

Hodgkin Lymphoma – Brief Information

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Hodgkin Lymphoma – Brief Information

1. General information

Hodgkin lymphoma, also known as Morbus Hodgkin, Hodgkin's lymphoma or Hodgkin's Disease, is a cancer of the lymphatic system. Like the large entity of Non-Hodgkin-Lymphomas (NHL), it belongs to the group of malignant lymphomas.

"Malignant lymphoma" literally means "malignant tumour of the lymph node". Medically speaking, the term summarises all cancers that arise from cells of the lymphatic system (lymphocytes) and that can cause lymph node swelling.

Malignant lymphomas are classified into two major groups: Hodgkin's lymphoma, which is named after the physician and pathologist Dr. Thomas Hodgkin, and the Non-Hodgkin lymphomas (NHL). Differentiation between these two types of lymphomas is only possible by analysing the affected tissue under the microscope (histological examination).

Hodgkin lymphoma develops from transformed B-lymphocytes, a type of white blood cells (leukocytes) found in lymphatic tissue. Hodgkin lymphoma can arise from every organ comprised of lymphatic tissue. The most common localisation is the lymph nodes, however, liver, bone marrow, lungs or spleen can also be affected, especially in advanced stages of the disease. Without adequate treatment, Hodgkin lymphoma is a fatal disease in most patients.

2. Incidence

Hodgkin lymphoma is the most frequent lymphoma disease in childhood. According to the German Childhood Cancer Registry in Mainz, about 80 children and teenagers aged younger than 15 are newly diagnosed with Hodgkin lymphoma in Germany per year. Counting all paediatric patients (under 18 years of age), the incidence is about 180 diagnoses per year. Thus, depending on the age range considered, Hodgkin lymphoma accounts for approximately 4.5 % and 7.5 % of all paediatric malignancies, respectively.

Hodgkin lymphoma is rarely diagnosed in children younger than 3 years. With increasing age, incidence gets more and more frequent, with boys being slightly more affected than girls. The incidence in children and adolescents (between 0 and 17 years) peaks at 15 years of age.

3. Causes

The causes of Hodgkin lymphoma still have to be elucidated. It is known so far that the disease arises from the malignant transformation of cells in the lymphatic system, the B-lymphocytes, and also, that this transformation is 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, is not known yet. Most certainly, Hodgkin lymphoma is caused by a specific combination of many factors.



A clustering of Hodgkin lymphoma patients within the white (Caucasian) population may suggest a genetic and also ethnological predisposition to the disease. Furthermore, children with certain congenital diseases of the immune system (such as Wiskott-Aldrich syndrome, Louis-Bar syndrome) or acquired immune deficiencies (for example due to HIV infection) are known to be at a higher risk to develop a Hodgkin lymphoma. In addition, the Epstein-Barr-Virus (EBV), which is well-known as the cause of infectious mononucleosis, seems to be associated with the development of Hodgkin lymphoma in some patients. Whether certain environmental factors (such as pesticides) promote Hodgkin lymphoma is currently being examined. However, for the majority of patients, no specific risk factor has been established yet.

4. Symptoms

Hodgkin lymphoma begins subtly and symptoms develop slowly in most cases, i.e. within weeks or months. First sign of the disease is usually a painless swelling of one or more lymph nodes in the regions of the neck, clavicles, armpits and/or groins.

However, the disease can also arise from lymph nodes that can not be seen or palpated at all, such as those behind the breastbone, in the chest, abdomen or along the spine. Since the cancer is continuously growing, the affected lymph nodes will soon become space occupying, thereby impairing inner organs and their functions. Therefore, enlarged lymph nodes in certain parts of the chest (mediastinum) may cause a dry cough or breathing difficulties, while others, in the abdomen for example, can result in diffuse abdominal pain and indigestion.

Enlargement of the spleen and liver (splenomegaly, hepatomegaly) due to lymphoma cell invasion is less frequent. If the lymphocytes in the bone marrow are involved, they occupy space within the hollow interior of bones. As a result, Hodgkin lymphoma can cause reduced production of red and white blood cells and, thus, anaemia and a predisposition for infections. However, these cases are rare.

Nonspecific (general) symptoms may include fever, weight loss, drenching night sweats, fatigue, and itchy skin. The first three symptoms are frequent in patients with Hodgkin lymphoma. They are called B-symptoms.

The following overview summarizes the most frequent symptoms caused by Hodgkin lymphoma.

4.1. General symptoms

- fever of unknown origin (over 38°C for three consecutive days) [B-symptom]
- night sweats [B-symptom]
- unexplained weight loss (more than 10 % in six consecutive months prior to admission) [B-symptom]
- fatigue, loss of appetite, malaise



· itchy skin

4.2. Specific symptoms

- in more than 90 % of patients: painless, palpable, superficial lymph node swellings, for example in the area of the neck (most frequent location), in the armpit, above the clavicle, in the groins or simultaneously at multiple sites
- chronic cough, shortness of breath (if thoracic lymph nodes, lungs or pleura are involved)
- abdominal pain, back pain, diarrhea (if abdominal lymph nodes or organs, such as liver or spleen, are involved)
- pallor due to lack of red blood cells (anaemia; if the bone marrow is involved)
- · bone or joint pain (if bones are involved)

Symptoms and complaints usually develop slowly in patients with Hodgkin lymphoma (over weeks or months). They can vary individually as to which symptoms prevail and how pronounced they are.

Good to know: The occurence of one or more of the above-mentioned symptoms does not necessarily mean that they are caused by a Hodgkin lymphoma. Several of these symptoms, such as lymph node swelling and fever, are exactly those often seen with common childhood diseases like common colds and other viral infections. Nevertheless, it is strongly recommended to have the child or teenager see a paediatrician, in particular, if symptoms persist or progress.

5. Diagnosis

If the paediatrician thinks that the young patient's history, physical exam and possibly even results from blood tests and/or imaging are suspicious of Hodgkin lymphoma, the child should be referred to a hospital with a childhood cancer program (paediatric oncology program), where further diagnostic tests can be initiated and performed by childhood cancer specialists. These tests serve to confirm or rule out the suspected diagnosis and to assess a possible spread of the disease ("staging").

5.1. Obtaining a tumour sample (biopsy)

For diagnosis, surgical removal and investigation of a lymph node or another tissue affected by the disease is required. Apart from histological investigation based on how the he cells look like under the microscope, im-munohistochemical and, if possible, investigations on molecular genetics in these samples allow both the confirmation of the diagnosis and the determination of the subtype of Hodgkin lymphoma. Knowing the subtype of Hodgkin lymphoma helps to plan the treatment.

5.2. Tests to assess spread of the disease

Once the diagnosis of Hodgkin lymphoma has been confirmed, further tests are required to find out if and to which extent the cancer has spread and which organs are involved. These tests include



imaging, such as ultrasound of the belly (abdomen) and lymph nodes, chest radiographs, magnetic resonance imaging (MRI) of the abdomen and pelvis, computed tomography (CT), and positron emission tomography (PET). Total body-PET is usually combined with a CT-scan (PET-CT) and/or an MRI (PET-MRI). Overall, MRI is the preferred imaging procedure, since it is not associated with radiation. However, to check the lungs and/or quickly assess the stage of the disease, CT is required. Sometimes, when bone involvement is suspected, a bone scan might be necessary as well.

In order to find out whether the bone marrow is affected by the disease, bone marrow biopsy and subsequent screening for lymphoma cells in the obtained bone marrow sample has been a diagnostic standard for a while. According to the current treatment protocol, EuroNet-PHL-C2, potential bone marrow involvement is assessed by PET, and biopsy is not required for these patients any more.

5.3. Tests before treatment begins

For treatment preparation, tests on the patient's cardiac function (electrocardiography and echocardiography) are performed. Furthermore, additional blood tests are needed to assess the patient's general health condition and to check whether the function of certain organs (such as liver and kidneys) is affected by the disease and whether there are any metabolic disorders to be considered prior or during therapy.

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. Also, the patient's blood group needs to be determined in case a transfusion is required during treatment.

Good to know: Not every patient needs the complete check-up. Your caregivers will inform you and your child, which diagnostic procedures are individually required in your case and why.

6. Treatment planning

After having established the diagnosis, the doctors will plan the treatment. In order to provide a therapy that is specifically designed for the patient's individual situation (risk-adapted therapy), the doctors will take into consideration certain factors that have been shown to have an impact on the prognosis (so-called risk factors or prognostic factors).

The following characteristics of Hodgkin lymphoma represent important prognostic factors and major criteria for treatment planning:

- histological characteristics (histological subtype): the subtype of Hodgkin lymphoma decides according to which therapy protocol or therapy optimizing trial the patient will be treated.
- stage of the disease: the extent of the disease in- and outside the lymphatic tissue as well
 as the presence (or absence) of other stage-defining factors (such as B-symptoms, elevated
 blood sedimentation rate, high tumour load) are crucial for assigning a patient to the appropriate



treatment group or treatment level, respectively. Three treatment groups / levels are currently being differentiated, considering patients with early, medium and advanced stages of the disease. Treatment intensities differ accordingly. This risk-adapted approach provides a strategy by which also patients with advanced stages of the disease have a chance of cure.

 response of the disease to chemotherapy: a major criteria for decision-making regarding the necessity of radiotherapy.

The following chapters provide information on the histological subtypes of Hodgkin lymphoma and on the different stages of the disease.

6.1. Types of Hodgkin Lymphoma

Based on the different characteristic microscopic features, the World Health Organisation (WHO) recognises five Hodgkin lymphoma subtypes, four of which are grouped as "classical Hodgkin lymphoma".

- a. Nodular lymphocyte-predominant Hodgkin lymphoma (LPHL)
- b. Classical Hodgkin lymphoma:
- Nodular sclerosis subtype (NS)
- Lymphocyte-rich subtype (LR)
- Mixed cellularity subtype (MC)
- Lymphocyte-depleted subtype (LD)

The different subtypes vary regarding incidences, courses of the disease as well as prognosis. In particular, LPHL is now considered a separate disease and treated differently than classical Hodgkin lymphoma. With an incidence of almost 70%, the NS subtype is the most frequent in Western countries, followed by the mixed cellularity subtype (MS). The other two subtypes are rather rare in children and adolescents.

6.2. Stages of Hodgkin Lymphoma

Staging of Hodgkin lymphoma is crucial for both treatment planning and estimating prognosis. The stage of the disease is primarily assessed based on its spread at the time of initial diagnosis. It describes which lymph node regions of the body are involved and how many. Staging also helps to assess whether the disease has spread to organs outside the lymphatic system (extranodal or extralymphatic disease). If such extralymphatic disease involves a single extralymphatic organ / site that lies adjacent to a known involved lymph node site, it is noted by an "E" (please see below).

The stages of Hodgkin lymphoma are classified according to the updated Ann Arbor staging using the terms I through IV as shown in the following table:



Hodgkin lymphoma stage grouping including E-stages:

Stage of Disease	Definition
Stage I	Lymphoma is found in one single lymph node region (stage 1). It may as well extend to one single extralymphatic organ or site, such as chest wall, heart sac or lung (stage IE).
Stage II	Lymphoma is found in two or more lymph node regions on the same side of the diaphragm (stage II). It may as well extend to a single adjacent extralymphatic organ or site, such as chest wall, heart sac or lung (stage IIE).
Stage III	Lymphoma is found in lymph node regions on both sides of the diaphragm (stage III). It may as well to an extralymphatic organ/site (stage IIIE) and/or the spleen (stage IIIES or IIIS, respectively).
Stage IV	Noncontiguos involvement of one or more extralymphatic organs or tissues (such as lungs, liver, bone, bone marrow) with or without involving (distant) lymph nodes

Abbreviations: \mathbf{E} – extralymphatic, notes that the cancer has spread to organs or tissues outside the lymphatic system (by infiltration from the affected lymph node region); \mathbf{S} – spleen, notes cancerous involvement of the spleen.

Each of the four stages are subgrouped either into the A- or B-category depending on the absence (category A) or presence (category B) of the following symptoms (B-symptoms):

- unexplained body weight loss of 10 % or more in the six months prior to admission and/or
- fever higher than 38°C for three consecutive days prior to admission
- drenching night sweats

The presence or absence of B-symptoms is labelled for all stage groups by the suffix B or A, respectively (for example: stage IB or IA).

Special considerations provided by the current treatment protocol:

In addition to E-stages and B-symptoms, trial EURONet-PHL-C2 also considers two additional factors for staging and treatment planning: elevated erythrocyte sedimentation rate ("sed rate"; ESR) and large tumour load ("bulky disease", "bulk").

Good to know: the presence of E-stages and/or B-symptoms, bulky disease exceeding a defined tumour load or elevated erythrocyte sedimentation rate has shown to negatively impact prognosis. Hence, patients presenting with these findings require a more intensive treatment than patients without these risk factors and are therefore assigned to higher treatment levels.



7. Treatment

Treatment of children and adolescents with Hodgkin lymphoma should take place in a children's hospital with a paediatric oncology program. Only such a treatment centre provides highly experienced and qualified staff (doctors, nurses and many more) that is 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 the treatment is to achieve high cure rates while avoiding acute or long-term side effects as much as possible.

7.1. Treatment methods

Treatment options for Hodgkin lymphoma include chemo- and radiotherapy as well as high-dose chemotherapy followed by stem cell transplantation.

Central backbone of current treatment concepts for Hodgkin lymphoma is chemotherapy. It uses drugs (so-called cytostatic agents) 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 lymphoma cells, a combination of cytostatics that function in different ways is given (polychemotherapy). The goal is to eliminate as many malignant cells as possible.

For some patients, low-dose radiation therapy of the affected regions is additionally recommended. However, in order to reduce radiation-induced late effects, radiotherapy has been used continuously less during the last years. Today, only certain patients receive radiotherapy, for example when their disease does not sufficiently respond to chemotherapy (*please see chapter "Course of treatment"*).

In very rare situations, for example in case of non-response to chemo- and radiotherapy or recurrent disease (relapse), respectively, high-dose chemotherapy followed by stem cell transplantation may be considered as an effective treatment option. The high doses of cytostatics given according to this treatment strategy are capable of eliminating the resistant lymphoma cells. Since high-dose chemotherapy also leads to the destruction of the blood-forming cells in the bone marrow, the patient will receive blood forming stem cells in a second step. Usually, these stem cells are obtained from the patient's blood or bone marrow prior to high-dose chemotherapy and are given back right after this treatment (so-called autologous stem cell transplantation, SCT).

The duration and intensity of chemotherapy, as well as the necessity of radiation or stem cell transplantation, and last but not least, the patient's individual prognosis is dependent on the extent (stage) of the disease at initial diagnosis and how it responds to treatment. The subtype of Hodgkin lymphoma only marginally determines the treatment strategies for children and adolescents.

Special considerations for patients with Lymphocyte Predominant Hodgkin Lymphoma (LPHL)

Certain treatment modifications are applied to children and adolescents with LPHL: in contrast to patients with classical Hodgkin lymphoma, patients with early stage LPHL (stage IA) do usually not receive any chemo- or radiotherapy, as long as only one lymph node is affected and can be easily



removed completely. Experience has shown that about two thirds of these patients will defeat their disease without chemo- and radiotherapy. However, regular follow-up examinations are necessary to closely observe the course of the disease (observatory approach). In case of recurrent disease, intensive treatment is recommended.

More than 80-85 % of patients with LPHL are diagnosed with stage IA or IIA. While patients presenting with stage IIA as well as with IA and residual tumour usually receive a rather mild chemotherapy, treatment as for classical Hodgkin lymphoma is recommended for those with higher stages of LPHL.

7.2. Course of treatment

The following information describes the treatment for patients with classical Hodgkin lymphoma. Therapy is currently given as per protocol of trial EuroNet-PHL-C2 (*please see chapter "Therapy optimising trials"*).

Chemo- and radiotherapy are important treatment modalities used in these protocols. If radiotherapy is indicated, it is usually performed after cessation of chemotherapy. The decision whether radiotherapy is necessary or not is primarily based on the response of the disease to chemotherapy (*please see below*).

Note regarding trial EuroNet-PHL-C2:

Within the framework of trial EuroNet-PHL-C2, current standard treatment is being compared with another promising, radiotherapy-sparing approach. The goal is to further reduce radiation-induced late-effects. After parents'/guardians' consent, patients with intermediate or advanced stages (stages II and III) of Hodgkin lymphoma are randomly assigned to two different treatment arms (standard and investigation arm). This strategy is called "randomisation". Chemotherapy as well as radiotherapy differ within the two treatment arms.

7.2.1. Chemotherapy

Chemotherapy for patients with classical Hodgkin lymphoma usually consists of multiple treatment cycles or blocks (blocks of chemotherapy). The quantity of blocks and, thus, treatment duration and intensity are based on the stage of the disease and the treatment group (TG) / treatment level (TL) they have been assigned to.

Usually, patients with

- early stages of the disease (TG / TL 1) receive 2 or 3 cycles of chemotherapy
- intermediate stages of the disease (TG / TL 2) receive 4 cycles of chemotherapy
- advanced stages of the disease (TG / TL 3) receive 6 cycles of chemotherapy

Every treatment block takes about two weeks and the different cycles partially contain different combinations of cytostatic agents. For example, "OEPA", a combination of vincristine (oncovin; "O"), etoposide (VP-16; "E"), prednisone ("P") and adriamycin (doxorubicin; "A") is the current standard for the first two blocks, the so-called "induction phase". All other blocks ("consolidation



phase") include "COPDAC", the standard combination of cyclophosphamide ("C"), vincristine ("O"), prednisone ("P") and dacarbacine ("DAC"). There are treatment breaks of about two weeks between single blocks. Duration of all chemotherapy is between two to six months if no relapse develops during or after treatment.

Note with regards to TG/TL: The term "treatment group" was routinely used in the context of the preceding trial EuroNet-PHL-C1. However, in the currently active trial EuroNet-PHL-C2, the term "treatment level" is used. Treatment group and treatment level do not only differ in naming (nomenclature-wise), but also regarding the contents they are referring to, meaning that patients with different risk factors are con-sidered. Therefore, both terms are mentioned here.

Note regarding trial EuroNet-PHL-C2:

In patients with advanced stages of Hodgkin lymphoma (TL 2 and 3), the standard consolidation therapy (COPDAC combination) is compared to a more intense consolidation treatment: Those patients who are randomly assigned to the standard arm receive the standard COPDAC combination (*please see above*) over 28 days, while patients in the investigation arm receive COPDAC as well, but in addition the agents etoposide and doxorubicin ("D"). This combination is called "DECOPDAC" and is given over 21 days ("DECOPDAC-21").

7.2.2. Radiotherapy

According to the recommendations of current trial EuroNet-PHL-C2 or the registry, respectively, less than half of all patients receive radiotherapy following chemotherapy. The prime decision-making factor regarding radiotherapy is not the stage of the disease (as it was a while ago), but the response of the disease to chemotherapy.

Standard treatment recommendations (also for patients in the trial's standard arm) are:

- Patients, whose disease shows good (adequate) response after two blocks of chemotherapy (assessed by PET) do not receive radiotherapy, regardless of the patient's treatment group or stage of the disease.
- Patients, whose disease does not sufficiently (not adequately) respond to the first two blocks of chemotherapy receive radiotherapy after chemotherapy.

"Good response" means, that the tumour as found at initial diagnosis now does not contain any live tumour cells any more, thus is PET-negative and also decreased in size for about 50% of its initial volume.

Radiotherapy usually starts about two weeks after cessation of chemotherapy, which is after a total of two or three (TL1), four (TL2) or six (TL3) blocks, depending on the patient's treatment level. The standard total radiation dose is 20 Gray (Gy) for all lymph node regions involved at initial diagnosis (more vulnerable organs are treated with lower doses in general, and in individual situations, higher doses are given as well).

In order to spare the healthy tissue that is surrounding the cancer, the total radiation dose is not given all at once. Instead, patients receive smaller portions of a maximum of 1.8 Gy per treatment.



Duration of radiotherapy comes to two to three weeks total. Radiotherapy is usually not performed over the weekends.

Note regarding trial EuroNet-PHL-C2

The standard radiotherapy as described above is given to all patients (treatment levels 1-3) of the standard chemotherapy arm (COPDAC-28). Patients in the investigation arm (DECOPDAC-21) only receive radiotherapy to those parts of the body that still show live tumour tissue with tumour diameters of more than 1 cm after completion of chemotherapy, thereby remaining PET-positive. Standard total radiation dose for these patients is 30 Gy.

The strategy applied to patients in the investigation arm helps to find out whether radiotherapy can be reduced after an intensified chemotherapy without jeopardizing treatment efficacy.

8. Therapy optimising trials

In Germany, treatment of almost all children and adolescents with Hodgkin lymphoma is performed according to the treatment plans (protocols) of therapy optimising trials. The term "therapy optimising trial" refers to a form of controlled clinical trial that aims at improving current treatment concepts for sick patients based on the current scientific knowledge. With many treatment centres being involved in this kind of standardised treatment, such studies are also called "multicentred" and "cooperative", and most often many countries participate.

The following trials for treatment of children and adolescents with Hodgkin lymphoma are currently active in Germany (with international participation):

- Trial EuroNet-PHL-C2: international multicentric therapy optimising trial for treatment of children and adolescents (under 18 years of age, in some European contries up to 25 years of age) with a newly diagnosed classical Hodgkin lymphoma. Trial EuroNet-PHL-C2 has been opened in October 2016 and represents the subsequent study of trial EuroNet-PHL-C1, which was closed in 2012. Many childrens' hospitals and paediatric oncology centres all over Germany as well as in other European and non-European countries are participating in the new trial.
- Trial EuroNet-PHL-LP1: an international multicentric therapy optimising trial for treatment of children and adolescents (under 18 years of age) with early stages of lymphocyte predominant Hodgkin lymphoma (LPHL, stages IA and IIA). Attention: this trial was closed for the enrollment of new German patients in November 2014. It was still active in other European countries until the end of 2018. The results of the study are currently being evaluated. German patients who had been enrolled prior to November 2014 are still receiving treatment as per protocol. Newly diagnosed patients are treated according to the recommendations of the study centre.

Note: the international and German study centre for the EuroNet-PHL-trials and the registry is located at the "Zentrum für Kinderheilkunde und Jugendmedizin der Universitätsklinik Gießen" (Department of Paediatrics, University of Gießen, Germany). The Pricipal Investigator is Prof. Dr. med. Dieter Körholz. "EuroNet-PHL" means "European Network Paediatric Hodgkin's Lymphoma".



9. Prognosis

Prognosis for newly diagnosed patients

Nowadays, long-term survival rates of children and teenagers after treatment of Hodgkin lymphoma are high: more than 9 out of 10 (95%) patients can be cured today, thanks to current modern diagnostics and standardised treatment concepts – and regardless of how advanced the disease had been at diagnosis. This is only possible due to the current treatment strategies that adjust the intensity of therapy (chemo- and radiotherapy) to the patient's individual situation by considering different treatment groups. Patients with more advanced stages of the disease (treatment groups II and III) need a more intensive therapy than patients presenting with earlier stages (treatment group I) in order to provide a comparably favourable prognosis.

Prognosis for patients with recurrent disease

According to the Morbus Hodgkin-Study Centre (Gießen, Germany), in about 11 % of patients aged younger than 18 years the disease does either not respond to current treatment strategies (progressive disease) or the patients later develop recurrent disease (relapse). In general, favourable long-term outcomes can be achieved for patients with relapsed Hodgkin lymphoma, too. Individual prognosis, however, depends primarily upon the timepoint of relapse and how intense primary treatment has been.

Patients with late relapse (more than one year after completion of therapy), who receive a second chemo- and radiotherapy for relapse treatment, have high survival rates (10-year survival of more than 90%). Patients with early stage of the disease at primary diagnosis (treatment group 1) and/ or those who have not received any radiotherapy as part of initial treatment also have a favourable prognosis.

The outcome of patients with early relapse (between three and twelve months after cessation of primary treatment) as well as with non-response or progressive disease have a less favourable outcome, even when given chemo- and radiotherapy for second therapy (10-year survival of about 75 or 50%, respectively). Comparable outcomes are seen for patients who already received intensified chemo- and radiotherapy for first treatment. Due to their high risk of developing recurrent disease, these patients may only benefit from the very intensive strategy of high-dose chemotherapy followed by autologous stem cell transplantation.

Note: The survival rates mentioned in the text above are statistical values. Therefore, they only provide information on the total cohort of patients with Hodgkin lymphoma. They do not predict individual outcomes. However, statistics help to estimate probabilities of survival.



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