NCCN GUIDELINES FOR PATIENTS®

2025

Hodgkin Lymphoma in Adults

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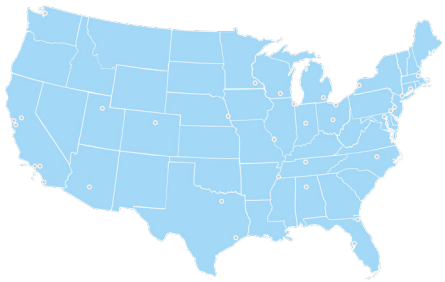
About the NCCN Guidelines for Patients®

National Comprehensive Cancer Network®



Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).

Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hodgkin Lymphoma, Version 2.2025 – January 30, 2025.

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NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

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1
About Hodgkin lymphoma

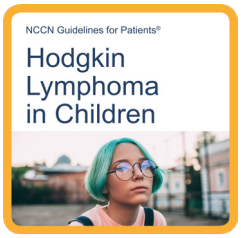
Hodgkin lymphoma is a highly curable cancer that usually starts in lymph nodes in the upper body. Most people are diagnosed between the ages of 15 to 30, or after age 55.

What is lymphoma?

Lymphoma is cancer that begins when white blood cells called lymphocytes grow out of control. Lymphomas are described as either Hodgkin or non-Hodgkin. Non-Hodgkin lymphomas are a large and varied group of cancers.

When viewed under a microscope, Hodgkin lymphoma cells look different than other lymphomas. The lymphocytes are abnormally large and may have more than one nucleus. These oversized lymphocytes are called Reed-Sternberg cells.

The focus of this resource is Hodgkin lymphoma in adults. Information on Hodgkin lymphoma in children and adolescents is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



What is the lymphatic system?

The lymphatic system is part of your immune system. It helps your body fight infection and disease.

The tissues and organs that make up the lymphatic system are described next. They are made mostly of lymphocytes. There are other types of white blood cells, but lymphocytes are the most important to understanding Hodgkin lymphoma.

Lymph and lymphatic vessels

There is a super-highway of ducts running through your body. These ducts are called lymphatic vessels. Much like how blood vessels transport blood, lymphatic vessels transport lymph. Lymph is a clear fluid that carries infection-fighting white blood cells (lymphocytes) throughout the body. It is also called lymphatic fluid.

Lymph nodes

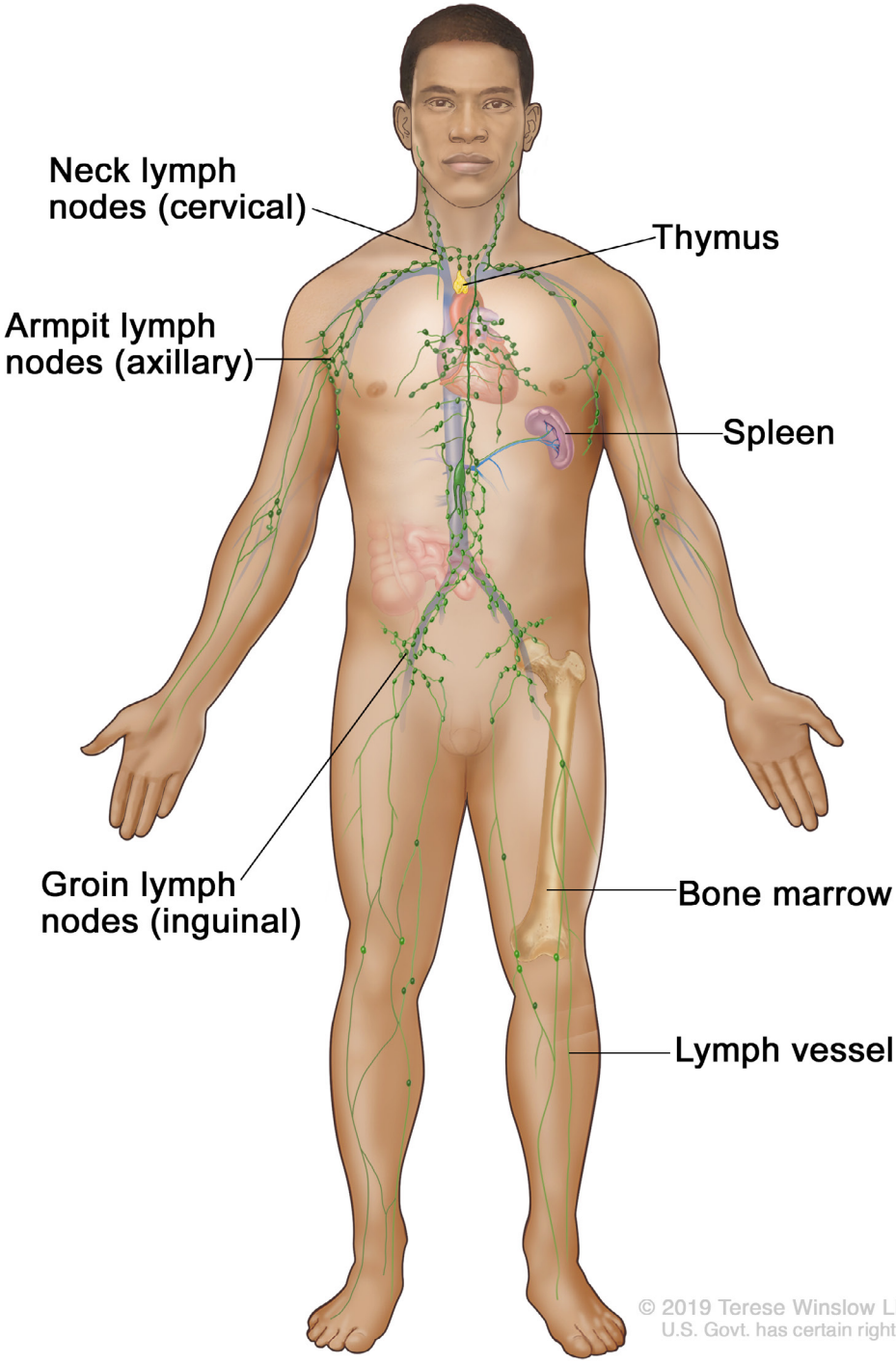
While lymph travels throughout your body in lymphatic vessels, it passes through hundreds of small bean-shaped structures called lymph nodes. Lymph nodes catch and filter out foreign particles and harmful cells, including cancer cells. Lymph nodes can't usually be seen or felt. The highest numbers of lymph nodes are found in the neck, groin, and armpits.

Spleen

The spleen is the largest organ of the lymphatic system. It is about 4 inches long and shaped like a fist. It makes lymphocytes and plays an important role in blood filtration and storage.

Lymphatic system

There are hundreds of small bean-shaped structures, called lymph nodes, throughout the human body. They catch and filter out foreign particles and harmful cells, including cancer cells.



Bone marrow

Most bones have soft, spongy tissue in the center called bone marrow. This is where new blood cells are made.

Thymus

After being made in bone marrow, lymphocytes travel to the thymus. The thymus is a small organ in the upper chest. Here lymphocytes develop into T lymphocytes (T cells), one of the two main types of lymphocytes.

The tonsils

Tonsils are small masses of lymph tissue found at the back of the throat. They help trap disease-causing germs that enter through your nose or mouth.

Types of Hodgkin lymphoma

There are 2 types of Hodgkin lymphoma, described next.

Classic Hodgkin lymphoma

Most people with Hodgkin lymphoma have classic Hodgkin lymphoma (CHL). CHL can be recognized by large lymphocytes called Reed-Sternberg cells.

While there are different subtypes of CHL, the same care is recommended for all of them.

NLPHL

While CHL is known for Reed-Sternberg cells, nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is known for popcorn-shaped cells.

This rare form of Hodgkin lymphoma usually grows slowly, but in rare cases behaves aggressively. Over time, it can transform into one of several types of fast-growing cancer, including diffuse large B-cell lymphoma (DLBCL).

What can you do to get the best care?

Advocate for yourself. You have an important role to play in your care. In fact, you're more likely to get the care you want by asking questions and making shared decisions with your care team.

The NCCN Guidelines for Patients will help you understand cancer care. With better understanding, you'll be more prepared to discuss your care with your team and share your concerns. Many people feel more satisfied when they play an active role in their care.

You may not know what to ask your care team. That's common. Each chapter in this book ends with an important section called Questions to ask. These suggested questions will help you get more information on all aspects of your care.

Why you should read this book

Making decisions about cancer care can be stressful. You may need to make tough decisions under pressure about complex choices.

The NCCN Guidelines for Patients are trusted by patients and providers. They clearly explain current care recommendations made by respected experts in the field. Recommendations are based on the latest research and practices at leading cancer centers.

Cancer care is not the same for everyone. By following expert recommendations for your situation, you are more likely to improve your care and have better outcomes as a result. Use this book as your guide to find the information you need to make important decisions.

2
Testing for Hodgkin lymphoma

This chapter explains how Hodgkin lymphoma is identified (diagnosed). Other testing and care you may have before treatment is described.

Biopsy and lab testing

The best way to diagnose Hodgkin lymphoma is to have 1 or more whole lymph nodes removed and tested. This is called an excisional lymph node biopsy.

While an excisional biopsy is preferred, a core needle biopsy may be done in some cases. In this method, a doctor uses a wide needle to remove a sample of tissue from a lymph node, but doesn't remove the entire node.

Guide 1
Testing for Hodgkin lymphoma

Necessary tests	• Your provider will gather your health history, perform a physical exam, and ask about your symptoms • Blood tests: complete blood count, differential, erythrocyte sedimentation rate, comprehensive metabolic panel, lactate dehydrogenase, liver function tests, HIV • Pregnancy test (if you can become pregnant and chemotherapy or radiation therapy is planned) • PET/CT scan from your skull to your thighs or feet
Tests used when needed	• Fertility preservation • Lung function tests, if ABVD chemotherapy is planned • Hepatitis B/C testing (encouraged) • Diagnostic CT with contrast • Chest x-ray (encouraged, especially if a large chest tumor) • Bone marrow biopsy • Echocardiogram or MUGA scan and possibly atorvastatin if anthracycline-based chemotherapy is planned • MRI with contrast of certain areas • PET/MRI scan from your skull to thighs (without contrast) • Help to quit smoking

A type of biopsy called a fine-needle aspiration (FNA) is not recommended to diagnose Hodgkin lymphoma. In this method, a thin needle is used to remove a sample of tissue from a lymph node.

Testing the removed lymph node(s)

The removed lymph nodes are examined using a process called immunohistochemistry (IHC). Using a microscope, this test looks for proteins on the surface of cells. A diagnosis can be made based on the proteins that can be seen (and not seen) using this technique.

For example, if you have CHL, proteins called CD15 and CD30 can usually be seen using immunohistochemistry, but CD3 and CD45 usually cannot.

Health history and physical exam

Your provider will review your health history and perform a complete physical exam.

Symptoms

Hodgkin lymphoma can cause symptoms. There are 3 symptoms in particular that are important for your provider to be aware of if you have them. These are called B symptoms or systemic symptoms. They are:

- Unexplained fevers (above 100.4 degrees Fahrenheit)
- Drenching night sweats
- Losing a lot of weight without trying

Also tell your provider if you have any of the symptoms listed below. These may also be related to Hodgkin lymphoma.

- Itchy skin (pruritus)
- Extreme tiredness despite sleep (fatigue)
- A bad reaction to alcohol

Physical exam

While lymph nodes can't usually be seen or felt, Hodgkin lymphoma can cause them to get bigger.

Using their hands, your doctor will feel your spleen, liver, and the areas of your body where there are the most lymph nodes. This includes the neck, armpits, and groin.

Performance status

Your doctor will also evaluate your ability to do daily tasks and activities. This is called your performance status. It helps decide if you can have certain treatments.

Blood tests

The blood tests typically done as part of testing for Hodgkin lymphoma are described below.

A complete blood count (CBC) measures the number of red blood cells, white blood cells, and platelets in a sample of blood.

An erythrocyte sedimentation rate (ESR) test measures how quickly red blood cells settle at the bottom of a test tube that contains a blood sample. A faster-than-normal ESR may be a sign of inflammation, infection, cancer, or other diseases.

A comprehensive metabolic panel (CMP) is a group of more than 10 blood tests. It provides information about the health of the kidneys, liver, and other organs and tissues. It also gives information on your blood sugar, calcium, and electrolytes.

Liver function tests are often done along with a CMP. The liver is an organ that does many important jobs, such as remove toxins from the blood. Liver function tests measure enzymes that are made or processed by the liver.

A high level of a protein called serum lactate dehydrogenase (LDH) in blood can be a sign of cell damage caused by cancer or other health problems.

Testing for human immunodeficiency virus (HIV) is also recommended.

Testing for hepatitis B and C is encouraged, especially if your provider thinks you may be at risk for these diseases.

Hodgkin lymphoma B symptoms

Fever

Heavy night sweats

Unexplained weight loss

Imaging tests

PET

Positron emission tomography (PET) scans use a small amount of radioactive glucose (sugar), called a radiotracer. Fluorodeoxyglucose (FDG) is most often used. The tracer gives off a small amount of energy that is detected by the scanner. Areas with cancer appear brighter (“hotter”) because cancer cells use sugar more quickly than normal cells.

FDG-PET scans are used to determine the cancer stage and to see how well treatment is working. It's common to have more than one during the course of treatment. FDG-PET is often combined with computed tomography (CT) or magnetic resonance imaging (MRI).

A 5-point system, called the Deauville criteria, is used to rate how much of the tracer is absorbed by areas with cancer compared to how much is absorbed by the liver and the mediastinum (the area between the lungs).

A score of 1, 2, or 3 means that there aren't any cancerous areas of concern. A score of 4 or 5 generally means that there are cancerous areas of concern. A score of 4 can be considered good or bad, depending on the situation, and a biopsy may be recommended.

Things like pneumonia and other infections can light up on PET scans. In these cases, or when a radiologist is unsure of the diagnosis, a Deauville score of X may be assigned.

The Deauville score given when you are first diagnosed isn’t important. How that score changes as a result of treatment is important. This is how your team learns how well treatment is working.

PET/CT

PET scans play a key role in the management of Hodgkin lymphoma. They are used to determine the stage of disease and to see how well treatment is working.

CT and MRI

Computed tomography and magnetic resonance imaging are other imaging tests used for Hodgkin lymphoma. Either may be combined with PET imaging.

CT takes many pictures of a body part from different angles using x-rays. A computer combines the x-rays to make detailed pictures.

MRI uses radio waves and powerful magnets to take pictures of areas inside the body. It doesn't use radiation. Because of the strong magnets used, tell the technician if you have any metal in your body. Also tell your care team if you are afraid of enclosed spaces. There are medications that can help.

Contrast

Contrast is a substance put into the body that makes imaging pictures clearer. It is often used for CT and MRI scans. The contrast is put into the bloodstream through a vein and may also be given as a drink.

Tell your care team if you've have had problems with contrast in the past. Allergic reactions, such as throat swelling and hives, are possible.

Chest x-ray

In some cases, a chest x-ray can help spot enlarged lymph nodes in the chest. It may be the first diagnostic test performed. The findings of a chest x-ray typically need to be confirmed with further imaging.

Receiving your test results

Think about how you want to get your test results. Accessing results online using a patient portal is often an option. But, trying to understand testing reports can be confusing and stressful. You may prefer for your provider to share your results in person or over the phone. Share your notification preferences with your care team.

Heart and lung tests

Some cancer treatments can damage your heart and lungs. In order to plan your treatment, your provider may test how well these organs work.

Heart tests

Doxorubicin (also known as Adriamycin, the “A” in ABVD) is an anthracycline. Among other side effects, it can cause heart damage.

If chemotherapy that includes doxorubicin is planned, you may have an echocardiogram or a multigated acquisition (MUGA) scan to learn about how your heart pumps blood.

An echocardiogram is a visual outline of your heart’s movement. A provider moves an ultrasound wand over your chest, creating images of your heart using sound waves.

In a MUGA test, a small amount of a radioactive chemical is put into one of your veins. Using a special camera, your provider can see how this tracer moves through the body as your heart beats.

Your provider may also prescribe a cholesterol-lowering medicine called atorvastatin.

Lung tests

The chemotherapy drug bleomycin (the "B" in ABVD) can damage the lungs. If chemotherapy that includes bleomycin is planned or being considered, you may have 1 or more of the lung function tests described next.

Spirometry measures the amount of air the lungs can hold, and how fast you can empty the air out of your lungs.

Heart tests

Doxorubicin is a chemotherapy drug called an anthracycline. Among other side effects, it can cause heart damage. An echocardiogram (shown here) or a MUGA scan is recommended to see how your heart pumps blood if chemotherapy that includes doxorubicin is planned.

A gas diffusion test involves breathing in a harmless gas and measuring how much of it you breathe out. It tells how much oxygen travels from your lungs into your blood.

Body plethysmograph involves sitting in a small room and breathing into a tube. This test measures how much air your lungs can hold and how much air is left in your lungs after you exhale.

Other testing and care

Everyone should get the influenza vaccine (the flu shot) and other vaccines as needed. Other care you may need is described next.

Help to quit smoking

If you use tobacco, learn about options to help you quit. Smoking and vaping can limit how well cancer treatment works and increase the risk of lung problems during chemotherapy.

Fertility and pregnancy

Anyone diagnosed with Hodgkin lymphoma who could become pregnant should be tested for pregnancy before starting treatment.

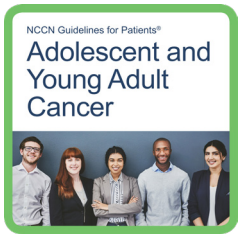
While most people will have chemotherapy with a regimen that is unlikely to affect fertility, there are regimens that can cause immediate and permanent infertility.

If you want the option of having children after treatment or are unsure, tell your provider. Common methods of fertility preservation are described next.

Sperm banking stores semen for later use by freezing it in liquid nitrogen. Like sperm, unfertilized eggs can be removed, frozen, and stored for later use.

Ovarian tissue banking involves removing part or all of an ovary and freezing the part that contains the eggs. The frozen tissue that contains the eggs can later be unfrozen and put back in the body.

More information on fertility preservation in adolescents and young adults is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Bone marrow biopsy

In general, bone marrow biopsies are no longer included in the initial testing for Hodgkin lymphoma. But if the cancer is advanced, you have lower-than-normal numbers of blood cells, and a PET scan doesn't suggest there is cancer in the marrow, a bone marrow biopsy may be needed.

Supportive care

Supportive care helps improve your quality of life during and after cancer treatment. The goal is to prevent or manage side effects and symptoms, like pain and cancer-related fatigue. It also addresses the mental, social, and spiritual concerns faced by those with cancer.

Supportive care is available to everyone with cancer and their families, not just those at the end of life. Palliative care is another name for supportive care.

Supportive care can also help with:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advanced care and end of life

Key points

- Tell your provider if you have unexplained fevers, drenching night sweats, significant weight loss, itchy skin, extreme tiredness, or a bad reaction to alcohol.
- An excisional lymph node biopsy is the most accurate way to diagnose Hodgkin lymphoma.
- Blood tests for Hodgkin lymphoma include a CBC, ESR, comprehensive metabolic panel, liver function tests, and measurement of lactate dehydrogenase.
- PET/CT scans are used to determine the stage of disease and to see how well treatment is working.
- Most people with Hodgkin lymphoma need testing of their heart and lungs to determine if they can have certain chemotherapy medicines.
- Fertility preservation methods are available if treatment with a regimen that could impair your fertility is planned.

Questions to ask

- Do I need heart and lung tests?
- Which imaging tests do I need?
- Will my fertility be impacted?
- Should I be concerned about radiation from imaging tests?
- What are the newest options for help to quit smoking?

3
Staging

Before starting treatment, it's important to know how far the cancer has spread. This process is called staging. The testing described in Chapter 2 is used to determine the stage (extent) of the cancer.

Staging Hodgkin lymphoma

The diaphragm is a thin muscle below the lungs and heart. It can be thought of as a dividing line between the chest and the abdomen.

Hodgkin lymphoma usually starts above the diaphragm, in lymph nodes in the neck, chest, or armpits. The cancer is staged (in part) based on whether it has spread to lymph nodes or other areas below the diaphragm.

There are 4 stages of Hodgkin lymphoma (1, 2, 3, and 4).

If there is cancer in only 1 group of lymph nodes and possibly in one small area or organ outside the lymphatic system, the cancer is stage 1.

If the cancer spreads to more lymph node groups on the same side of the diaphragm, it is stage 2.

If Hodgkin lymphoma is found in lymph nodes above and below the diaphragm, it is stage 3.

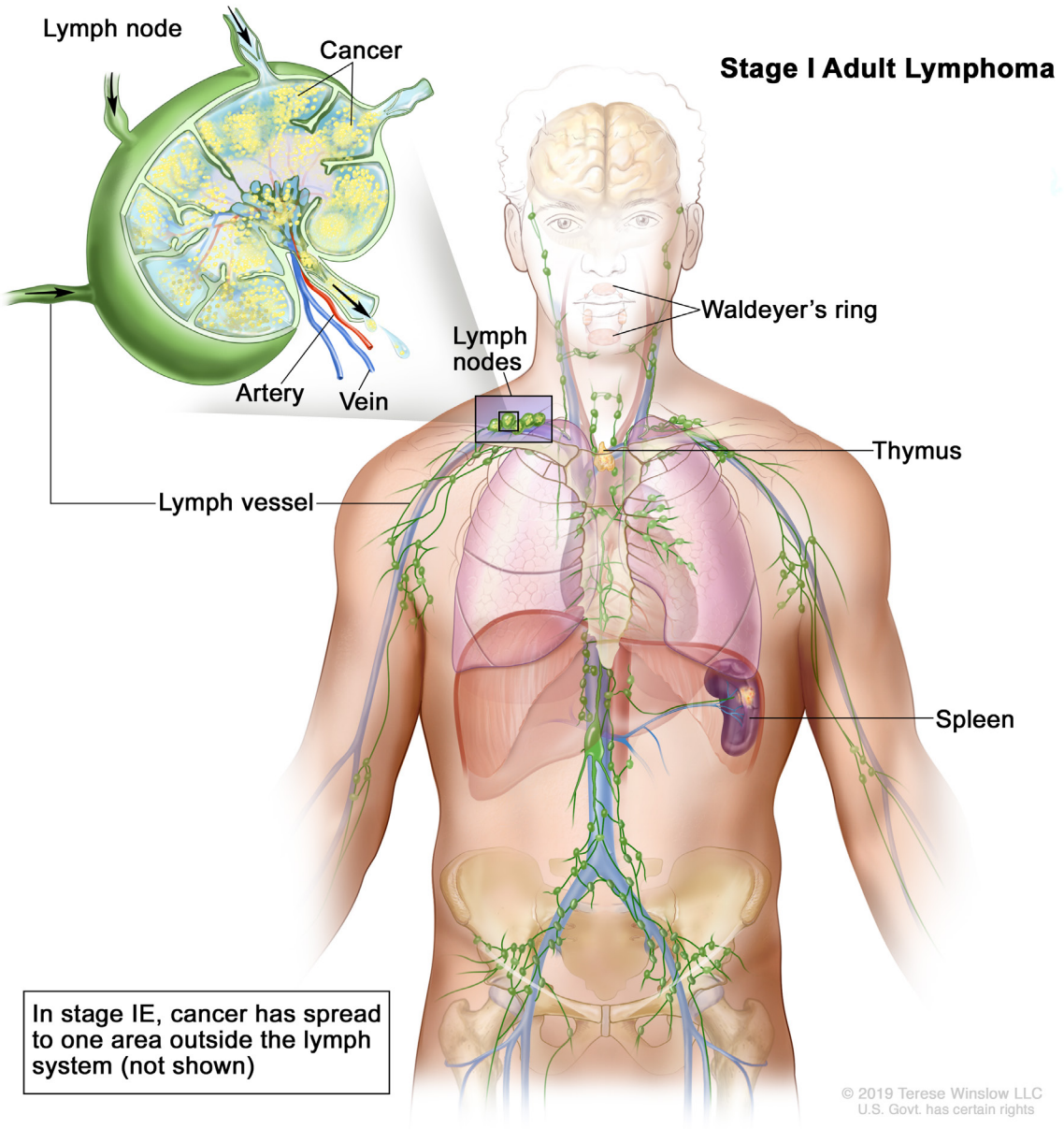
Hodgkin lymphoma that has spread to multiple areas outside of the lymphatic system is stage 4.

A "B" after the stage means that the cancer is causing B symptoms (unexplained fevers, drenching night sweats, and extreme weight loss). An "A" after the stage means that the cancer isn't causing B symptoms.

Stages 1 and 2 are considered early CHL. Stages 3 and 4 are considered advanced CHL.

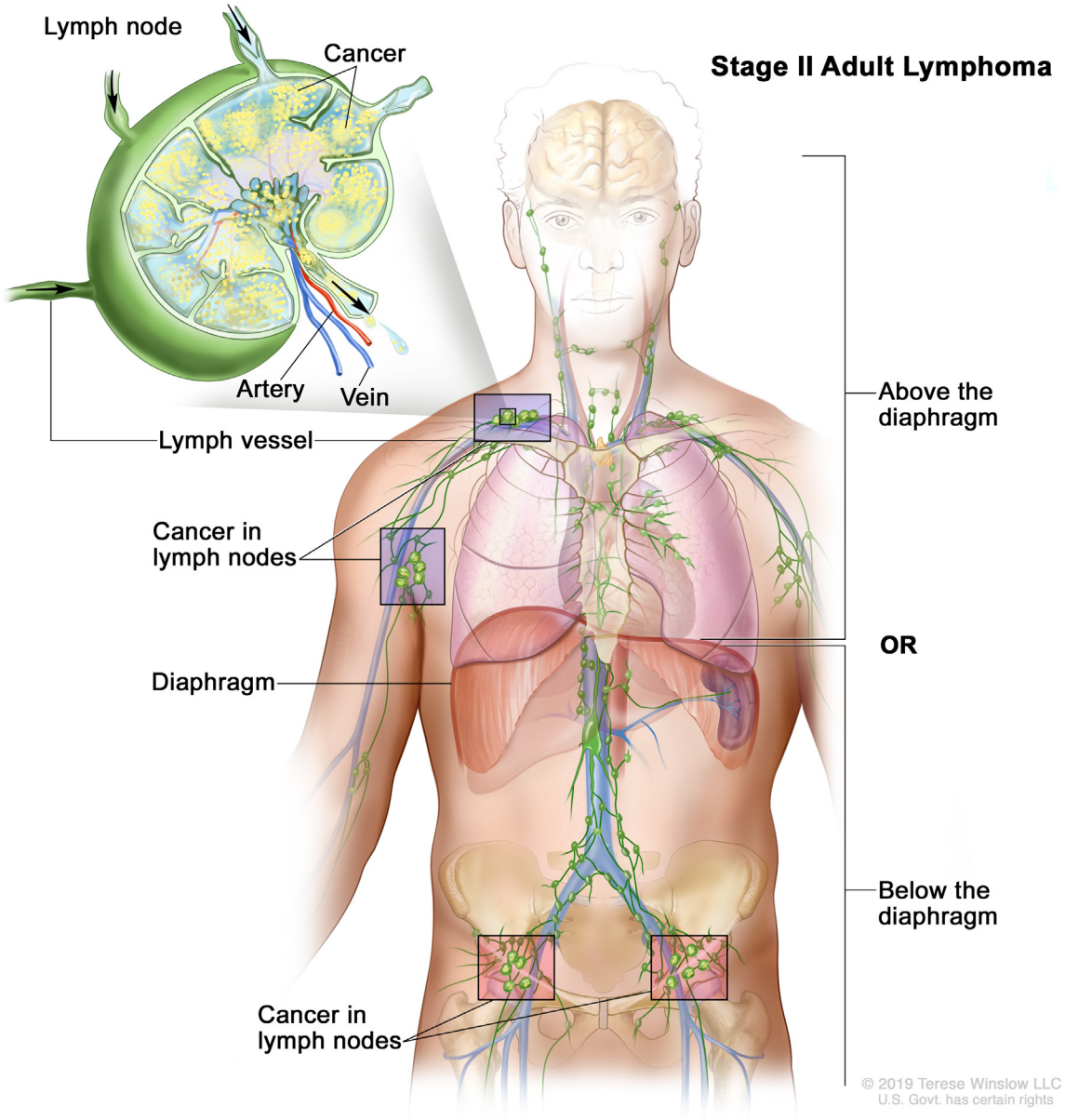
Stage I

There is cancer in one group of lymph nodes, and possibly in one small area or organ outside the lymphatic system.



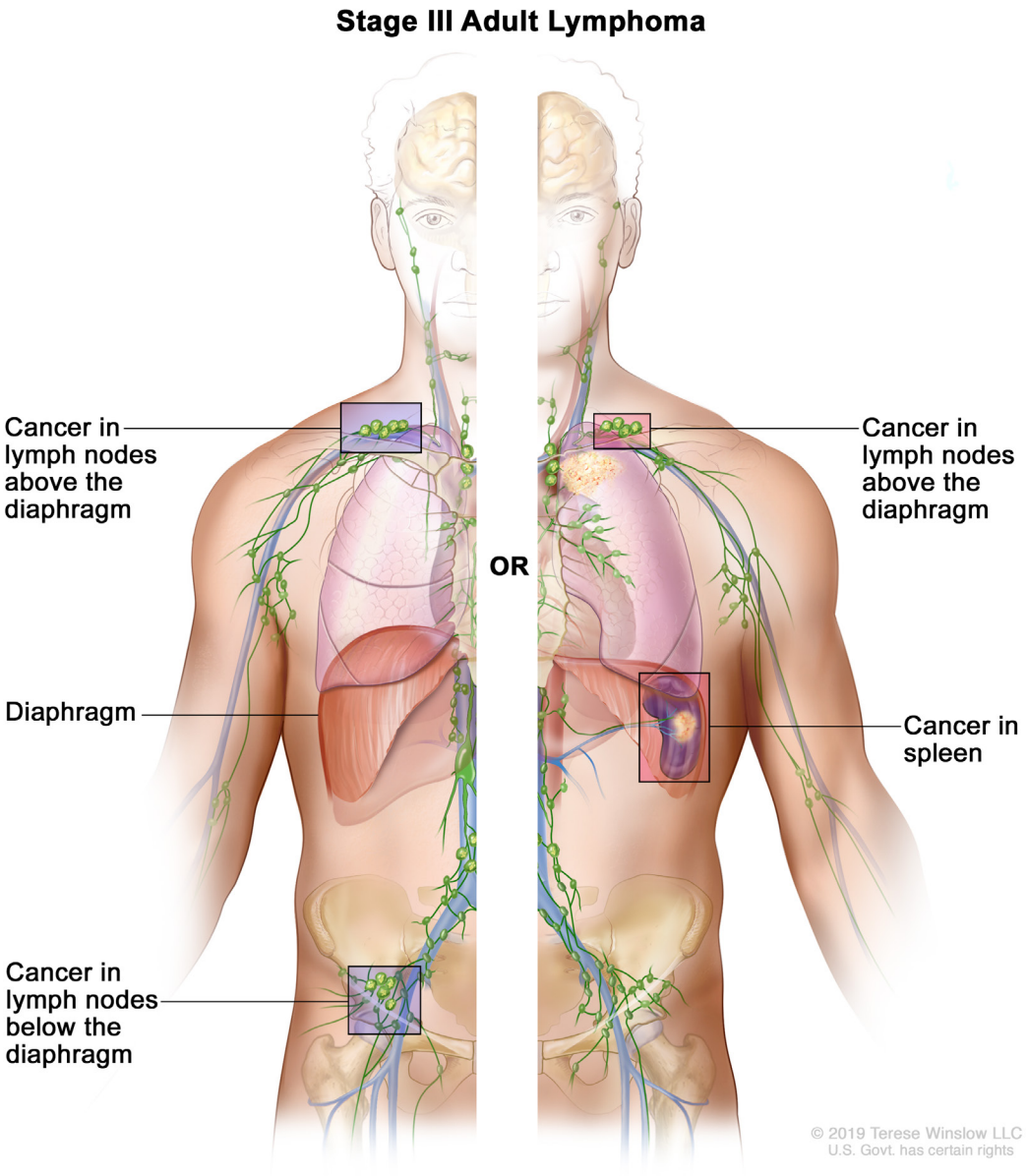
Stage II

There is cancer in 2 or more groups of lymph nodes on the same side (above or below) of the diaphragm, and possibly in one area or organ and its nearby lymph nodes outside the lymphatic system.



Stage III

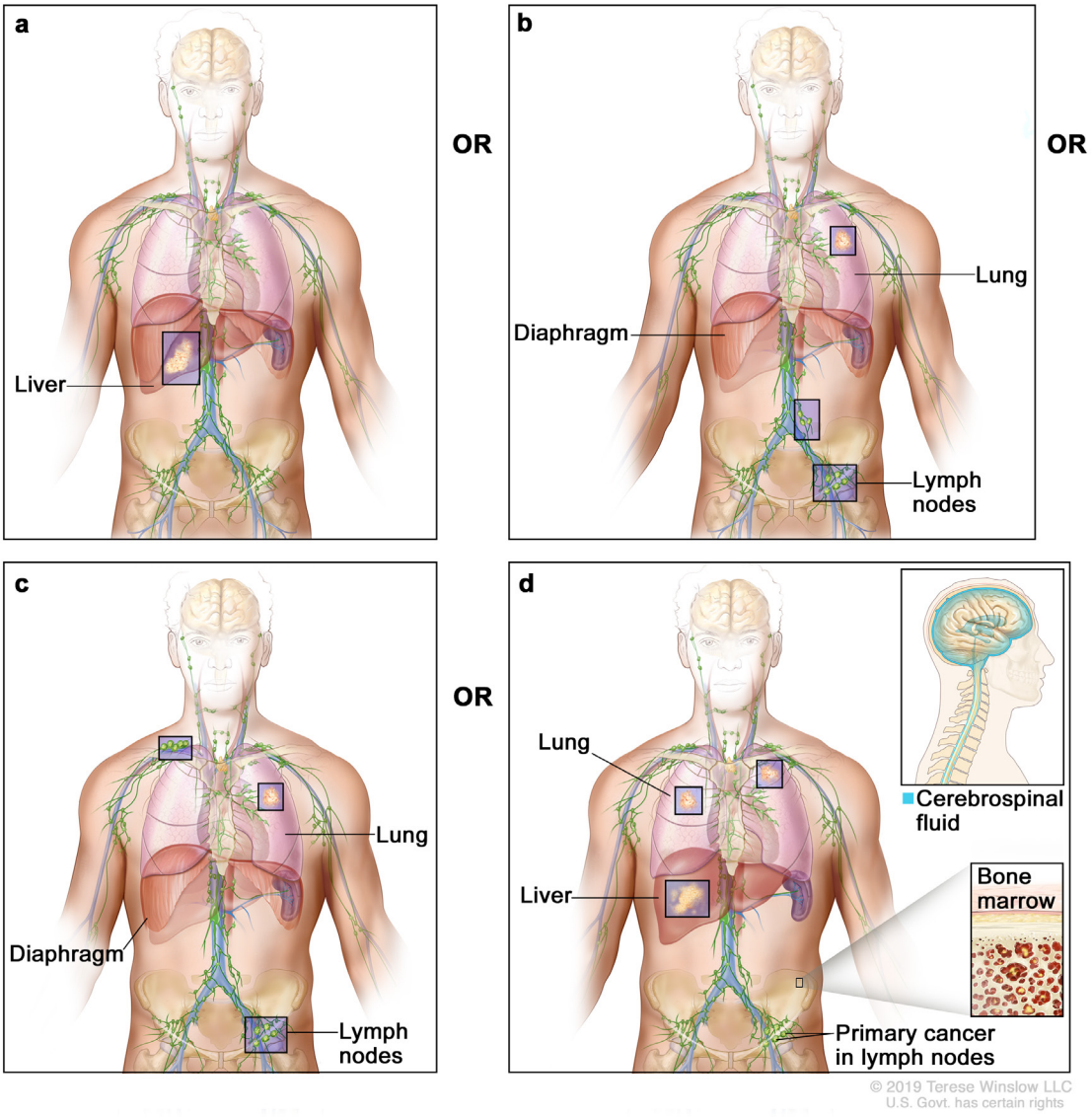
There is cancer in lymph nodes on both sides (above and below) of the diaphragm. There may also be cancer in one area or organ outside of the lymphatic system, in the spleen, or both.



Stage IV

There are multiple areas of cancer in one or more organs outside the lymphatic system, and possibly in the neighboring lymph nodes. Or, there may be cancer in one organ outside of the lymphatic system and also in distant lymph nodes.

Stage IV Adult Lymphoma



Key points

- There are 4 stages of Hodgkin lymphoma (1, 2, 3, and 4).
- If there is cancer in only 1 group of lymph nodes, the cancer is stage 1.
- If the cancer spreads to more lymph node groups on the same side of the diaphragm, it is stage 2.
- If Hodgkin lymphoma is found in lymph nodes above and below the diaphragm, it is stage 3.
- Hodgkin lymphoma that has spread to multiple areas outside of the lymphatic system is stage 4.
- A “B” after the stage means that the cancer is causing B symptoms (unexplained fevers, drenching night sweats, and extreme weight loss). An “A” after the stage means that the cancer isn’t causing B symptoms.
- Stages 1 and 2 are considered early CHL. Stages 3 and 4 are considered advanced CHL.

Questions to ask

- What stage is the cancer?
- Has it spread below my diaphragm?
- If the cancer spreads, does the stage change?

4

Treatment for classic Hodgkin lymphoma (CHL)

Classic Hodgkin lymphoma (CHL) is treated with chemotherapy, sometimes combined with radiation therapy. If possible, experts in different areas of cancer treatment (a multidisciplinary team) should review your treatment plan before it is finalized.

Types of treatment

Systemic therapy

Systemic therapy is the use of medicine to kill cancer cells. Chemotherapy, targeted therapy, and immunotherapy are types of systemic therapy.

Most systemic therapies are given by infusion (slow injection through a vein). The drugs travel in your bloodstream to kill cancer cells throughout the body. Healthy cells are also affected in the process, which is why side effects can occur. Treatment is given in cycles of treatment and rest to allow the body to recover between infusions.

CHL is most often treated with chemotherapy, which may be paired with immunotherapy or radiation therapy. Commonly used regimens are listed in **Guide 2.**

Guide 2
Commonly used chemotherapy regimens for CHL

ABVD	Includes doxorubicin, bleomycin, vinblastine, and dacarbazine
BrECADD + G-CSF	Includes brentuximab vedotin (BV), etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone, and growth factors
BV-AVD + G-CSF	Includes brentuximab vedotin, AVD (doxorubicin, vinblastine, and dacarbazine), and growth factors
Nivolumab and AVD	Includes nivolumab (an immunotherapy) and AVD chemotherapy

Because chemotherapy can weaken your immune defense, some regimens include a medicine called granulocyte colony-stimulating factor (G-CSF). This type of growth factor boosts your immune system by driving your body to make more white blood cells.

Some regimens include a steroid, such as dexamethasone or prednisone. These are included because they relieve inflammation and also have anti-cancer effects.

Brentuximab vedotin (also called BV or Adcetris) is an antibody drug conjugate. This means it combines two drugs in one medicine. The antibody part (brentuximab) finds and attaches to cancer cells that have a specific protein (CD30) on their surface. Once attached, a chemotherapy drug is released into the cancer cell.

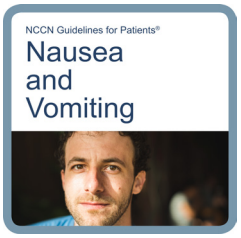
Immunotherapy medicines called checkpoint inhibitors may also be used to treat Hodgkin lymphoma. They include nivolumab (Opdivo) and pembrolizumab (Keytruda). Immunotherapy increases the activity of your immune system, improving the body's ability to find and destroy cancer cells.

For information on the side effects of immune checkpoint inhibitors, see the *NCCN Guidelines for Patients: Immunotherapy Side Effects – Immune Checkpoint Inhibitors* at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Side effects

Managing side effects is a shared effort between you and your care team. It is important to speak up about bothersome side effects, such as nausea and vomiting. Ask about your options for managing or relieving the effects of treatment.

More information on nausea and vomiting is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Radiation therapy

Radiation therapy is often used in addition to chemotherapy to treat Hodgkin lymphoma. Radiation therapy kills existing cancer cells, stopping new cancer cells from being made. Radiation can also affect the surrounding normal cells.

Involved-site radiation therapy (ISRT) is recommended to treat Hodgkin lymphoma. ISRT only targets the lymph nodes in which the cancer first started.

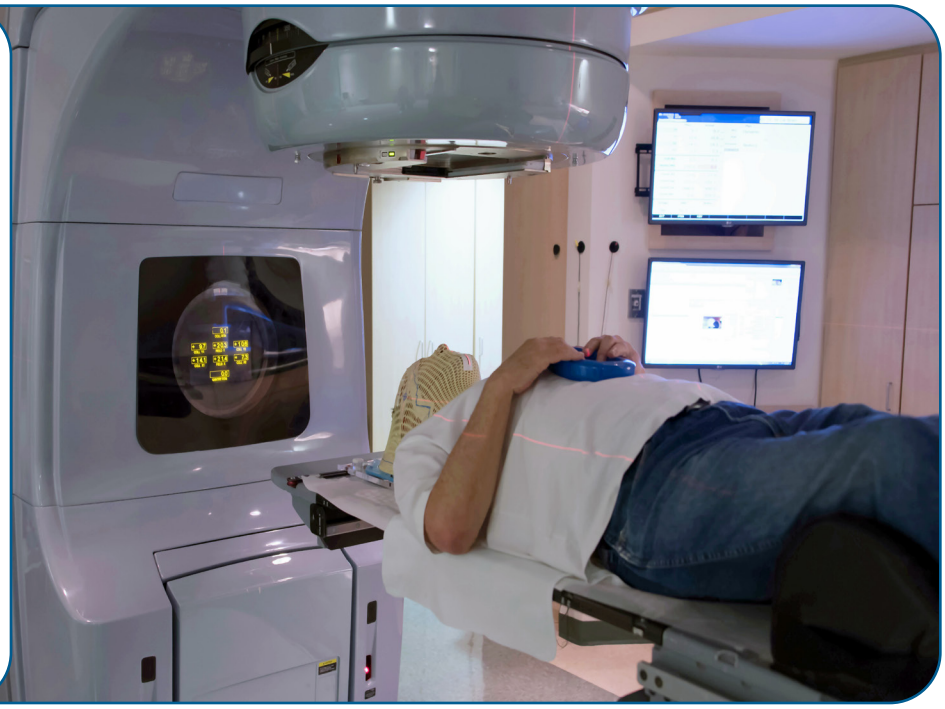
In some cases, particle-based methods, such as proton therapy, may be used. This is especially used for younger people with lymphoma in the area of the chest between the lungs (the mediastinum). Proton therapy may reduce late side effects caused by treatment with radiation, such as heart disease and second cancers. The type of radiation used will be decided based on where the cancer started in the body.

If radiation therapy is planned, a simulation (planning) session is needed before the start of treatment. During simulation, pictures of the tumor will be taken, usually using a CT scan in the radiation treatment position. The scan images are used to plan the radiation dose and the setup of the radiation beams.

You may be asked to hold your breath during the simulation scan or treatment. This limits the movement of your heart and lungs and helps reduce extra radiation to these organs. During treatment, you will lie on a table in the same position as you did for the simulation. Devices, like a mesh mask or a body mold, may be used to keep you from moving.

Radiation therapy

Radiation therapy is often used in addition to chemotherapy to treat Hodgkin lymphoma. A type of external beam radiation called ISRT is recommended in most cases.



About treatment for early CHL

Treatment for stage 1–2 CHL depends on whether the cancer has the following features, which can make it harder to treat:

- B symptoms (unexplained fevers, drenching night sweats, weight loss)
- Bulky (larger than 10 cm) tumors
- Elevated erythrocyte sedimentation rate (ESR)
- Having cancer in more than 2 areas
- Involvement of areas other than lymph nodes, such as a lung

If the cancer has any of these features, it is described as unfavorable or high-risk. Cancers without any of these features are described as favorable or low-risk.

There are 2 main approaches to treating stage 1–2 CHL:

- Combination therapy (chemotherapy and radiation therapy)
- Chemotherapy alone

Your provider will recommend one of these approaches based on the following factors:

- Your age
- Your sex assigned at birth
- Your family history of cancer or heart disease
- Your overall health
- The specific areas with cancer

Managing breast cancer risk

For those assigned female at birth who are under age 30, combination therapy (including radiation to breast tissue) may increase the risk of developing breast cancer later. But if the doxorubicin dose needed would be too high using chemotherapy alone, combination therapy may be preferred.

Favorable stage 1–2

Treatment for favorable early CHL begins with 2 cycles of ABVD chemotherapy, followed by a PET/CT scan to check the results. Further treatment depends on the Deauville score and the cancer features. Next steps for a score of 1, 2, or 3 are listed in **Guide 3.**

Deauville score of 4

For a Deauville score of 4, having 2 more cycles of ABVD is often the next step. After finishing chemotherapy, you will have another PET scan. Further treatment depends on the results of the interim (new) Deauville score. If the score is 1, 2, or 3, radiation therapy is recommended.

If the interim score is 4 or 5, a biopsy is needed. If the biopsy is negative for lymphoma, radiation therapy is recommended. If the biopsy is positive, treatment for refractory CHL is recommended.

Deauville score of 5

A biopsy is needed before having more treatment. If the biopsy is negative, the cancer is treated as if the Deauville score were 4 (see "Deauville score of 4" above).

If the biopsy is positive, or if a biopsy cannot be performed, treatment for refractory CHL is recommended.

Guide 3
Deauville score of 1, 2, or 3 after ABVD chemotherapy

Cancers with all of these features: • **ESR slower than 50** • **no e-lesions** • **cancer in 2 or fewer lymph node sites**	If the Deauville score is 1 or 2, recommended options include: • Radiation therapy • 2 more cycles of ABVD If the Deauville score is 3, there are 2 recommended options: • Radiation therapy • 4 cycles of AVD chemotherapy
All other cancers	If the Deauville score is 1 or 2, recommended options include: • 2 more cycles of ABVD • 1 cycle of ABVD and radiation therapy If the Deauville score is 3, recommended options include: • 4 cycles of AVD chemotherapy • 2 cycles of ABVD and radiation therapy

Unfavorable stage 1–2

Unfavorable early disease means that the cancer has 1 or more of the following features:

- B symptoms
- Bulky (larger than 10 cm) tumors
- Lymphoma outside the lymph nodes (such as in the lung)

There are 4 possible treatment pathways, described next.

ABVD pathway

This pathway starts with 2 cycles of ABVD chemotherapy, followed by a PET/CT scan to check the results. Further treatment depends on the results of the PET scan (the Deauville score).

For a Deauville score of 1, 2 or 3, there are 2 options:

- 4 cycles of AVD (not ABVD) chemotherapy
- 2 cycles of ABVD chemotherapy + radiation therapy

For a Deauville score of 4 or 5, there are 2 options:

- 2 more cycles of ABVD
- 2 cycles of BrECADD + granulocyte colony-stimulating factor (G-CSF)

After finishing chemotherapy, you will have another PET scan. Further treatment depends on the results of the interim (new) Deauville score. If the interim score is 1, 2, 3, or 4, radiation therapy is recommended.

If the interim score is 5, a biopsy is needed. If the biopsy is negative, radiation therapy is recommended. If the biopsy is positive, or if a biopsy cannot be performed, treatment for refractory CHL is recommended

Immunotherapy pathway

This pathway starts with the following:

- 4 cycles of nivolumab (Opdivo) and AVD chemotherapy
- Radiation therapy

For a Deauville score of 1, 2 or 3 after restaging, you can begin follow-up care.

For a Deauville score of 4 or 5, a biopsy is needed. If the biopsy is negative, you can begin follow-up care. If the biopsy is positive, or if a biopsy cannot be performed, treatment for refractory CHL is recommended.

For information on the side effects of immune checkpoint inhibitors, see the N*CCN Guidelines for Patients: Immunotherapy Side Effects – Immune Checkpoint Inhibitors* at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Brentuximab vedotin pathway

This pathway starts with the following:

- 4 cycles of brentuximab vedotin with growth factors and AVD chemotherapy
- Radiation therapy

For a Deauville score of 1, 2 or 3 after restaging, you can begin follow-up care.

For a Deauville score of 4 or 5, a biopsy is needed. If the biopsy is negative, you can begin follow-up care.

If the biopsy is positive, or if a biopsy cannot be performed, treatment for refractory CHL is recommended.

BrECADD pathway

This pathway involves 2 cycles of BrECADD and growth factors, followed by a PET/CT scan to check the results. Further treatment depends on the Deauville score.

For a score of 1, 2, or 3, two more cycles of BrECADD and growth factors is recommended, followed by restaging. If the interim (new) score is 1, 2, or 3, you can start follow-up care.

If the interim score is 4 or 5, a biopsy is needed to guide your care. If the biopsy is negative, 4 cycles of BrECADD and growth factors is recommended. If the results are good, follow-up care will begin.

If the biopsy is positive, treatment for refractory CHL is recommended.

Advanced CHL (stage 3–4)

This section explains the treatment options for CHL that has spread below the diaphragm, and possibly outside the lymphatic system.

Preferred regimens

The chemotherapy regimens in **Guide 4** are preferred for treating advanced CHL. Preferred therapies have the most evidence they work better. They may also be safer than other therapies.

If you can't have either of the preferred regimens, other recommended options are available.

The following features can lead to poor treatment outcomes for stage 3–4 CHL:

- Age 45 or over
- Male sex assigned at birth
- Stage 4 disease
- Albumin level below 4 g/dL
- A low hemoglobin level for your age and sex (commonly known as anemia)
- A high number of white blood cells in the blood (called leukocytosis)
- A low level of lymphocytes in the blood (called lymphocytopenia)

A scoring system is used to help guide treatment decisions for advanced CHL. The score is calculated by adding the number of these risk factors that apply to you or your cancer. The total is called the International Prognostic Score (IPS).

Guide 4
Preferred regimens for advanced CHL

Nivolumab + AVD	This pathway begins with 6 cycles of nivolumab (Opdivo) given with AVD chemotherapy. For a Deauville score of 1, 2 or 3, no further treatment is needed. For a score of 4 or 5, a biopsy is needed to guide your care.
BrECADD + growth factors	This pathway begins with 2 cycles of BrECADD chemotherapy (includes growth factors). For a Deauville score of 1, 2 or 3, two more cycles of BrECADD is recommended. If the results are good, no further treatment is needed. For a Deauville score of 4 or 5 after the first 2 cycles of BrECADD, a biopsy is needed to guide your care.

Regimens used in certain cases

If the preferred regimens in Guide 4 aren't available or you aren't a candidate for them, your provider may recommend one of the regimens described next.

BV-AVD with growth factors

This regimen begins with 6 cycles of brentuximab vedotin (BV) plus AVD and growth factors.

If the Deauville score is 1, 2, or 3 after restaging, no further chemotherapy is needed. You can begin follow-up care. If the Deauville score is 4 or 5, a biopsy is needed to guide your care.

Regardless of Deauville score, radiation therapy may be used after chemotherapy to treat high-risk areas.

ABVD chemotherapy

This regimen begins with 2 cycles of ABVD chemotherapy, followed by a PET/CT scan.

For a Deauville score of 1, 2, or 3, the next step is to have 4 cycles of AVD chemotherapy. Radiation therapy may also be used to treat high-risk areas.

For a Deauville score of 4 or 5, switching to BrECADD chemotherapy for 3 cycles is recommended. If the results are good, 1 more cycle of BrECADD is recommended. Radiation therapy may follow. If the results aren't as good, a biopsy is recommended to guide your next steps of care.

CHL during pregnancy

Classic Hodgkin lymphoma is the most common blood cancer diagnosed during pregnancy. Treatment should be individualized based on all of the following:

- Your symptoms and general health
- How far along you are in your pregnancy
- Your wishes

Cancer care during pregnancy requires a multidisciplinary approach. Experts in medical oncology, high-risk obstetrics, and neonatology should be involved.

A pharmacist is also needed to make sure that supportive medications, like anti-nausea aids, are safe to use in pregnancy. Ondansetron and metoclopramide are the preferred anti-nausea medications for pregnant people.

To stage CHL during pregnancy, imaging should include a single-view chest X-ray (your abdomen will be shielded from the radiation) and an ultrasound or MRI of your abdomen (without gadolinium contrast).

Tests and treatments that should be avoided during pregnancy include:

- FDG-PET and CT imaging
- Intensive regimens such as escalated BEACOPP and BV + AVD
- Radiation therapy

First trimester

Chemotherapy should generally be avoided in the first trimester. If you have few or no

symptoms, treatment can be safely delayed until the second or third trimester. During this time you will be closely monitored.

If your symptoms are severe or a major organ problem is suspected, you and your provider will make decisions about the following:

- Referral to a center with expertise
- Pregnancy management and urgent treatment
- Chemotherapy with vinblastine, followed by ABVD chemotherapy after the first trimester

Second or third trimester

If you have few or no symptoms, treatment can often be safely delayed until after childbirth. During this time you will be closely monitored.

If your symptoms are severe or a major organ problem is suspected, ABVD chemotherapy is recommended. It is perfectly safe for you (and the unborn baby) to receive ABVD in the second or third trimester.

Breastfeeding

Breastfeeding should be avoided if you are receiving chemotherapy in the post-partum period.

CHL during pregnancy

Classic Hodgkin lymphoma is the most common blood cancer diagnosed during pregnancy. Treatment should be individualized based on your symptoms, general health, how far along you are, and your wishes.

CHL in older adults

CHL can be harder to treat in older adults, and outcomes often aren't as good. Seeking treatment as part of a clinical trial is recommended, if one is available to you.

Treatment for CHL in older adults involves chemotherapy and sometimes radiation therapy. If you aren't well enough to have chemotherapy, radiation therapy alone may be considered.

Doxorubicin (Adriamycin, the "A" in ABVD) is an anthracycline. Among other side effects, it can cause heart damage. Your provider will suggest a regimen based on whether you can safely have doxorubicin. If you can, recommended regimens are listed in **Guide 5**.

Guide 5
Regimens for adults over 60 who can have doxorubicin (an anthracycline)

Stage 1-2 favorable	There are 2 recommended options: • 2 cycles of A(B)VD **and** radiation therapy • 3 cycles of A(B)VD. If there is a complete response, radiation therapy may follow.
Stage 1-2 unfavorable	There are 4 recommended options: • 2 cycles of A(B)VD followed by a PET scan. If the scan is negative after 2 cycles of ABVD, 4 cycles of AVD will follow. If the scan is positive, your care will be individualized. • 4 cycles of A(B)VD **and** radiation therapy • 2 cycles of brentuximab vedotin followed by 6 cycles of AVD. If the results are good, you may have 2 more cycles of brentuximab vedotin • 4 cycles of nivolumab (Opdivo) with AVD chemotherapy **and** radiation therapy
Stage 3-4	If you are a candidate for immunotherapy, the **preferred** treatment for advanced CHL is: • 6 cycles of nivolumab (Opdivo) with AVD If you cannot have checkpoint inhibitor immunotherapy: • 2 cycles of brentuximab vedotin followed by 6 cycles of AVD. If results are good, you may have 2 more cycles of brentuximab vedotin.

If you can't receive doxorubicin, brentuximab vedotin is often used instead, together with either dacarbazine or nivolumab. If you can't have brentuximab vedotin, immunotherapy with either nivolumab or pembrolizumab is recommended. All of these regimens can and may be paired with radiation therapy.

Bleomycin is the "B" in the ABVD regimen. This chemotherapy drug can cause a lung problem (pulmonary fibrosis) that makes it hard to breathe. It may be too harsh for older adults. If used, it shouldn't be given for more than 2 cycles.

Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.
NCCN.org/patients/response

Older adults with CHL are more likely to have:

- **B symptoms**
- **Other health problems**
- **The Epstein-Barr virus**
- **A subtype of CHL called mixed cellularity Hodgkin lymphoma (MCHL)**

Key points

- Chemotherapy is the most effective and widely used treatment for Hodgkin lymphoma. Some regimens may be paired with immunotherapy or radiation therapy.
- Treatment for stage 1–2 CHL depends on whether the cancer has unfavorable features like B symptoms, an elevated erythrocyte sedimentation rate, bulky (large) tumors, or spread to 2 or more groups of lymph nodes.
- Early-stage CHL is treated with chemotherapy, either alone or with radiation therapy. Your age, health, sex assigned at birth, family health history, and the cancer features are used to select a regimen.
- Advanced (stage 3–4) CHL has spread to both sides of the diaphragm or outside the lymphatic system. Preferred regimens include nivolumab with AVD and BrECADD chemotherapy. Radiation therapy may be used with either regimen.
- Treatment for CHL during pregnancy is personalized based on your symptoms, general health, how far along you are, and your wishes. Experts in medical oncology, high-risk obstetrics, and neonatology should be involved in your care.
- If you are an older adult with CHL, your provider will suggest a regimen based on whether you can safely have doxorubicin and bleomycin. If used, bleomycin should only be given for 1 or 2 cycles. Joining a clinical trial is recommended.

Questions to ask

- What is the cancer subtype? Does this matter?
- Which systemic therapy regimen do you recommend for me? Will you stop or change regimens if there are serious side effects?
- Will I need radiation therapy after chemotherapy?
- If so, how long will radiation therapy last? Which areas will be treated?
- What are the chances of the cancer worsening or returning?

5
Refractory or relapsed CHL

Classic Hodgkin lymphoma (CHL) that doesn't respond to recommended treatment is described as primary refractory. Seeking treatment at a center with expertise in this cancer is recommended for refractory or relapsed CHL, ideally within a clinical trial.

After being confirmed by biopsy, treatment for refractory or relapsed CHL depends on whether you are a candidate for high-dose chemotherapy with hematopoietic cell transplant (HCT).

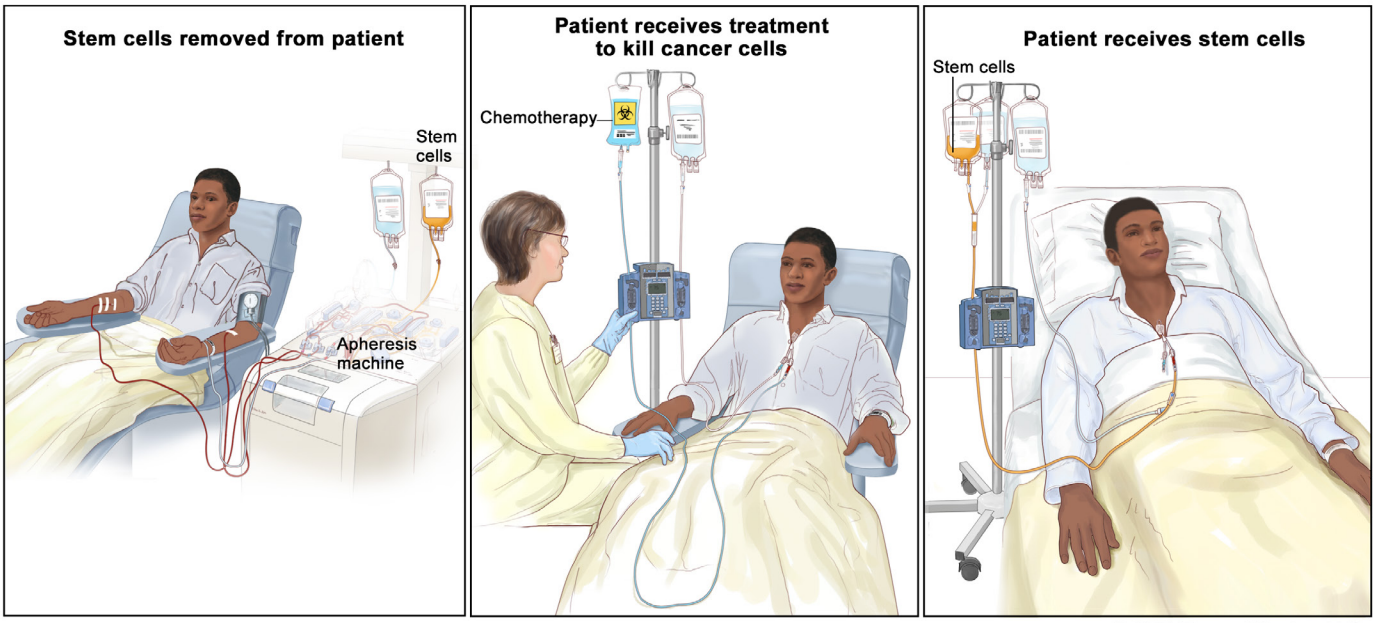
High-dose chemotherapy with HCT

When possible, high-dose chemotherapy is used to treat refractory or relapsed Hodgkin lymphoma. But the high dose needed can damage or destroy hematopoietic (blood-forming) stem cells in your bone marrow.

When damaged, hematopoietic stem cells they may not form the blood cells needed by the body. To protect these important blood-making cells, they are first removed (rescued) from your blood or bone marrow.

After chemotherapy, your rescued, healthy stem cells are transplanted back into your body. They form new red blood cells, white blood cells, and platelets. This process, called

Autologous hematopoietic cell transplant (HCT)



engraftment, restores your body's ability to protect itself from infection.

Until engraftment is achieved, you will likely feel tired and weak. In order to prevent infection, you will stay in a very clean room at the hospital and may be given an antibiotic. You may also receive blood transfusions to prevent bleeding and to treat low red blood counts (anemia) and low platelets (thrombocytopenia).

A number of names are used to refer to this procedure, including:

- High-dose chemotherapy with autologous stem cell rescue (HDT/ASCR)
- Autologous bone marrow transplant
- Autologous stem cell transplant

Allogeneic (donor) transplants aren't used often for CHL, but may be considered if the cancer doesn't respond to recommended treatment.

Candidate for high-dose chemotherapy and HCT

If you are healthy enough to have high-dose chemotherapy, your options for treatment are described next.

Refractory or recently relapsed

The following information applies to those with:

- Primary refractory CHL
- Recently relapsed CHL (relapse within 3 months of treatment)

Treatment begins with systemic therapy. If you've never had immunotherapy, a regimen that includes a checkpoint inhibitor is preferred. Recommended regimens are listed in **Guide 6.**

After systemic therapy, the cancer will be restaged. Further treatment is based on the Deauville score.

For a **score of 1 to 3**, an autologous stem cell transplant is recommended for everyone who can tolerate it. Radiation therapy may be used to treat areas that haven't already been treated. After the transplant, maintenance therapy with brentuximab vedotin will be considered if the cancer has features that make it likely to return.

If you can't have a stem cell transplant, observing the cancer without treatment is recommended. Radiation therapy may also be an option.

For a **score of 4**, an autologous stem cell transplant is a recommended option for those

healthy enough to have it. Radiation therapy may also be used. After the transplant, maintenance therapy with brentuximab vedotin will be considered if the cancer has features that make it likely to return.

Other options for those with a score of 4 after second-line therapy include:

- Radiation therapy alone
- Systemic therapy **(see Guide 6),** possibly paired with radiation therapy

If one of these approaches works well, a stem cell transplant (either autologous or allogeneic) will be considered.

For a Deauville score of 5, there are 2 options:

- Radiation therapy alone
- Systemic therapy **(see Guide 6),** possibly with radiation therapy

If one of these approaches works well, a stem cell transplant (either autologous or allogeneic) will be considered.

Guide 6
Second-line and subsequent regimens for refractory or relapsed CHL

Regimens that include a checkpoint inhibitor	• Brentuximab vedotin and nivolumab (Opdivo) • GVD and pembrolizumab (Keytruda) • ICE and nivolumab • ICE and pembrolizumab
Regimens that don't include a checkpoint inhibitor	• Brentuximab vedotin • Brentuximab vedotin and bendamustine • DHAP • Gemcitabine, bendamustine, and vinorelbine • GVD and ICE • ICE and brentuximab vedotin • IGEV

What's in each regimen?

DHAP (dexamethasone, cisplatin, high-dose cytarabine)

GVD (gemcitabine, vinorelbine, liposomal doxorubicin)

ICE (ifosfamide, carboplatin, etoposide)

IGEV (ifosfamide, gemcitabine, vinorelbine)

Relapse after 3 months

The following information applies to CHL that returned more than 3 months after treatment.

Second-line systemic therapy is recommended, and may be paired with radiation therapy. If you've never had immunotherapy, a regimen that includes a checkpoint inhibitor is preferred. **See Guide 6.**

Depending on the cancer stage at diagnosis and your treatment history, high-dose chemotherapy with HCT may follow systemic therapy.

Treatment for relapsed CHL is often individualized, especially for those who have been cancer-free for some time.

Not a candidate for high-dose chemotherapy and HCT

A stem cell transplant isn't always possible. In this case, treatment for relapsed or refractory CHL is individualized.

Systemic therapy that includes either a checkpoint inhibitor or brentuximab vedotin (BV) is recommended. The choice depends on your history of treatment with these medicines, if any. Neither has been found to work better than the other in this case.

How you feel during treatment and how the cancer appears on imaging scans may not align. With checkpoint inhibitors, sometimes what looks like progression (worsening) on scans is immune flare-up. If a checkpoint inhibitor is helping you feel better, you can continue taking it, even if the scans show what looks like progression.

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a lab, potential new ways of fighting cancer need to be studied in people.

If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment and are done in phases.

- Phase 1 trials study the safety and side effects of an investigational drug or treatment approach.
- Phase 2 trials study how well the drug or approach works against a specific type of cancer.
- Phase 3 trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- Phase 4 trials study the safety and benefit of an FDA-approved treatment.

Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a research team. This group of experts will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this

Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov/

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with people you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is often covered by insurance.

Key points

- Classic Hodgkin lymphoma (CHL) that doesn't respond to recommended treatment is described as primary refractory.
- Treatment for refractory or relapsed CHL depends on whether you are a candidate for high-dose chemotherapy with hematopoietic cell transplant (HCT).
- Seeking treatment at a center with expertise in CHL, ideally within a clinical trial, is recommended for refractory or relapsed cancer.
- Clinical trials provide access to investigational treatments that may, in time, be approved by the FDA.

Questions to ask

- Should I consider a clinical trial?
- Do you know of any clinical trials I am eligible for?
- Am I candidate for high-dose chemotherapy with HCT?
- I've already received immunotherapy. If I can't have it again, are my other options just as good?

6
Treatment for NLPHL

Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is a rare type of Hodgkin lymphoma. It is often slow-growing and may return long after treatment.

Initial treatment

After diagnosis, your treatment options are based on the cancer stage and other features and may include any of the following:

- Radiation therapy
- Rituximab (Rituxan)
- Chemotherapy

Rituximab is an antibody therapy. It targets and attaches to a protein (CD20) on the surface of NLPHL cells (and some healthy blood cells). This helps your immune system find and attack the cancer cells.

Non-bulky stages 1A and 2A

Radiation therapy is recommended to treat these small, early-stage tumors.

If you had cancer in only 1 lymph node and it was totally removed, safely skipping radiation therapy may be an option.

Transformation

While uncommon, a slow-growing lymphoma like NLPHL can transform into a fast-growing lymphoma over time. This is one reason your doctor may want to do a bone marrow biopsy. NLPHL is more likely to transform if it has any of these features at diagnosis:

- Bulky (large) tumors
- Cancer below the diaphragm
- Cancer in the spleen

Transformed lymphoma is often treated like a type of fast-growing non-Hodgkin lymphoma called diffuse large B-cell lymphoma (DLBCL). More information is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Bulky stages 1A and 2A

While uncommon, stage 1A and 2A tumors can be bulky. Treatment with all of the following is recommended for bulky, early-stage tumors:

- Chemotherapy + rituximab **(Guide 7)**
- Radiation therapy

Non-contiguous stage 2A

Stage 2A disease may be non-contiguous. This means that there is cancer in 2 groups of lymph nodes above the diaphragm, but the groups aren't next to each other.

Treatment with both chemotherapy and rituximab is recommended. In some cases, radiation therapy is given in addition to systemic therapy.

Radiation therapy alone may be an option for selected people with non-contiguous stage 2A disease.

Treatment with rituximab by itself may be used to relieve pain or other symptoms in some people with stage 2A non-contiguous disease.

Stages 1B and 2B

Treatment with all of the following is recommended for stage 1B and 2B cancers:

- Chemotherapy rituximab **(Guide 7)**
- Radiation therapy

Radiation therapy alone may be an option for a small number of people with stage 1B disease.

Stages 3 and 4

If you don't have symptoms, it is safe to monitor stage 3 and stage 4 cancers without treatment. Or, your provider may recommend one of the treatments below:

- Chemotherapy with rituximab, and possibly also radiation therapy
- Rituximab alone
- Radiation alone to relieve symptoms

Guide 7
First-line systemic therapy regimens for NLPHL

ABVD and rituximab	Includes doxorubicin, bleomycin, vinblastine, dacarbazine, and rituximab
CHOP and rituximab	Includes cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab
CVbP and rituximab	Includes cyclophosphamide, vinblastine, prednisolone, and rituximab
Rituximab alone	(an option for stage 3 and stage 4 NLPHL)

If chemotherapy and radiation therapy are being used together, chemotherapy is usually only given for 2 to 4 months.

After finishing treatment, expect to have a positron emission tomography/computed tomography (PET/CT) scan to learn if the cancer improved. This is called restaging.

If the cancer improves but you are still having symptoms, radiation therapy is recommended (if you haven't already had it).

Refractory or relapsed NLPHL

Cancer that doesn't improve with initial treatment is described as refractory. Cancer that returns after a cancer-free period is described as relapsed.

Seeking treatment at a center with expertise in this rare cancer is encouraged, ideally within a clinical trial.

For refractory NLPHL, or if a relapse is suspected, a biopsy is needed to guide your care. This involves removing samples from at least 1 tumor and testing them in a lab.

If the cancer hasn't transformed, you may not need treatment. Options for care are based on your general health and the features of the cancer. Details are provided below.

If the biopsy is negative and you don't have any symptoms, a period of observation is recommended before re-assessing for relapse.

Non-bulky and not causing symptoms

If the cancer is small and not causing symptoms, options include observation, rituximab, and radiation therapy.

If rituximab is planned, some people may continue treatment with rituximab alone for 2 years. This is called maintenance therapy.

If the cancer improves after treatment and you don't have symptoms, observation is recommended. If you have symptoms, high dose chemotherapy with stem cell rescue is an option. See page 40 for more information about this treatment.

Guide 8
Second-line and beyond regimens for NLPHL

- Rituximab
- Rituximab + bendamustine
- Rituximab + DHAP (dexamethasone, cisplatin, high-dose cytarabine)
- Rituximab + ICE (ifosfamide, carboplatin, etoposide)
- Rituximab + IGEV (ifosfamide, gemcitabine, vinorelbine)
- Certain first-line regimens in **Guide 7** (if not already used)

If the cancer doesn't improve or gets worse, treatment with rituximab, alone or with chemotherapy is recommended. Regimens are listed in **Guide 8**.

Bulky or causing symptoms

If the cancer is bulky (large) or causing symptoms, second-line systemic therapy is recommended. There are no preferred options. Your provider will recommend a regimen based on your treatment history. See **Guide 8**.

In addition to systemic therapy, your provider may recommend radiation therapy or high dose chemotherapy with stem cell rescue.

Key points

- NLPHL is a rare type of Hodgkin lymphoma that is usually found at an early age. Over time it can become a fast-growing non-Hodgkin lymphoma.
- Rituximab (Rituxan) is an antibody therapy widely used alone or in combination with chemotherapy to treat NLPHL
- Radiation therapy is the preferred treatment for most non-bulky stage 1A and 2A cancers.
- Treatment with chemotherapy, rituximab, and radiation therapy is recommended for stage 1B–2B cancers and bulky stage 1A–2A cancers.
- Treatment with chemotherapy and rituximab is recommended for most people with non-contiguous stage 2A cancers. Radiation therapy may be added.
- Initial treatment options for stage 3-4 NLPHL may include observation, chemotherapy, rituximab, or radiation therapy to relieve symptoms.
- After being confirmed by biopsy, relapsed or refractory NLPHL may be observed or treated with rituximab, chemotherapy, radiation therapy, or all of these.

Questions to ask

- What are the odds that the cancer will transform?
- What are the most common side effects of rituximab?
- Is it safe to observe advanced NLPHL without treatment?

7
When treatment is over

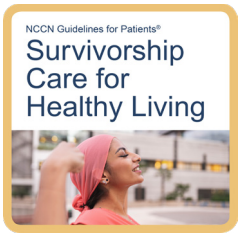
Classic Hodgkin lymphoma can usually be cured. But, its treatment can cause other cancers and health problems later in life. It's important to see a provider who understands the health issues and risks faced by Hodgkin lymphoma survivors.

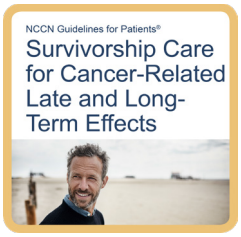
After Hodgkin lymphoma is cured, there isn't a one-size-fits-all strategy for follow-up care. The types of surveillance tests and how often you should have them are based on:

- Your age
- The cancer stage at diagnosis
- Your social habits
- Your treatment history

For more information on cancer survivorship, the following are available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

- *Survivorship Care for Healthy Living*
- *Survivorship Care for Cancer-Related Late and Long-term Effects*





The first 5 years

During the first 5 years after treatment, it is important to monitor for the return of Hodgkin lymphoma. The recommended care during this time is explained below.

Physical exams

During the first 1 to 2 years, a physical exam is recommended every 3 to 6 months. They are then given every 6 to 12 months until 3 years after treatment. Yearly exams are recommended after that.

Imaging tests

Imaging is only generally needed if your provider strongly suspects the cancer has come back.

If needed, imaging may include a CT scan every 3 to 6 months for up to 2 years, or after 2 years if relapse is suspected.

You may need another PET/CT if the results of your last one suggested a poor response to treatment. But, having PET scans on a regular basis to monitor for the return of Hodgkin lymphoma is not recommended.

Blood tests

There is no recommended schedule for bloodwork in the first 5 years after treatment. Your doctor may order blood tests at the time of your physical exams, or may only order them if relapse is suspected.

Blood tests your doctor may order include a complete blood count (CBC), erythrocyte sedimentation rate (ESR), and chemistry

profile. An ESR is usually only needed if your initial ESR was high. If you had radiation therapy to the neck, a thyroid-stimulating hormone (TSH) test is recommended at least once a year.

Long-term care (after 5 years)

Some side effects of Hodgkin lymphoma and its treatment can start years after treatment. These are called late effects. The most serious late effects that survivors experience are described next, along with recommendations for managing your risk.

The longer you are monitored after finishing treatment, the more likely you are to experience some of these side problems. Recommended long-term care is described next.

Physical exams

Physical exams continue to be an important part of follow-up care. You should continue having a physical exam once a year.

Your provider will closely monitor changes in your blood pressure. Any signs of heart damage or disease should be noted and promptly managed.

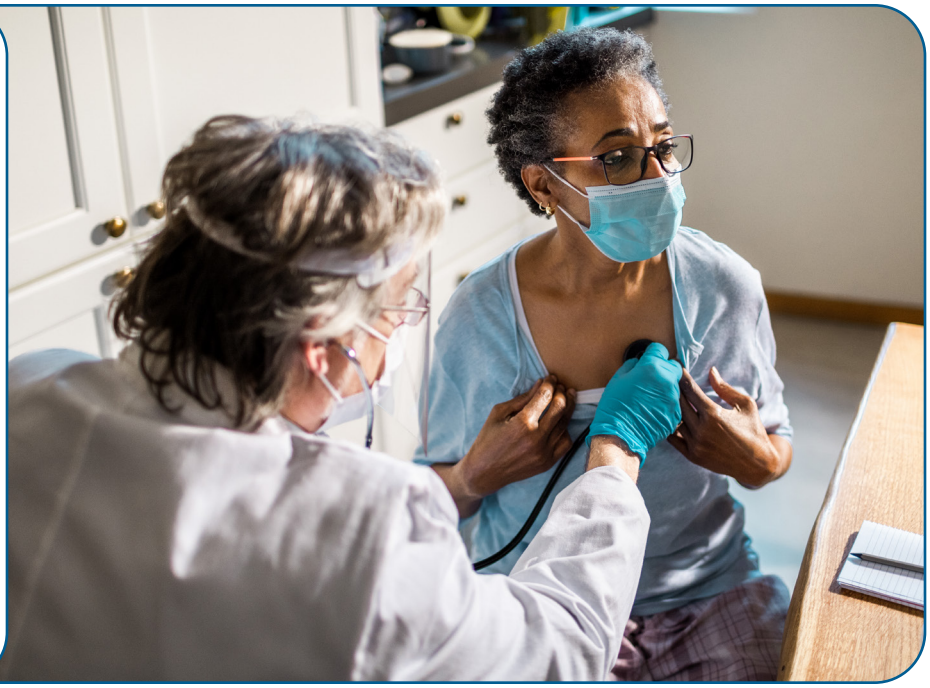
Blood tests

A yearly CBC and a chemistry profile are recommended beginning in the sixth year after treatment. If your neck was treated with radiation, continue to have your TSH level measured at least once a year.

Due to the increased risk of heart damage or disease over time, extra bloodwork to test for lipid disorders and diabetes is needed after 5 years. Lipids are fats that your body uses for energy. Cholesterol is a lipid. You should have

Physical exams

Physical exams are needed more often right after treatment and then spaced farther apart. Starting in the third year after treatment, a physical exam is recommended once per year.



a test called a lipids panel twice per year. A lipids panel typically measures your:

- Total cholesterol level
- Triglyceride level
- The levels of “good” (HDL) and “bad” (LDL) cholesterol

Glucose—a simple sugar—is your body’s main source of energy. A fasting glucose test measures the amount of glucose in your blood. If the level is high, it could be a sign of diabetes. If the level is low, it could be a sign of hypothyroidism. A fasting glucose test is recommended once a year beginning in the sixth year after finishing treatment.

Thyroid problems

The thyroid is a small, butterfly-shaped gland in the front of the neck. About half of Hodgkin lymphoma survivors who receive radiation therapy to the neck or upper chest have thyroid problems later in life.

The most common problem is that the thyroid gland doesn’t make enough thyroid hormone. This is called hypothyroidism or underactive thyroid. Symptoms include weight gain, constipation, dry skin, and sensitivity to cold temperatures.

Your provider should do a careful thyroid exam during your annual physical exam. Thyroid function tests should also be done at least once a year, especially in people who had radiation therapy to the neck.

Thyroid exams

About half of Hodgkin lymphoma survivors who had radiation therapy to the neck or upper chest have thyroid problems later in life. A careful thyroid examination is an important part of your annual physical exam.

Heart disease

Hodgkin lymphoma survivors are at increased long-term risk of heart or blood vessel problems. This is called heart disease or cardiovascular disease. Symptoms of heart disease can start at any age, but damage to the heart or blood vessels is usually found more than 5 to 10 years after finishing treatment.

If you had radiation therapy to the area between your lungs, you are at increased risk for developing heart disease.

The other main risk factor is treatment with the chemotherapy drug doxorubicin. Doxorubicin is an anthracycline used in ABVD and some other recommended regimens. Among other side effects, it can cause heart damage.

Your blood pressure should be taken at least once a year and closely monitored, even if you don't have symptoms of heart disease.

Your provider may order an exercise stress test or heart ultrasound (echocardiogram) when you are done treatment. If you had radiation therapy to the neck, you may also have an ultrasound of your carotid artery. The goal of this testing is to get a baseline (starting) measurement of your heart health. The testing may be repeated every 10 years and compared to your baseline results.

Exercise stress test

To check for signs of heart disease, you may have an exercise stress test every 10 years after finishing treatment.

Screening for secondary cancers

Hodgkin lymphoma survivors are at risk of other types of cancer, especially if radiation therapy was included in first-line treatment.

Secondary cancers often develop more than 10 years after finishing treatment for Hodgkin lymphoma. Lung cancer and breast cancer are the most common. Skin cancers can also occur in areas treated with radiation.

Screening for breast cancer is important for those assigned female at birth who have intact breast tissue. If you had radiation therapy to the chest or armpit area, start getting mammograms 8 years after finishing treatment, or at age 40 (whichever comes first).

If you had radiation therapy to the chest between the ages of 10 and 30, screening with **both** mammography and breast magnetic resonance imaging (MRI) is recommended.

In addition to imaging, a health care professional should examine your breasts once or twice a year. You are also encouraged to become familiar with your breasts and report any changes you notice to your provider. In some cases, seeing a breast specialist may be recommended.

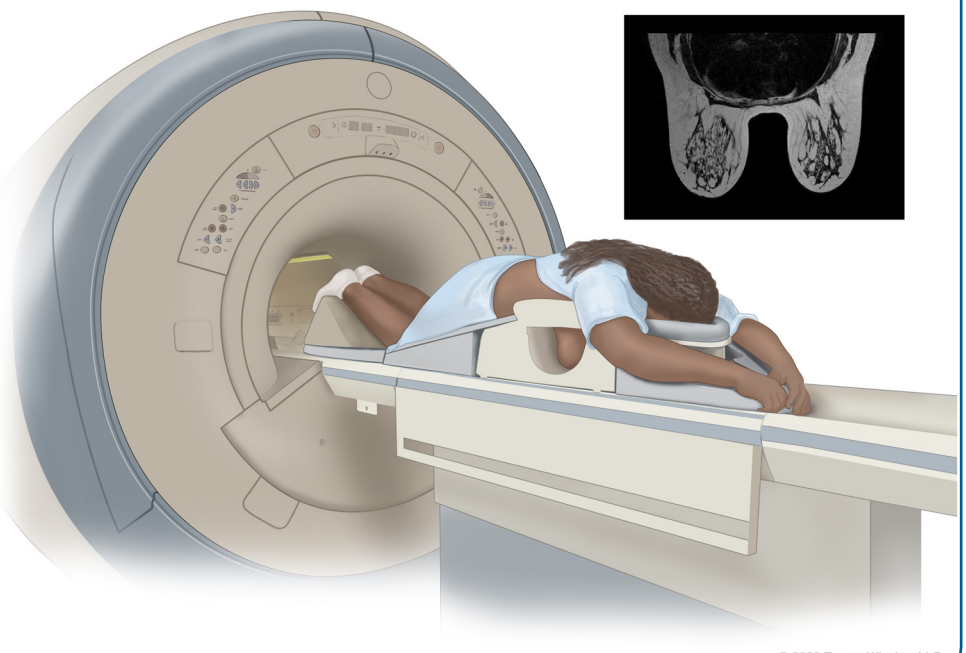
Screening for cervical, colorectal, endometrial, lung, and prostate cancer is recommended. Screening should follow NCCN recommendations and those of the American Cancer Society (ACS).

Vaccines

Everyone should continue to get the influenza vaccine (the flu shot) every year, and other vaccines as needed.

Screening for breast cancer

Hodgkin lymphoma survivors assigned female at birth are at increased risk of breast cancer. If you had radiation therapy to the chest between the ages of 10 and 30, screening with both breast MRI (shown here) and mammography is recommended.



Key points

- Hodgkin lymphoma survivors are at increased risk of second cancers, heart disease, and underactive thyroid. Follow-up care is personalized and based on your cancer circumstances.
- Physical exams are given more often in the first 2 years after treatment. Beginning in the third year, they are recommended yearly. To check for signs of heart disease, your blood pressure will be checked at least once a year.
- Imaging is only generally ordered if your provider strongly suspects the cancer has come back. If needed, imaging may include a CT scan every 3 to 6 months for up to 2 years.
- If you received radiation therapy to the neck or upper chest, you may develop underactive thyroid. Symptoms include weight gain, constipation, dry skin, and sensitivity to cold temperatures.
- Survivors assigned female at birth who had radiation therapy to the chest should start getting mammograms 8 years after treatment, or at age 40 (whichever is first). If the radiation was received between the ages of 10 and 30, you should also have breast MRI scans.
- Screening for cervical, lung, skin, and prostate cancers is recommended for Hodgkin lymphoma survivors. Screening should follow NCCN recommendations and those of the American Cancer Society (ACS).

Questions to ask

- How common are second cancers in Hodgkin lymphoma survivors?
- My chemotherapy regimen included doxorubicin. What am I at risk for?
- What else can I do to mange my risk of late side effects?

8
Other resources

Want to learn more? Here's how you can get additional help.

What else to know

This book can help you improve your cancer care. It plainly explains expert recommendations and suggests questions to ask your care team. But it's not the only resource that you have.

You're welcome to receive as much information and help as you need. Many people are interested in learning more about:

- The details of their health and treatment
- Being a part of a care team
- Getting financial help
- Finding a care provider who is an expert in their field
- Coping with health problems

What else to do

Your health care center can help you with next steps. They often have on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself. Look through the list and visit the provided websites to learn more about these organizations.

Where to get help

AnCan Foundation
Ancan.org

Blood & Marrow Transplant Information Network
bmtinfonet.org

Cancer*Care*
Cancercare.org

Cancer Hope Network
Cancerhopenetwork.org

Imerman Angels
Imermanangels.org

Lymphoma Research Foundation
lymphoma.org

National Bone Marrow Transplant Link (nbmtLINK)
nbmtlink.org

National Coalition for Cancer Survivorship
canceradvocacy.org

NMDP
NMDP.org

The Leukemia & Lymphoma Society
LLS.org/PatientSupport

Triage Cancer
triagecancer.org

Words to know

hematopoietic cell transplant (HCT)
A treatment that destroys your bone marrow then rebuilds it with your healthy stem cells. Also called high-dose therapy with autologous stem cell rescue (HDT/ASCR).

B symptoms
Unexplained fevers, heavy night sweats, and fast weight loss without dieting caused by Hodgkin lymphoma.

bone marrow
Soft, sponge-like tissue in the center of most bones where blood cells are made.

cancer stage
A rating of the extent of cancer in the body.

classic Hodgkin lymphoma (CHL)
The most common type of Hodgkin lymphoma. Subtypes include nodular sclerosis, mixed cellularity, lymphocyte-rich, and lymphocyte-depleted.

clinical trial
A type of research that studies how well investigational treatment approaches work in people.

computed tomography (CT)
A test that uses x-rays from many angles to make pictures of areas inside the body.

contiguous lymphoma
Lymphoma in which the lymph nodes with cancer are next to each other.

contrast
A substance put into your body to make clearer pictures during imaging tests.

core needle biopsy
The removal of a tissue sample with a wide needle for examination under a microscope. Also called core biopsy.

Deauville scale
A rating scale used to describe how Hodgkin lymphoma is responding to treatment.

diaphragm
The thin muscle below the lungs and heart that helps a person to breathe.

echocardiogram
An ultrasound of the heart. Recommended if chemotherapy containing an anthracycline is planned.

erythrocyte sedimentation rate (ESR)
A test for inflammation based on how much clear liquid is at the top of a tube of blood after one hour.

excisional lymph node biopsy
The preferred biopsy method for diagnosing Hodgkin lymphoma. Involves removing entire lymph nodes in order to test them for cancer cells.

fatigue
Severe tiredness despite getting enough sleep that limits one's ability to function.

granulocyte colony-stimulating factor (G-CSF)
A type of growth factor that drives bone marrow to make white blood cells. Included in some chemotherapy regimens to boost the immune system.

immune system
The body's natural defense against infection and disease.

involved-site radiation therapy (ISRT)
A type of external radiation therapy often used to treat Hodgkin lymphoma. Radiation is delivered to the lymph nodes in which the cancer started and nearby areas of cancer.

liver function test
Test that measures chemicals in the blood that are made or processed by the liver.

lung function test
A test used to measure how well the lungs work. Also called pulmonary function test.

lymph
A clear fluid containing white blood cells called lymphocytes.

lymphatic system
The tissues and organs that produce, store, and carry white blood cells that fight infections and other diseases. Part of the immune system.

lymph node
Small groups of disease-fighting cells located throughout the body.

lymphocyte
A type of immune cell that's made in the bone marrow and is found in the blood and in lymph tissue.

mediastinum
The area of the chest between the lungs.

nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL)
A rare form of Hodgkin lymphoma that can transform into a fast-growing type of non-Hodgkin lymphoma.

noncontiguous lymphoma
Lymphoma in which the lymph nodes containing cancer are on the same side of the diaphragm, but are not next to each other.

positron emission tomography (PET) scan
A test that uses a small amount of radioactive glucose (sugar) and a scanner to see where cancer may exist in the body.

spleen
An organ in the lymphatic system that helps protect the body from disease. It is located on the left side of the abdomen near the stomach.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hodgkin Lymphoma, Version 2.2025. It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • pennmedicine.org/cancer

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • cityofhope.org

Dana-Farber/Brigham and Women's Cancer Center |
Mass General Cancer Center
Boston, Massachusetts
877.442.3324 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah
800.824.2073 • healthcare.utah.edu/huntsmancancerinstitute

Indiana University Melvin and Bren Simon
Comprehensive Cancer Center
Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Johns Hopkins Kimmel Cancer Center
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

Robert H. Lurie Comprehensive Cancer Center
of Northwestern University
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Roswell Park Comprehensive Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute
Columbus, Ohio
800.293.5066 • cancer.osu.edu

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

The University of Texas MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

UC Davis Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • uclahealth.org/cancer

UCSF Helen Diller Family Comprehensive Cancer Center
San Francisco, California
800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW • yalecancercenter.org

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