Acute Myeloid Leukaemia (AML) - Brief Information

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1. General disease information

Acute myeloid (or nonlymphocytic) leukaemia (AML) is a malignant disease that arises within the haematopoietic system. AML usually originates from the *bone marrow*, where the blood cells are produced. It is characterised by an overproduction of impaired white blood cells.

Healthy blood cells reproduce and regenerate at a normal, balanced rate. They undergo a complex maturation process. AML interferes with this process: The white blood cells (*leukocytes*) are unable to mature into functional cells and instead multiply rapidly and uncontrollably. This disturbs normal blood cell formation, so that healthy white blood cells, red blood cells (*erythrocytes*), and platelets (*thrombocytes*) can no longer be produced to the extent that is necessary.

Anaemia, *infection*s, and bleeding tendencies can result and may be the first signs of acute leukemia. Since AML is not limited to one specific region of the body, but can spread from the bone marrow into the blood and the *lymphatic system*, it can affect all organs and organ systems and is therefore – like all leukaemias – known as a malignant systemic disease.

AML progresses rapidly. The spread of leukaemia cells and the resulting damage to other body parts can cause serious diseases, which – without the appropriate treatment – are lethal within a few weeks or months.

2. Incidence

Comprising about 20 % of childhood *leukaemia*, acute myeloid leukaemia (AML) is, following *acute lymphoblastic leukaemia* (ALL), the second most frequent leukaemia in children and adolescents. AML accounts for about 4 % of all cancers in this age group. According to the German Childhood Cancer Registry in Mainz, about 90 children and adolescents aged between 0 and 17 years are newly diagnosed with AML every year.

In general, AML can occur at any age, with a peak during adulthood. The frequency of childhood AML is highest during the first two years of life. After that, incidence decreases and remains stable throughout childhood. It shows a mild increase again during adolescence. The young patients' average age at diagnosis is approximately seven years. Boys are slightly more affected than girls (sex ratio: 1,1:1). .

3. Types of acute myeloid leukaemia

AML is caused by a malignant transformation of immature "myeloid cells". These are blood precursor cells in the bone marrow (*blood stem cells*), which finally develop either into red blood

cells (erythrocytes), certain types of white blood cells (*granulocytes* or *monocytes*), or platelets (thrombocytes), depending on which kind of precursor myeloid cell is involved.

AML is mainly characterised by a malignant transformation of granulocyte precursor cells (so-called myeloblasts). However, AML can derive from any immature myeloid cell, i.e. from monocytes, young red blood cells or platelets, and even from the very young precursor (stem) cell of all of them. Furthermore, the development of immature into mature blood cells of any kind comprises several developmental stages, each of which can be affected by malignant transformation. This is why there are different forms of AML, such as acute myeloblastic, monocytic, erythroid, or megacaryocytic leukaemia and many more, including various mixed forms.

According to the French-American-British (FAB) classification, eight major subtypes of AML are differentiated based on how the leukaemia cells look under the microscope, meaning based on their *cytomorphological* appearance; in the past, these were relevant for the classification of AML. Today, the FAB classification is increasingly being replaced by the *WHO classification* (2021), which is based on cytomorphological, *cytogenetic* and *molecular genetic* features of the abnormal cells.

Good to know: Various subtypes of childhood AML have been characterised so far, the courses and prognoses of which can differ significantly. Current treatment strategies for children and adolescents with AML consider these different subtypes. Therefore, children and adolescents with AML do not all receive the same treatment.

4. Causes

The causes of acute myeloid leukaemia (AML) are largely unknown. It is known so far that the disease arises from the malignant transformation of certain (myeloid) precursor blood *cell*s in the bone marrow, and also, that this transformation can be associated with *genetic* alterations of these cells. Why these genetic alterations exist and why they cause the disease in some children but not in others, remains to be discovered. Most certainly, AML is caused by a specific combination of many genetic factors, that have not yet been identified.

AML is primarily not an inherited disease. However, the risk of developing this type of malignancy is increased in individuals with a positive family history for cancer: for example, siblings of a child with leukaemia have a slightly increased risk (about 1.1-fold) to develop leukaemia as well. The identical twin of a leukaemia patient has a risk of 15 % to also develop this disease. Therefore, it is recommended to check on blood and maybe even on bone marrow of the healthy twin, too.

It is known that children with certain inherited or acquired immunodeficiencies [*immunodeficiency*] as well as young patients with chromosomal abnormalities have a higher risk of developing acute leukaemia than their healthy peers. Hereditary concomitant diseases promoting the development of AML are, for example, *Down syndrome*, *Fanconi anaemia*, *neurofibromatosis* or *monosomy 7*. Since these (very rare) diseases are associated with a predisposition to develop cancer, they are also called *cancer predisposition syndrome*s.

Both *radiation therapy* (radiotherapy) and *chemotherapy* given in childhood harbour a certain risk to develop a secondary malignancy later in life. For example, AML can develop as a

secondary malignancy after radio- and/or chemotherapy of a different malignancy, such as an acute lymphoblastic leukemia (ALL) or *Hodgkin lymphoma*. These forms of AML are also known as treatment-induced secondary AML. Also (prenatal exposure to) *radioactive radiation* or *X-rays* and to certain genotoxic chemicals and drugs, prenatal exposure to parental nicotine or alcohol abuse, and maybe certain *virus*es have been reported to play a role in the development of leukaemia. However, for most of the patients, no specific risk-factor for the development of AML has been identified yet.

5. Symptoms

The health problems (*symptom*s) caused by of most children and adolescents with AML develop within only a few weeks. They mainly occur due to the increase of malignant cells within the *bone marrow* as well as their spread into other organs and tissues. The uncontrolled production of leukaemia cells in the bone marrow increasingly suppresses the production of normal blood cells.

Children and adolescents suffering from AML initially experience general symptoms such as fatigue, pain, and pallor. This is due to the lack of red blood cells (*anaemia*), the function of which it is to carry oxygen to cells throughout the body. The lack of functional white blood cells (i.e. *lymphocytes* and *granulocytes*) prevents pathogens from being attacked and eliminated properly, thereby causing *infection*s and fever. Another frequent symptom is bleeding, for example, under the skin (bruises, *petechiae*) or from mucous membranes such as the gums, owing to impaired *blood coagulation* as a result of low platelet counts.

The growth of leukaemia cells in the marrow of the long bones can cause bone and joint pain, especially in the limbs (arms and legs) and back. This pain can be so intense that the affected child may refuse to walk or run. The malignant cells can also spread into the liver, spleen, and *lymph nodes*. Therefore, these organs may enlarge and subsequently cause problems, such as abdominal pain. In general, all organs can potentially be affected by AML. If AML spreads to the brain and its *meninges*, patients may suffer from headache, visual disturbances, nausea, vomiting, and other central nervous system impairments.

Presenting symptoms in patients with AML are as follows:

Very frequent (over 60 % of patients):

- fatigue, exhaustion, weariness, malaise, pallor (caused by the lack of red blood cells, *anaemia*)
- fever and/or frequent nonspecific infections (due to the lack of white blood cells, *neutropenia*)
- abdominal pain and loss of appetite (due to the enlargement of spleen and/or liver)

Frequent (between 20 and 60 % of patients)

- increased risk of bleeding, for example, frequent spontaneous nose bleeding, gum bleeding (for example while brushing teeth), excessive bruising, pinpoint, round and red spots on the skin (petechiae); rare: cerebral haemorrhage (due to lack of platelets)
- enlarged *lymph nodes* (for example, in neck, armpits, groin)

- bone and joint pain (mostly limbs and back)

Rare (under 20 % of patients)

- headache, visual disturbances, vomiting, cranial nerve palsies (due to involvement of the *central nervous system*)
- shortness of breath (in case of high count of white blood cells, *hyperleukocytosis*)
- skin changes and chloroma (myeloid blastoma or myeloud sarcoma): tumour-like local masses of leukaemia cells in the skin, lymph nodes, bone, and, sometimes around the eyes; coloured, partly bluish-green in colour
- gingival (gum) enlargement (gingival hyperplasia)
- enlargement of testicles

Good to know: The type and degree of symptoms of AML vary individually. It is also important to know that a child or teenager showing one or more of these symptoms does not necessarily suffer from AML. Many of the symptoms described above, such as fever, fatigue, or headaches, are also regularly seen with frequent and rather harmless childhood diseases, like common colds and other viral infections. Nevertheless, if these symptoms recur frequently or persist,a doctor should be consulted as soon as possible. If acute leukaemia is diagnosed, treatment must be started promptly.

6. Diagnosis

If the doctor, based on the young patient's history (*anamnesis*) and *physical examination*, suspects acute leukaemia, he or she will first initiate a blood test (*blood count*). If the results promote the diagnosis of an acute leukaemia, a sample of the bone marrow (*bone marrow puncture*) is required for confirmation. For bone marrow tests and other diagnostic procedures, the doctor will refer the patient to a children's hospital with a childhood oncology program (paediatric oncology unit) and childhood cancer specialists.

6.1. Blood and bone marrow tests

Blood and bone marrow tests are needed to confirm the diagnosis of leukaemia as well as to determine the type. The tests include microscopic (*cytomorphological*), *immunological*, and *genetic* laboratory analysis of blood and bone marrow samples that distinguish AML from other kinds of leukaemia (such as ALL) and, furthermore, allow to define the specific subtype of AML. Knowing the subtype of AML is necessary for appropriate therapy planning, because different forms of AML have different biological characteristics and also vary regarding their response to treatment and, thus, *prognosis*.

6.2. Tests to assess spread of the disease (staging)

Following the diagnosis of AML and its subtype, it is important for treatment planning to know whether the leukaemia cells have spread to additional body compartments (other than the bone

marrow), including the brain, liver, spleen, *lymph nodes*, testicles, or bones. Therefore, various imaging techniques, such as *ultrasound*, *X-ray examination*, *magnetic resonance imaging* (MRI) and/or *computed tomography* (CT), may be used to evaluate spread of the disease. To find out whether the central nervous system (brain and spinal cord) is affected, a sample of cerebrospinal fluid is taken and analysed for leukaemia cells (*lumbar puncture*).

6.3. Additional diagnostics before treatment begins

To prepare the patient for the intensive treatment, several organ functions must be checked, since certain anticancer agents have specific side effects that can damage different organs. To have an initial assessment later helps to detect and appropriately interprete potential functional changes. These preparatory diagnostics usually include various tests of the heart function (such as *electrocardiography* (ECG) and *echocardiography*) and the brain function (*electroencephalography*, EEG) as well as a variety of different blood tests that will give information on how well liver, bone marrow, and kidneys are working. Furthermore, the patient's *blood group* will be defined, which is essential in case a *blood transfusion* may be necessary during the course of treatment.

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.

7. Treatment planning

After the diagnosis has been confirmed, therapy is planned. In order to design an individual, risk-adapted treatment regimen for the patient, certain factors influencing the patient's chance of recovery (prognosis) – called risk factors or prognostic factors – are being considered during treatment planning (risk-adapted treatment strategy).

Important *prognostic factors* are the subtype of AML (*see chapter „types of acute myeloid leukaemia“*), the extent of leukemia cell spread throughout the body at diagnosis, and the response of the disease to *chemotherapy*. The exact knowledge of the tumour type helps the caregiver team to assess how sensitive the tumour cells might be to the chemotherapy and, thus, how intensely patients need to be treated in order to keep the risk of relapse as low as possible. Extent of the disease and response to treatment impact the decision whether, aside from chemotherapy, additional treatment methods (for example *radiation therapy* of the brain or *high-dose chemotherapy* followed by *stem cell transplantation*) are necessary to increase the probability of cure.

All these factors are included in treatment planning in order to achieve the best outcome possible for each patient. Hence, each individual clinical situation is crucial for assigning a patient to the appropriate treatment group and for choosing the optimal treatment protocol, in order to guarantee he or she will receive the most appropriate (risk-adapted) treatment. Currently, three treatment groups are differentiated: standard-risk group, medium- (intermediary-)risk group, and high-risk group.

8. Treatment

If acute myeloid leukaemia (AML) is being suspected or has been diagnosed, treatment should be started as soon as possible in a children's hospital with a paediatric oncology program. Only in such a treatment centre, highly experienced and qualified staff (doctors, nurses and many more) is guaranteed, since they are specialised and focus on the diagnostics and treatment of children and teenagers with cancer according to the most advanced treatment concepts. The doctors (such as oncologists, radiologists, surgeons) 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 the treatment is to achieve high cure rates as well as low rates of side effects.

8.1. Treatment methods

Treatment options for acute myeloid leukaemia include **chemotherapy**, **targeted therapies**, **radiotherapy** (rarely) and **high-dose chemotherapy** followed by **stem cell transplantation** (stem cell therapy).

- **Chemotherapy:** is the major backbone of AML treatment. It uses drugs (so-called cytostatic agents or *cytostatics*) that can kill fast-dividing cells, such as cancer cells, or inhibit their growth, respectively. Since one cytostatic agent alone may not be capable of destroying all the leukaemia cells, a combination of cytostatics that function in different ways are usually given (polychemotherapy). The aim is to achieve the greatest possible effect against the malignant cells.

- **Chemotherapy concepts for patients with Down syndrome or APL:** Patients with Down syndrome do not require a chemotherapy as intensive as oth-er patients with AML do. Patients with acute promyelocytic leukaemia (APL) – a subtype of AML – may do completely without chemotherapy. They receive other substances instead.

- **Radiation therapy:** In few cases, radiotherapy of the brain (cranial irradiation) is performed in addition to chemotherapy to treat *central nervous system* (CNS) involvement. This may be the case if CNS involvement persists, that means, if the leukaemia cells do not respond to chemotherapy of the CNS (*intrathecal chemotherapy*).

- **Targeted therapy:** In patients with certain *immunological* subtypes of AML (for example, FLT3-ITD/TKD-positive AML), targeted therapy with *tyrosine kinase* inhibitors (FLT3 inhibitors such as sorafenib) may be considered in addition to chemotherapy. In these patients, the leukaemia cells harbour a *mutation* in the *FLT3* gene. This leads to an altered FLT3 receptor protein on

the surface of the leukaemia cells, which stimulates their growth and proliferation. The FLT3 inhibitor halts the growth of the leukaemia cells; they die off (*apoptosis*). The FLT3 mutation occurs in approximately 10–15% of AML patients.

- **Stem cell therapy:** For patients who do not respond to treatment from the very beginning or who develop recurrent disease, *high-dose chemotherapy* followed by *allogeneic stem cell transplantation* may be an option. The major goal of treatment is to eliminate the leukaemia cells in the body as extensively as possible, so that the *bone marrow* can resume its function as a blood cell-producing organ.

In order to prevent or adequately manage the side effects of the intensive therapy, specific supportive care regimens have been established and now represent an important and efficient component of AML treatment.

Good to know: The intensity and duration of *chemotherapy*, the need for *radiation therapy* and/or *stem cell transplantation*, as well as the *prognosis* of the disease, depend on the subtype of AML, on how extensively the leukaemia cells have spread throughout the body, whether the patient tolerates the treatment, and whether the leukaemia responds to it (*see chapter "Treatment planning"*).

8.2. Treatment courses (chemotherapy)

In general (i.e. apart from for above-mentioned specific cases in patients with Down syndrome or APL), *chemotherapy* of children and teenagers with AML consists of different steps. These steps (or phases) have different purposes. Therefore, they vary regarding their duration, treatment intensity, and the drug combinations applied. Major treatment elements are:

1. **Induction therapy:** Induction consists of an intensive chemotherapy with various anticancer agents (polychemotherapy). It aims at achieving *remission*, i.e. elimination of most of the leukaemia cells, in a relatively short period of time. Induction therapy usually takes about two months, comprising two courses of chemotherapy, with a phase of recovery in between.

2. **Consolidation therapy:** Consolidation follows induction therapy. It includes two to three courses of intensive chemotherapy, however, partially with different agents than those used during induction. With consolidation therapy, which takes about three to four months, the remaining leukaemia cells are to be further reduced, thus minimising the patient's risk of developing recurrent disease.

3. **CNS-directed therapy:** Treatment of the *central nervous system* (CNS-directed therapy) is recommended for all patients with AML. It is meant to either prevent a spread of leukaemia cells to the CNS (prophylactic treatment) or, in case the CNS is already affected, to stop them from being dispersed any further (therapeutic treatment). In any case, CNS-treatment occurs during systemic therapy and includes the application of anticancer drugs into the spinal canal via a *lumbar puncture* (*intrathecal chemotherapy*). If CNS involvement persists, *radiotherapy* of the brain may be recommended after intensive chemotherapy, that is, in addition to intrathekal

chemotherapy. Radiation takes about two to three weeks and is carried out subsequent to consolidation therapy.

4. **Maintenance therapy:** Maintenance therapy consists of a less intense polychemotherapy. It is mostly given orally while the children are out-patients. The goal of performing maintenance therapy is to fight all leukaemia cells that might have survived the intensive treatment over a long period of time, usually about a year after cessation of intensive therapy. **Important note:** Recently, maintenance therapy has no longer been part of the treatment!

Some patients, for example children with high numbers of leukaemia cells (high white blood cell counts) at diagnosis or patients with severe involvement of other organs, receive a so-called **pretreatment** prior to the induction therapy (*cytoreductive* preliminary phase). The treatment consists of a short, approximately one week long, phase of chemotherapy using moderate dosages of one or two different agents. The purpose of this phase is to reduce the often initially heavy burden of leukaemia cells gradually. This relatively gentle start helps the doctors to keep the metabolic products released by the dying leukaemia cells under control, which is important, because such metabolites can seriously harm the patient's organs, especially the kidneys (so-called *tumour lysis syndrome*).

The **overall treatment time** is about half a year without maintenance therapy (as long as no *stem cell transplantation* is required, the patient responds to therapy and does not suffer disease relapse). These intensive six months of treatment require various times as an inpatient. Recovery breaks between chemotherapy cycles, however, can be spent at home as long as the patient does not experience any serious complications such as fever and/or infections. During the moderately intense, longer time (about a year) of maintenance therapy, which until recently formed part of the treatment, the patient was allowed be at home. However, regular follow-up visits in the outpatient clinic were to be attended.

9. Therapy optimising trials and registries

In Germany, diagnosis and treatment of almost all children and adolescents with first diagnosis of acute myeloid leukaemia (AML) are performed according to the treatment plans (protocols) of *therapy optimising trial*s, so named because the treatment concepts of such trials are continously being optimised based on the respective current status of medical knowledge. Therapy optimising trials are standardised, controlled studies which aim at steadily developing and improving treatment possibilities for cancer patients. With many treatment centres being involved, such trials are also called "multicenter" or "multicentric" trials, and most often many countries participate.

Patients who are not included in any trial, either because they suffer disease while there is no trial available or because they do not, for some reason, fit into one of the existing trials, are often included in so-called **registries**. The patients are generally treated according to the recommendations of the trial centre, thus receiving the current best therapy available.

Currently, the following therapy optimising trials and registries are available for children and adolescents with AML in Germany:

- **AIEOP-BFM-AML 2020**: Since the end of February 2023, children and adolescents with AML can be included in the international therapy optimising trial AIEOP-BFM-AML 2020. Eligible are patients (under 18 years) with primary AML diagnosis and patients (under 21 years) with AML relapse, respectively. AML patients with acute promyelocyte leukaemia, *Down syndrome*, and/or a transient myeloproliferative syndrome are not included. Aim of the study is to increase cure rates as well as to reduce side-effects of the treatment by means of new agents or such with a different mechanism of action. Numerous treatment centres throughout Germany as well as other European countries participate in this trial. **Note:** Randomization for patients with newly diagnosed AML was closed on February 19, 2026. All patients will be treated in the standard-of-care arm.

- **Registry AML-BFM 2017:** Since the beginning of 2018, all AML patients under 18 years of age can register in the registry AML-BFM 2017 (which is the subsequent version of the registry AML-BFM 2012). This applies to patients with primary AML diagnosis as well as with AML relapse or AML as a secondary malignancy, respectively. The registry also documents patients with acute promyelocytic leukaemia (APL) and patients with down syndrome and AML, if they are not treated within a trial (*see below*). Infants with Down syndrome, who have been diagnosed with a so-called transient myeloproliferative syndrome (TMD), are registered as well. TMD is a disease that frequently transforms into an AML. The registry aims at collecting disease- and treatment-associated data of as many AML patients as possible in order to further optimise the understanding and treatment of the disease. It also provides treatment recommendations for patients who are not eligible for / participating in any trial in order to maintain optimal treatment options for them.

- **Trial ML-DS 2018:** For children with Down syndrome and AML (briefly ML-DS), the therapy optimising trial ML-DS 2018 has been open since February 2018. Eligible are patients with or without *GATA1* mutation who are older than 6 months and younger than 4 years of age OR patients with *GATA1* mutation who are older than 4 years and younger than 6 years of age. Goal of the study is to analyse whether reducing treatment intensity, and thereby further minimizing side effects, is an option for patients with good response to therapy. Multiple treatment centres throughout Germany and other European countries are participating in this trial.

Note: The trial centre for above-mentioned trials/registry is located at the University Hospital Frankfurt (principal investigator: Prof. Dr. Jan-Henning Klusmann).

10. Prognosis

Thanks to the immense progress in diagnostics and treatment over the last four decades, the chances of cure for children and adolescents with acute myeloid leukaemia (AML) have significantly improved. Today's modern diagnostic procedures and the use of intensive, standardised polychemotherapy protocols combined with optimised supportive care regimens result in current 5-year survival rates of 75 to 80 %.

However, this also means that in approximately 20 to 25 % of the young patients the disease cannot be controlled, which is mainly due to the high rates of disease relapses: nearly one third of

the children and adolescents diagnosed with AML in Germany per year suffer recurrent disease. Furthermore, about 10 % of patients do not respond to therapy and, thus, do not attain *remission* after the intensive treatment phase.

The individual prognosis of a patient primarily depends on the genetic subtype of AML as well as on how well the disease responds to therapy. Patients with favourable genetic subtype and good treatment response can achieve cure rates up to 90 %. The cure rates for patients with unfavourable *prognostic factors*, however, are far beyond 70 %, even when treated according to intensified regimens. Due to their low risk of relapse, patients with newly diagnosed acute promyelocytic leukaemia (APL) have a 10-year-survival rate of more than 90 % and, thus, a far better prognosis than patients with other AML subtypes.

In case of a relapse, prognosis is generally worse, in particular, if the disease comes back early, such as within a year after achievement of the first remission. This also applies to patients with no response to therapy. However, prognosis after relapse has improved during the last decade due to better therapy regimens including stem cell transplantation. The 5-year survival rates in children and adolescents with AML relapse are currently in the range of 40 %. The major goal of the current therapy optimising trials and future studies is to find ways to further improve the chances of cure for all AML patients, including those with recurrent disease.

Note: The survival rates mentioned in the text above are statistical values. Therefore, they only provide information on the total cohort of patients with childhood AML. They do not predict individual outcomes. Acute leukaemias can show unpredictable courses, in both patients with favourable and patients with unfavourable preconditions.

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Glossary

acute lymphoblastic leukaemia	lymphoblastic leukaemia, predominant form of leukaemia in childhood and adolescence
allogeneic stem cell transplantation	transfer of stem cells from a donor to a recipient. The prerequisite for an allogeneic transplant is that the tissue characteristics of the donor and recipient are largely identical. The stem cells are obtained from the blood or bone marrow.
anaemia	„lack of blood“; reduction of the red blood pigment (haemoglobin) and/or the proportion of red blood cells (haematocrit) in the blood below the normal value typical for a given age. Signs of anaemia include palor, headache, dizziness, and fatigue.
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.
apoptosis	programmed cell death; form of cell death, which is triggered by various mechanisms in the cell itself; this can happen naturally in the context of cellular aging, but also, for example, in response to cell damage (e.g. caused by cytostatics, radiotherapy).
blood coagulation	phased solidification of the liquid blood; intact blood clotting is important, for example, in haemostasis and wound healing during or after surgery. Impaired blood clotting leads to an increased tendency to bleed and/or prolonged bleeding time (e.g. after an injury). Increased blood clotting can cause thrombosis, for example.
blood count	blood test to determine the qualitative and quantitative composition of the blood in a blood sample: the number of red and white blood cells as well as platelets, the haemoglobin content (Hb value) of the blood and the volume fraction of red blood cells in the entire blood volume (haematocrit) are assessed. The "complete blood count" also includes a so-called differential blood cell count, in which the white blood cells in particular are examined more precisely for their composition (percentages of the various subtypes) and their appearance.
blood group	hereditary, usually stable, structural characteristics (blood group antigens) of blood components (e.g. AB0 blood groups) located on the cell walls of blood and other tissue cells;

blood stem cells	precursor cells of all blood cells, which give rise to red blood cells (erythrocytes), white blood cells (leukocytes), platelets (thrombocytes) and some other cells. This process is called blood formation. The various blood cells are formed in the bone marrow before they enter the blood stream.
blood transfusion	transfer of blood (whole blood) or blood components (e.g. red blood cells or platelets) from a donor to a recipient
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.
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)
cytogenetic	the number and structure of the chromosomes contained in the nucleus
cytomorphological	referring to the shape and structure of the cells (under the microscope); the cytomorphological assessment of bone marrow and blood smears is part of the basic diagnosis if a blood disease, such as leukemia, is suspected.
cytoreductive	cyt-: part of the word meaning „cell“; reductive means „reducing“; decreasing the number of cells
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.
Down syndrome	congenital disorder associated with maldevelopment of tissues and organs, mental retardation that varies from person to person, short stature and malformations in the facial area; patients with Down syndrome also have an increased risk of developing cancer, especially leukaemia. Down syndrome is caused by a chromosomal alteration: chromosome 21 is present in every cell of the body in three copies instead of two (Trisomy 21). As a result, tissues and organs grow more slowly, remain immature, age faster and have malformations.
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.

erythrocytes	red blood cells, the most abundant cells in the blood, they are mainly used to transport oxygen in the body; erythrocytes are formed in the bone marrow (erythropoiesis). The red blood pigment (haemoglobin) inside the erythrocytes is responsible for binding and transporting the oxygen absorbed in the lungs. If red blood cells are not present in sufficient quantities or, due to a lack of haemoglobin, are not functional, it is referred to as anaemia.
Fanconi anaemia	hereditary haematopoietic disorder; it is mainly characterized by a progressive dysfunction of the bone marrow, which leads to a reduced formation of blood cells (bone marrow insufficiency), as well as by chronic anaemia and a high risk of cancer (especially for acute myeloid leukaemia). Other concomitant symptoms include skeletal malformations (e.g. short stature, malformations of the thumbs and arms). Fanconi anemia is one of the cancer predisposition syndromes. At the cellular level, there is an increased chromosomal fragility; this leads to chromosomal changes and, as a result, to disorders of cell cycle control.
genetic	concerning the (level of) inheritance or genes; inherited
granulocytes	subgroup of white blood cells (leukocytes); they are mainly responsible for defending against bacteria and other pathogens (such as viruses, parasites and fungi); granulocytes are also involved in allergic and inflammatory reactions, as well as pus formation. Granulocytes make up about 60 – 70% of the leukocytes in the blood. Due to their differently colourable granules and their different tasks, they are divided into three subtypes: neutrophils (90 %), eosinophils (2 – 4 %) and basophilic granulocytes (up to 1 %). The neutrophils (neutrophils for short) play the most important role in the defense against infections.
high-dose chemotherapy	the use of a particularly high dose of cell growth-inhibiting drugs (cytostatics); in the case of cancer, it aims to destroy all malignant cells. Since the haematopoietic system in the bone marrow is also destroyed, the patients own or foreign blood stem cells must then be transferred (autologous or allogeneic stem cell transplantation).
Hodgkin lymphoma	malignant disease of the lymphatic system; belongs to the malignant lymphomas and accounts for about 5% of malignant diseases in childhood and adolescence.
hyperleukocytosis	severe leukocytosis, i.e. a greatly increased number of white blood cells (leukocytes) in the blood compared to the age-

	appropriate norm (over 100,000 compared to 5,000 to 8,000 leukocytes per microlitre of blood).
immunodeficiency	congenital or acquired disorder of the immune system that results in a weakening of the bodys immune response; this leads to the fact that pathogens and consequently infections cannot be sufficiently or adequately fended off.
immunological	associated with the structure and function of the bodys own defense system (immune system); includes the recognition and defense mechanisms of an organism for foreign and endogenous substances and tissues.
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.
intrathecal chemotherapy	administration of cell growth-inhibiting drugs (cytostatics) into the cerebrospinal fluid (CSF) canal, which contains the CSF
leukaemia	malignant disease of the blood forming (haematopoietic) system and the most common cancer in children and adolescents (about 33%); depending on the origin of the malignant cells, a distinction is made between lymphoblastic and myeloid leukaemias. Depending on the course of the disease (fast or slow), a distinction is made between acute and chronic leukaemias.
leukocytes	white blood cells; they serve as cells of the immune system, defending against pathogens and fighting infections. In addition, they remove the cell debris produced by the decay of body cells. Leukocytes include granulocytes (with 60 – 70 %), lymphocytes (20 – 30 %) and monocytes (2 – 6 %). Leukocytes are mainly produced in the bone marrow. This process is called leucopoiesis.
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.
lymphatic system	collective term for lymphatic vessels, lymphatic vessel trunks, lymph nodes, lymphatic tissues (lymphocytes in connective tissue, mucous membranes, glands) and lymphatic organs (spleen, pharyngeal tonsils, bone marrow, thymus gland).
lymphocytes	subgroup of white blood cells that are responsible for the bodys own defenses, especially the defense against viruses; there are B and T lymphocytes. They are formed in the bone marrow, but partly only mature to full functionality in the lymphatic tissue (e.g. lymph nodes, spleen, thymus gland). They eventually enter the blood via the lymphatic vessels, where they take over their respective tasks.
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.
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.
monocytes	subtype of white blood cells (leukocytes); after maturing in the bone marrow, they circulate in the blood for one to two days and serve as an immune defense. Subsequently, they migrate into various tissues and develop there into local, tissue-typical macrophages ("large scavenger cells").
monosomy 7	congenital condition associated with an increased risk of developing acute myeloid leukaemia (AML); the disease is caused by a genetic change (mutation) in which chromosome 7 is only present in a single rather than double version due to chromosome loss.

mutation	alteration of genetic material; it can arise without any identifiable external cause (so-called spontaneous mutation) or be caused by external influences (induced mutation). External influences include, for example, ionizing radiation or certain chemical substances (mutagens). If somatic cells are affected, it is referred to as a somatic mutation, and if germ cells are affected, it is referred to as a generative mutation. Somatic mutations are not heritable, while germ cell mutations can lead to hereditary damage. Depending on the extent of the change (single or multiple genes, larger chromosome segments or complete chromosomes), a distinction is made between point and block mutations as well as numerical and structural chromosomal aberrations.
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.
neutropenia	reduction of neutrophils in the blood, increasing susceptibility to bacterial infections; the extreme form of neutropenia is agranulocytosis.
petechiae	smallest, punctual bleedings of the skin and/or mucous membranes
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.
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);

radioactive radiation	radiation produced by the decay (nuclear decay) of radioactive substances; these are substances with unstable atomic nuclei that spontaneously transform by releasing energy. The energy released is emitted as ionizing radiation (high-energy particles and/or gamma radiation).
radiotherapy	controlled use of ionizing (high-energy) radiation for the treatment of malignant diseases
remission	temporary or permanent decrease or disappearance of the signs of cancer.
stem cell transplantation	transfer of haematopoietic stem cells after conditioning chemotherapy, radiation or immunosuppression of the recipient; the stem cells can be obtained either from the bone marrow or from the bloodstream. In the first case, the procedure of their transfer is called bone marrow transplantation, in the second case peripheral stem cell transplantation. Depending on the type of donor, a distinction is made between two forms of SCT: allogeneic SCT (stem cells from a foreign donor) and autologous SCT (own stem cells).
symptom	sign of illness
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.
thrombocytes	blood cells that are responsible for haemostasis; they ensure that, in the event of an injury, the walls of the blood vessels are sealed within a very short time, thus stopping the bleeding.
tumour lysis syndrome	metabolic changes due to tumour cell death as a consequence of cancer treatment, usually with large masses or cell counts, after chemotherapy; the changes are manifested by increased uric acid, potassium and phosphate levels, as well as a decrease in serum calcium concentrations, which can result in acute renal failure.
tyrosine kinase	enzymes from the protein kinase family; they particulalrly contribute to the transmission of signals within a cell and are important for embryonic development as well as the regeneration and maintenance of tissues. Functional disorders can play a role in the development of cancer, among other pathological conditions.

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.
virus	viruses are infectious particles that do not have their own metabolism and therefore depend on host cells for their reproduction, on which they often have a pathogenic effect.
WHO classification	international guideline developed by the World Health Organization (WHO) for classification, diagnosis and differentiation/grading of (malignant) diseases
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.