these types of tumour. They do not predict individual outcomes. It should also be noted that soft tissue tumours constitute a highly heterogeneous group of diseases, meaning that general figures, such as those mentioned above, are not particularly meaningful. Please ask the doctor, who is responsible for your child, for competent information on the individual prognosis

Bibliography

[1] Bisogno G, Brack E, Merks JHM, Sparber-Sauer M, Ebinger M „, GPOH-Leitlinie Rhabdomyosarkom (S1-Leitlinie)“ *AWMF online* 2023, https://register.awmf.org/assets/guidelines/025-007l_S1_Rhabdomyosarkome_2024-03.pdf [uri]

[2] Bisogno G, Chisholm J, Hladun R, De Salvo GL, Guerin F, Casanova M, Mandeville H, Alaggio R, Coppadoro B, Orbach D, Ferrari A, van Rijn R, Defachelles AS, Ben-Arush M, Glosli H, Cesen M, Merks JHM, Minard-Colin V „, Maintenance Chemotherapy in Patients With High-Risk Rhabdomyosarcoma: Long-Term Survival Analysis of the European Paediatric Soft Tissue Sarcoma Study Group RMS 2005 Trial.“ *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2025 Jun;43(16):1856-1862, 40053891 [pubmed]

[3] Chisholm J, Mandeville H, Adams M, Minard-Collin V, Rogers T, Kelsey A, Shipley J, van Rijn RR, de Vries I, van Ewijk R, de Keizer B, Gatz SA, Casanova M, Hjalgrim LL, Firth C, Wheatley K, Kearns P, Liu W, Kirkham A, Rees H, Bisogno G, Wasti A, Wakeling S, Heenen D, Tweddle DA, Merks JHM, Jenney M „, Frontline and Relapsed Rhabdomyosarcoma (FaR-RMS) Clinical Trial: A Report from the European Paediatric Soft Tissue Sarcoma Study Group (EpSSG).“ *Cancers* 2024 Feb 29;16(5), 38473359 [pubmed]

[4] Defachelles AS, Bogart E, Casanova M, Merks JHM, Bisogno G, Calareso G, Gallego Melcon S, Gatz SA, Le Deley MC, McHugh K, Probst A, Rocourt N, van Rijn RR, Wheatley K, Minard-Colin V, Chisholm JC „, Randomized Phase II Trial of Vincristine-Irinotecan With or Without Temozolomide, in Children and Adults With Relapsed or Refractory Rhabdomyosarcoma: A European Paediatric Soft Tissue Sarcoma Study Group and Innovative Therapies for Children With Cancer Trial.“ *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2021 Sep 20;39(27):2979-2990, 34343032 [pubmed]

[5] Defachelles AS, Breunis WB, Casanova M, Minard-Collin V, Hjadun R, Wasti A, Dávila Fajardo R, Terwisscha van Scheltinga S, Heenen D, Heinz AT, Sparber-Sauer M, Merks JHM, Chisholm JC, Gatz SA „, Relapsed rhabdomyosarcoma: treatment recommendations from the European pediatric soft tissue sarcoma study group (EpSSG).“ *British journal of cancer* 2025:1591-1598, 40913059 [pubmed]

[6] Ferrari A, Orbach D, Sparber-Sauer M, Walterhouse DO, Pajtler KW, Meyer WH, Spunt SL, Weiss AR „, The treatment approach to pediatric non-rhabdomyosarcoma soft tissue sarcomas: a critical review from the INternational Soft Tissue SaRcoma ConsorTium.“ *European journal of cancer* 2022 Jul;169:10-19, 35490564 [pubmed]

[7] Ferrari A, van Noesel MM, Brennan B, Zanetti I, Corradini N, Casanova M, Berlanga P, Merks JHM, Alaggio R, Schifflers S, Ramirez-Villar GL, Giraudo C, Burrieza GG, Safwat A, Bisogno G, De Salvo GL, Orbach D „, Paediatric non-rhabdomyosarcoma soft tissue sarcomas: the prospective NRSTS 2005 study by the European Pediatric Soft Tissue Sarcoma Study

Group (EpSSG).“ *The Lancet. Child & adolescent health* 2021 Aug;5(8):546-558, 34214481 [pubmed]

[8] Heinz AT, Schönstein A, Koscielniak E, Ebinger M, Fuchs J, Harrabi S, Vokuhl C, Imle R, Stegmaier S, Brecht IB, Ljungman G, Juntti H, Ladenstein R, Kazanowska B, Klingebiel T, Pajtler KW, Sparber-Sauer M „, Children and Adolescents With Localised Non-Rhabdomyosarcoma Soft Tissue Sarcoma: Results of the CWS-96 and CWS-2002P Prospective Trials With Reclassification of the Trial Data Incorporating the Recent Soft Tissue Sarcoma Registry.“ *Pediatric blood & cancer* 2026;73(2):e32159, 41216926 [pubmed]

[9] Koscielniak E, Klingebiel T „, Weichteilsarkome“ *in: Niemeyer C, Eggert A (Hrsg.): Pädiatrische Hämatologie und Onkologie, Springer-Verlag GmbH Deutschland* 2. vollständig überarbeitete Auflage 2018, 475, 978-3-662-43685-1 [isbn]

[10] Koscielniak E, Sparber-Sauer M, Scheer M, Vokuhl C, Kazanowska B, Ladenstein R, Niggli F, Ljungman G, Paulussen M, Bielack SS, Seitz G, Fuchs J, Hallmen E, Klingebiel T, On Behalf Of The Cws Study Group „, Extraskeletal Ewing sarcoma in children, adolescents, and young adults. An analysis of three prospective studies of the Cooperative Weichteilsarkomstudiengruppe (CWS).“ *Pediatric blood & cancer* 2021;e29145, 34089219 [pubmed]

[11] Koscielniak E, Blank B, Vokuhl C, Kazanowska B, Ladenstein R, Niggli F, Ljungman G, Handgretinger R, Seitz G, Fuchs J, Fröhlich B, Scheer M, Wessalowski R, Schmid I, Sparber-Sauer M, Klingebiel T „, Long-Term Clinical Outcome and Prognostic Factors of Children and Adolescents with Localized Rhabdomyosarcoma Treated on the CWS-2002P Protocol.“ *Cancers* 2022 Feb 11;14(4), 35205646 [pubmed]

[12] Merks, E Brack, M Ebinger et al. „, European standard clinical practice recommendations for children and adolescents with Rhabdomyosarcoma a joint EpSSG, CWS and ERN PaedCan project.“ *JHM EJC Paediatric Oncology* 2025 June; Vol.5, https://doi.org/10.1016/j.ejcped.2025.100229 [doi]

[13] Ronckers CM, Spix C, Grabow D, Erdmann F. „, German Childhood Cancer Registry - Annual Report 2022 (1980-2021)“ *Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI) at the University Medical Center of the Johannes Gutenberg University Mainz* 2025, https://www.kinderkrebsregister.de/fileadmin/kliniken/dkkr/pdf/jb/jb2022/JB_2022_final.pdf [uri]

[14] Rudzinski ER, Kelsey A, Vokuhl C, Linardic CM, Shipley J, Hettmer S, Koscielniak E, Hawkins DS, Bisogno G „, Pathology of childhood rhabdomyosarcoma: A consensus opinion document from the Children's Oncology Group, European Paediatric Soft Tissue Sarcoma Study Group, and the Cooperative Weichteilsarkom Studiengruppe.“ *Pediatric blood & cancer* 2021;68(3):e28798, 33306276 [pubmed]

[15] Sparber-Sauer M, Ferrari A, Kosztyla D, Ladenstein R, Cecchetto G, Kazanowska B, Scarzello G, Ljungman G, Milano GM, Niggli F, Alaggio R, Vokuhl C, Casanova M, Klingebiel T,

Zin A, Koscielniak E, Bisogno G „, Long-term results from the multicentric European randomized phase 3 trial CWS/RMS-96 for localized high-risk soft tissue sarcoma in children, adolescents, and young adults.“ *Pediatric blood & cancer* 2022 Apr 19;:e29691, 35441463 [pubmed]

[16] Stanulla M, Erdmann F, Kratz CP „, Risikofaktoren für Krebserkrankungen im Kindes- und Jugendalter“ *Monatsschrift Kinderheilkunde 169, 30-38* 2021, 10.1007/s00112-020-01083-8 [doi]

[17] Weihkopf T,Blettner M,Dantonello T,Jung I,Klingebiel T,Koscielniak E,Lückel M,Spix C,Kaatsch P „, Incidence and time trends of soft tissue sarcomas in German children 1985-2004 - a report from the population-based German Childhood Cancer Registry.“ *European journal of cancer* 2008 ;44(3):432-40, 18077150 [pubmed]

[18] WHO Classification of Tumours Editorial Board „, Soft Tissue and Bone Tumours“ *5th ed. Lyon: IARC Press* 2020, https://publications.iarc.who.int/Book-And-Report-Series/Who-Classification-Of-Tumours/Soft-Tissue-And-Bone-Tumours-2020 [uri]

Glossary

anamnesis	medical interview, a patient's history, development of signs of illness; the type, onset and course of the (current) symptoms as well as any risk factors (e.g. hereditary diseases) are evaluated during a medical interview.
audiometry	method of studying auditory function using special tone generators that produce individual frequencies at a specific volume; it is used, among other things, to diagnose diseases of the hearing organs. A distinction is made between subjective and objective audiometric methods. An example of a subjective audiometric method is the tone audiogram. It requires the assistance of the person whose hearing is to be examined.
Beckwith-Wiedemann syndrome	congenital or acquired clinical condition, characterized in particular by a pathologically increased one-sided growth of the body (hemihypertrophy), enlargement of the liver, spleen or kidneys, considerably enlarged tongue, umbilical (cord) rupture, maldevelopment of the auricles, kidney abnormalities and an increased risk to develop certain malignant diseases (especially Wilms tumours); BWS is one of the cancer predisposition syndromes and is caused by various genetic changes (on chromosome 11).
BERA hearing test	ENT examination to determine hearing damage; it essentially measures the electrical activity of the auditory nerve and the auditory pathways to the brain stem and does not require the patients assistance (objective hearing test). In the BERA test, certain auditory stimuli (sounds) are emitted via headphones: with the help of an electroencephalogram (EEG), the reaction (in the form of brain waves, so-called acoustically evoked potentials) is measured. This is the brainstems response to the acoustic stimulus. The measurement of these brain waves makes it possible to detect hearing disorders or abnormalities in the cranial nerve or brainstem.
biopsy	removal of a tissue sample for subsequent (mainly microscopic) examination; this can be done, for example, by puncture with a hollow needle, with the use of special instruments (such as forceps, punching instruments, probes) or surgically with a scalpel.
bone marrow	site of blood formation; spongy tissue with a strong blood supply that fills the cavities inside many bones (e.g., vertebrae, pelvic

	and thigh bones, ribs, sternum, shoulder blade, and collarbone); in the bone marrow, all forms of blood cells develop from blood progenitor cells (blood stem cells).
bone marrow puncture	removal of bone marrow tissue to examine the cells; during the puncture, a few milliliters of liquid bone marrow are drawn from the pelvic bone or sternum into a syringe with the help of a thin hollow needle. The puncture is performed under local anaesthesia in older children; a sedative may also be administered (sedation). For smaller children, a short period of anesthesia may be appropriate.
cancer predisposition syndrome	genetic disorders that can include malformations and intellectual disability in addition to an increased risk of tumors; according to current knowledge, about 10% of childhood and adolescent cancers develop due to a known hereditary change or cancer predisposition syndrome. Cancer predisposition syndromes include Louis Bar syndrome (= ataxia telangiectatica), Beckwith-Wiedemann syndrome, Down syndrome, Hippel-Lindau syndrome, Li-Fraumeni syndrome, MEN syndrome, neurofibromatosis and WAGR syndrome. The familial form of retinoblastoma is also part of it.
carcinoma	malignant tumour resulting from degenerated epithelial tissue (e.g. skin, mucous membranes, glandular tissue);
cell	the smallest functional unit in organisms with the ability to perform metabolism, involuntary muscle movement and reproduction and to respond to stimuli; each cell contains a nucleus and a cell body (cytoplasm) and is externally bounded by the cell membrane.
central nervous system	comprises the brain and spinal cord and is separated from the so-called peripheral nervous system; as a central organ of integration, coordination and regulation, it serves to process external sensory impressions as well as stimuli produced by the organism itself.
chemotherapy	here: use of drugs (chemotherapeutic agents, cytostatics) for the specific inhibition of tumor cells in the organism
computed tomography	imaging, X-ray diagnostic procedure; it produces an image by computer-controlled evaluation of a large number of X-rays from different directions. This makes it possible to produce sliced images of body parts (tomograms, transverse or longitudinal sections of the human body)

contrast agent	substance that can be used to improve the visualization of structures and functions of the body in imaging techniques; contrast agents are mainly used in X-ray diagnostics (X-ray examination, computed tomography), magnetic resonance imaging (MRI) and ultrasound examinations.
cytostatics	drugs that inhibit cell growth; cytostatics can affect the metabolism of different types of cells, thereby destroying them and/or preventing them from multiplying. Cells that divide frequently are particularly affected.
DICER1 syndrome	congenital disease associated with an increased risk (predisposition) in children and adults of developing lung tumours (pleuropulmonary blastoma, PPB), kidney tumours (cystic nephroma), ovarian and thyroid tumours , as well as many other benign and malignant tumours; the condition is caused by a change in the genetic material in the DICER1 gene. 80% of patients with DICER1 syndrome have inherited the disease from their parents (through an autosomal dominant inheritance pattern). The probability that a child of affected parents will also develop DICER1 syndrome is 50%. In 20% of patients, the syndrome is caused by a spontaneous (de novo) mutation.
DNA	abbreviation for deoxyribonucleic acid; it carries the genetic information and is found in all living beings. DNA contains the genes that provide the information for the production of ribonucleic acids (RNA) or proteins. It is a large molecule consisting of two nucleic acid chains twisted into a double helix. The individual chains consist of a sequence of four different building blocks (bases), the order (sequence) of which determines the genetic code.
echocardiography	ultrasound examination of the heart to check its performance (cardiac function); the position or structure of the heart valves and walls, the wall thickness of the heart muscle, the size of the heart and the ejected blood volume (pumping function of the heart) are examined and assessed, among other things.
electrocardiography	method of measuring the electrical activity of the heart
electroencephalography	method of recording the electrical activity of the brain; the electroencephalogram (also abbreviated EEG) is the graphical representation of this electrical brain activity. Its evaluation can provide evidence of brain dysfunctions.
electromagnetic	electromagnetic rays (also known as electromagnetic waves) consist of coupled electric and magnetic fields; examples of

	electromagnetic radiation are X-rays and gamma rays as well as radio waves, thermal radiation and light.
Epstein-Barr virus	causative agent of glandular fever;
Ewing sarcoma	highly malignant (malignant) sarcoma originating in the bone (rarely in soft tissue); second most common malignant bone tumour in children and adolescents (after osteosarcoma), occurring mainly from the second decade of life onwards.
exophthalmus	pathological protrusion of the eyeball from the eye socket on one or both sides;
genetic	concerning the (level of) inheritance or genes; inherited
Gorlin-Goltz syndrome	a hereditary disease associated with a number of developmental disorders and a predisposition to various cancers, the most common being a form of skin cancer (basal cell carcinoma);
GPOH	Society for Paediatric Oncology and Hematology (GPOH), the German professional society for childhood and adolescent cancers and blood diseases; in the GPOH, doctors, scientists, nurses and psychologists, among others, work together on the research, diagnosis, treatment and aftercare of malignant diseases and blood diseases in children and adolescents. in the GPOH, doctors, scientists, nurses and psychologists, among others, work together on the research, diagnosis, treatment and aftercare of malignant diseases and blood diseases in children and adolescents.
gray	unit of measurement for the dose of energy caused by ionising radiation (e.g. in the context of radiotherapy) and absorbed by a given mass (kilogram of body weight)
haemangioma	benign neoplasms of blood vessels (sometimes also referred to as blood sponges) mainly in the skin, but also, depending on the type of haemangioma, in other organs; haemangiomas develop in the first few weeks of life or are already present at birth, but usually regress on their own within a few years.
histological	concerning the tissues of the body; in a histological (fine tissue) examination, tissue samples are examined under the microscope after special preparation (preparation of tissue sections and use of certain staining techniques).
histology	study of the tissues of the body
HIV	abbreviation for "human immunodeficiency virus"; HIV belongs to the retrovirus family. After an incubation period of varying lengths,

	usually several years, an infection leads to AIDS (acquired immunodeficiency syndrome), an immunodeficiency disease that is currently still incurable.
imaging	diagnostic procedures generating images of the inside of the body, such as ultrasound and X-ray examination, computed tomography, magnetic resonance imaging, and scintigraphy
immunohistochemical	in an immunohistochemical or immunohistological examination, proteins or other cell or tissue structures are visualized with the help of labeled antibodies (e.g. bound to dyes).
infection	penetration of the smallest organisms (e.g. bacteria, viruses, fungi) into the body and subsequent multiplication within it. Depending on the characteristics of the microorganisms and the immune system of the infected person, various infectious diseases can occur after infections.
inhibitor	the term derives from „inhibition“ (= hindering); a substance that influences one or more biochemical reactions thereby slowing it down or completely preventing it
intensity-modulated radiotherapy	modern radiation technology, which provides maximum protection for the surrounding healthy tissue from radiation exposure by means of a highly precise distribution of the radiation dose at the tumour site; the intensity of the radiation dose can be precisely adjusted to the irradiation field only; this may also allow the use of a higher radiation dose.
Li-Fraumeni syndrome	cancer predisposition syndrome characterized by the increased occurrence of various solid tumours within a family; in childhood and adolescence, tumours of the adrenal glands, as well as soft tissue sarcomas, leukaemias and CNS tumours are most commonly observed, in adulthood mainly bone tumours (osteosarcomas), breast cancer and lung tumours. In most cases, there is a change (mutation) of the so-called tumour suppressor gene TP-53 (protein p53).
lipoma	benign tumour that develops from cells of adipose tissue
lumbar puncture	puncture of the spinal canal in the lumbar spine, e.g. to remove cerebrospinal fluid (CSF) or for the purpose of administering medication (so-called intrathecal treatment); in the case of cancer, a sample and examination of cerebrospinal fluid can be used to detect malignant cells; in the case of increased intracranial pressure due to a CNS tumour, cerebrospinal fluid removal (CSF) is also used to relieve pressure.

lymph nodes	small lenticular to bean-shaped organs that are part of the bodys immune system and are located in many parts of the body; they serve as filter stations for the tissue water (lymph) of a region of the body and contain cells of the immune system.
magnetic resonance imaging	diagnostic imaging method; very precise, radiation-free examination method for the visualization of structures inside the body; with the help of magnetic fields, cross-sectional images of the body are generated, which usually allow a very good assessment of the organs and many organ changes.
meninges	layers of connective tissue that protectively envelop the brain; the three meninges are joined to the outside by the skull bones. In the area of the spinal cord, the meninges merge into the three-layered spinal cord membrane, which surrounds the rest of the central nervous system.
mesenchymal stem cells	stem cells of connective tissue; they are found in various types of tissues (such as bone marrow, bones, skeletal muscles, cartilage, blood, adipose tissue, connective tissue of the skin) and can develop into different types of cells (including bone, cartilage, muscle, fat cells).
metastasis	1. tumour spread from the primary site of tumour to other parts of the body; characteristic feature of malignant tumours (cancer). 2. collective term for a disease process characterized by malignant cells spreading from their primary site to other areas of the body via the bloodstream and/or the lymphatic system.
molecular genetic	referring to structure, formation, development, function and interactions of cells and cell building blocks (e.g. nucleic acids, proteins) at the molecular level; the focus is on the analysis of the genetic information stored in the nucleic acids (DNA and RNA) and its processing in the context of protein synthesis as well as gene regulation.
MRI	abbreviation for magnetic resonance imaging, a very precise, radiation-free examination method for imaging structures inside the body
neurofibromatosis	hereditary disease that leads to tumours of the nerve sheaths, meninges and glia (the "connective tissue" of the nervous system). Clinically and molecular-genetically, two forms of neurofibromatosis can be distinguished, which are caused by different genetic defects: 1. Peripheral neurofibromatosis (NF1, also known as Recklinghausens disease): this is characterized by so-called café-au-lait spots on the skin and a predisposition

	to various tumours (including neurofibromas, gliomas of the optic nerve, iris hamartomas as well as astrocytomas and pheochromocytomas). 2. Central neurofibromatosis (NF2): it is characterized by mostly (bilateral) neuromas of the auditory nerve (acusticus), which can lead to deafness, facial paralysis and mental disturbances. There is also an increased risk of tumours (e.g. astrocytomas, spinal ependymomas). Neurofibromatosis is one of the so-called phacomatoses.
otoacoustic emissions	very quiet sounds that the inner ear emits when hearing sounds (sound waves hitting the ear); these can be registered by highly sensitive microphones. The measurement of OAE is used to check the function of the inner ear; the patients assistance is not required (objective hearing test). This form of hearing test is therefore also suitable for infants and toddlers. During the examination, tiny measuring microphones are inserted into the external ear canal. The supplied sound waves cause the outer hair cells in the inner ear to vibrate, i.e. move mechanically. This generates the quiet but measurable otoacoustic emissions.
paediatric oncologist	paediatrician who is specialized on the management of children and adolescents with cancer
pathologist	a physician who identifies diseases and determines the malignancy of tumours by means of histological and molecular genetic examination of cells and tissues
peripheral nervous system	can be described as the receiving and executing organ of the central nervous system (CNS); it consists of the numerous nerves that run through the body; they carry impulses either from the periphery to the CNS (sensory nerve pathways) or from the CNS to the periphery (motor nerve pathways). The peripheral nervous system includes, for example, the cranial nerves, spinal cord nerves and peripheral nerve cells.
physical examination	an important part of diagnostic examinations; includes palpation and listening to certain body organs as well as testing reflexes to obtain indications of the nature or course of a disease.
positron emission tomography	an imaging, nuclear medicine procedure based on the principle of scintigraphy, which can be used in cancer medicine to visualize tumours or metastases. To detect tumour tissue, a radioactively labeled sugar compound is administered. Since tumours have a higher metabolism than healthy tissue, the radioactive substance is increasingly taken up and stored by the tumour cells. The tumour cells enriched with this substance emit signals that are

	captured by a special camera (PET scanner) and converted into an image (tomogram).
primary tumour	the tumour that developed first, from which metastases can originate
prognosis	prediction of the course and outcome of a disease / prospect of recovery
prognostic factors	factors that allow an approximate assessment of the further course of the disease (i.e. the prognosis);
proton therapy	modern form of radiotherapy using protons for the treatment of malignant tumours; compared to conventional radiotherapy with photons, this type of radiation can specifically target the tumour area, thereby sparing adjacent, healthy tissue from the effects of radiation.
radiation exposure	the dose of ionising radiation to which humans are exposed from natural, civilised or artificial sources of radiation; natural sources of radiation include cosmic, terrestrial and natural radioactive substances produced by the decay of natural radioactive substances, which are absorbed into the body with drinking water, food and breathing air. Artificial sources include radiation produced by the technical and medical use of nuclear and atomic forces, such as X-rays.
radiologist	a physician specialized in diagnostic imaging and radiotherapy
radiotherapy	controlled use of ionizing (high-energy) radiation for the treatment of malignant diseases
recurrence	relapse, recurrence of a disease after recovery
resistance	here: insensitivity of cancer cells to certain cell growth-inhibiting drugs (cytostatics)
rhabdomyosarcoma	the most common soft tissue sarcoma in childhood and adolescence
sarcoma	malignant tumour that arises from degenerated nerve, connective or supporting tissue (e.g. bones, cartilage, tendons, muscle, fat); the name is given according to its origin: for example, rhabdomyosarcoma is a malignant tumour of the striated muscles, osteosarcoma a malignant tumour of the bone-forming tissue.
soft tissue	soft tissues include connective, fat, and muscle tissue, as well as blood vessels and peripheral nerve tissue (nervous system without the brain and spinal cord). The soft tissues thus include

	all non-epithelial tissues of the body with the exception of the supporting tissue (bone and cartilage). They connect, support and surround the other parts of the body and organs.
solid tumour	solid, localized increase of the bodys own tissue; solid tumours can originate from various tissues and can be benign or malignant; only the malignant ones are considered as cancers. Solid tumours include all cancers that do not affect the haematopoietic or lymphatic system. The latter are systemic malignancies. The most common solid tumours in childhood and adolescence are brain tumours, followed by neuroblastoma and soft tissue sarcomas.
supportive therapy	supportive treatment measures to prevent, alleviate or treat disease and/or treatment-related side effects or complications; supportive therapy is designed to improve the patients quality of life.
surgery	surgical intervention on or in the body of a patient for the purpose of treatment, less often also in the context of diagnostics; the surgical intervention is carried out with the help of special instruments, generally with the patient under anesthesia.
symptom	sign of illness
systemic	covering/includiing the entire body
therapy optimising trial	a controlled clinical trial (study) that aims to provide the best possible treatment for patients and at the same time to improve and develop treatment options; therapy optimisation is aimed not only at improving the chances of recovery, but also at limiting treatment-related side effects and long-term effects.
ultrasound	an imaging technique used to examine organs, in which ultrasound waves are sent through the skin into the body; at tissue and organ boundaries, the sound waves are reflected back, picked up by a receiver (transducer) and converted into corresponding images with the help of a computer.
vaccination	a preventive measure against infectious diseases, sometimes also a therapeutic measure in cancer patients; vaccination involves introducing an agent, the vaccine, into the body in ordert o achieve vaccine protection (immunisation of the organism). It is usually administered by injection. There are two different vaccination approaches: active vaccination and passive vaccination.
Werner`s syndrome	very rare, genetic disease associated with premature aging and an increased risk of cancer; the first symptoms appear

	in early puberty (short stature; weak, high-pitched voice), the full manifestation of the disease presets around the age of 30 years. Symptoms include, for example, characteristic skin changes, whitish and sparse scalp hair, bilateral cataracts, type II diabetes mellitus, arteriosclerosis, muscle breakdown and osteoporosis. In addition, patients with Werner syndrome have an increased risk of malignant tumours. The disease is inherited in an autosomal recessive manner and is one of the cancer predisposition syndromes.
WHO	abbreviation for World Health Organization; international federation for cooperation in the field of public health
X-ray examination	imaging procedure that uses X-rays to visualize organs or parts of organs
X-rays	high-energy electromagnetic radiation, discovered by W. C. Röntgen in 1895; X-rays can partially penetrate matter, so that insights into the interior of the human body are possible, among other things. Since X-rays have an ionising effect (ionising rays), they can also change matter, e.g. damage cells and possibly cause cancer. In diagnostics, X-rays are used to examine certain parts of the body. Depending on the type of irradiated tissue, the radiation is intercepted (absorbed) to varying degrees and displayed on a film plate as a two-dimensional image. Since every X-ray examination is associated with a certain amount of radiation, particularly sensitive parts of the body (such as gonads) must be protected. In the context of X-ray therapy (e.g. radiotherapy), very high-energy X-rays are used to kill tumour cells.