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GUIDELINES  
FOR PATIENTS®

2024

# Diffuse Large B-Cell Lymphomas



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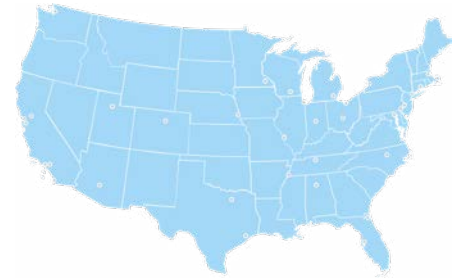
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Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).



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 B-Cell Lymphomas Version 1.2024 – January 18, 2024.**

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# 1

## Lymphoma basics

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**Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma (NHL). NHLs develop from lymphocytes, a type of white blood cell. DLBCL is a fast-growing cancer, affecting tissues and organs such as bone marrow, spleen, thymus, lymph nodes, lymphatic vessels, and other parts of the body.**

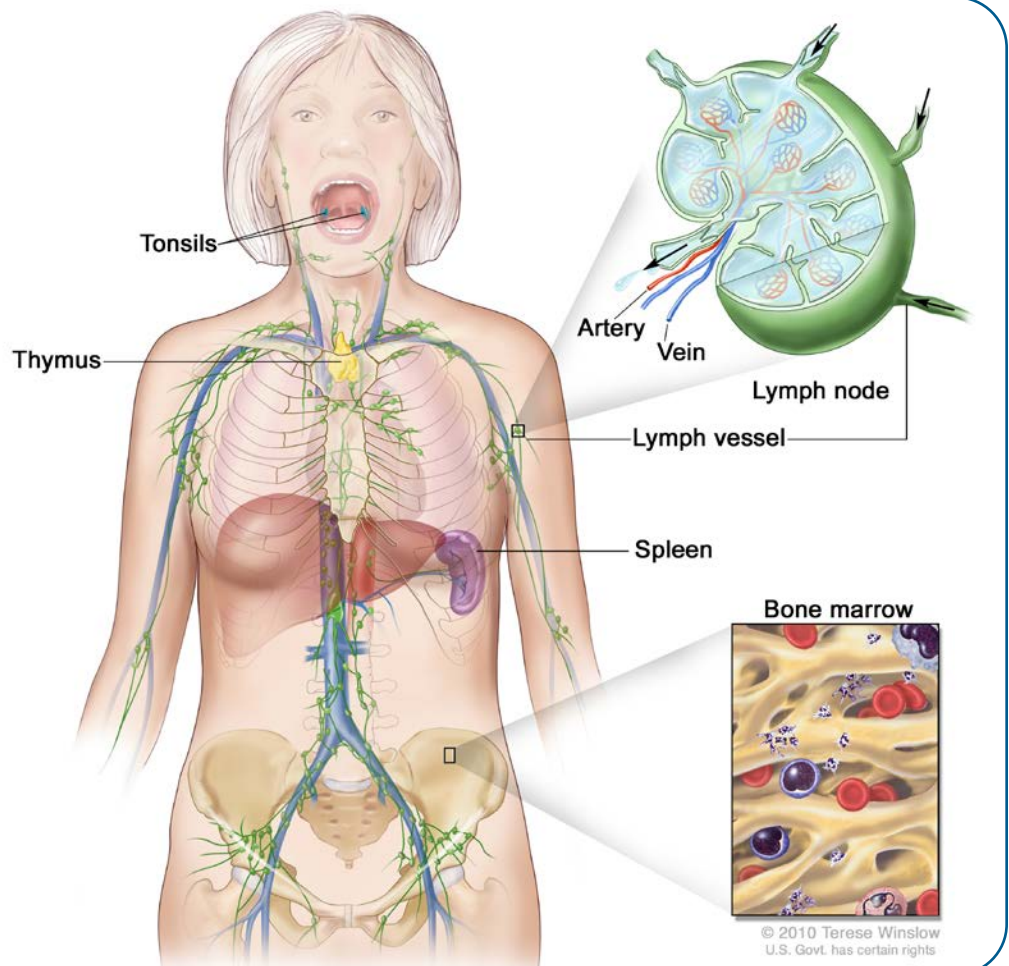
## Lymphatic system

Non-Hodgkin lymphoma (NHL) begins in the lymphatic system. The lymphatic or lymph system is a major part of the body's immune system. It is a germ-fighting network of tissues and organs that includes the bone marrow, spleen, thymus, lymph nodes, and lymphatic vessels.

Lymphatic vessels are a network of thin tubes that carry lymphatic fluid (lymph) and white blood cells into all the tissues of the body. Lymph gives cells water and food. White blood cells, such as lymphocytes, help fight infection and disease.

### Lymphatic system

The lymphatic or lymph system is part of the immune system. It includes lymph vessels, lymph nodes, tonsils, thymus, spleen, and bone marrow.



As lymph travels throughout your body, it passes through hundreds of small bean-shaped structures called lymph nodes. Lymph nodes make immune cells that help the body fight infection. They also filter the lymph fluid and remove foreign material such as bacteria and cancer cells.

## Lymphocytes

Non-Hodgkin lymphoma (NHL) is a cancer of lymphocytes. A lymphocyte is a type of white blood cell that helps fight and prevent infection. Lymphocytes are found in blood and lymph tissue, and every organ in the body. Lymph tissue includes lymph vessels and lymph nodes. Lymphocytes normally grow in response to infection or inflammation. When they grow on their own without proper regulation, they can develop into lymphoma.

There are 3 main types of lymphocytes:

- **B lymphocytes or B cells** make antibodies. An antibody is a protein.
- **T lymphocytes or T cells** help fight infections, kill tumor cells, and control immune responses.
- **Natural killer (NK) cells** can kill tumor cells or virus-infected cells.

Non-Hodgkin lymphoma can develop from B-cell, T-cell, or NK-cell lymphocytes. Diffuse large B-cell lymphoma (DLBCL) starts in B cells. B cells mature into plasma cells, which produce antibodies that are used to attack invading bacteria, viruses, and toxins. The antibody molecules latch onto and destroy invading viruses or bacteria by recruiting other components of the immune system. Cancers of plasma cells are multiple myeloma and not lymphoma.

## DLBCL

Diffuse large B-cell lymphoma (DLBCL) is the most common type of NHL. It accounts for about 3 out of every 10 NHLs. DLBCL tumors consist of fast-growing, large B cells. They are commonly found in lymph nodes, spleen, liver, bone marrow, or other tissues and organs. Symptoms can include fever, night sweats, fatigue, and weight loss. These symptoms are referred to as B symptoms. Not everyone has the same symptoms and tumors can be found anywhere in the body.

### LBCL subtypes

There are many subtypes of large B-cell lymphoma (LBCL). Diffuse large B-cell lymphoma DLBCL is one type. For types of LBCL, **see Guide 1.**



## Key points

- ▶ The lymphatic or lymph system is a network of tissues and organs that helps your body fight infections and disease. It is part of the immune system.
- ▶ Non-Hodgkin lymphoma (NHL) is a cancer that develops from lymphocytes, a type of white blood cell.
- ▶ Lymphocytes normally grow in response to infection or inflammation. When they grow on their own without proper regulation, they can develop into lymphoma.
- ▶ Diffuse large B-cell lymphoma (DLBCL) is the most common type of NHL. There are many types of large B-cell lymphoma (LBCL).
- ▶ DLBCL tumors consist of fast-growing, large B cells. They are commonly found in lymph nodes, spleen, liver, bone marrow, or other tissues and organs.

### Guide 1

#### Large B-cell lymphoma (LBCL) types

Diffuse large B-cell lymphoma (DLBCL)

DLBCL, not otherwise specified (NOS)

ALK-positive large B-cell lymphoma (LBCL)

Mediastinal gray zone lymphoma (MGZL)

Primary mediastinal large B-cell lymphoma (PMBL)

High-grade B-cell lymphoma (HGBL)

High-grade B-cell lymphoma, not otherwise specified (HGBL-NOS)

Intravascular LBCL

DLBCL associated with chronic inflammation (includes fibrin-associated DLBCL)

EBV-positive DLBCL, NOS

T-cell/histiocyte-rich LBCL

LBCL with *IRF4/MUM1* rearrangement

Primary cutaneous DLBCL, leg type (PC-DLBCL, leg type)

# 2

## Testing for DLBCL

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15	Biopsy	25	Key points

**Accurate testing is essential to diagnose and treat diffuse large B-cell lymphoma (DLBCL). This chapter presents an overview of possible tests you might receive and what to expect.**

### Test results

Results from biopsy and imaging studies will be used to determine your treatment plan. Treatment will be based on these findings. It is important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a great way to access your test results. Please discuss your results with your doctor or health care team.

Keep these things in mind:

- Choose a friend, family member, or peer who can drive you to appointments, provide meals, or offer emotional support during diagnosis and treatment.
  - Bring someone with you to doctor visits, if possible.
  - Write down questions and take notes during appointments. Don't be afraid to ask your care team questions. Get to know your care team and help them get to know you.
  - Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
  - Keep a list of contact information for everyone on your care team. Add it to your phone. Hang the list on your refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician (PCP) informed of changes to this list. You are encouraged to keep your PCP in the loop. They are great partners in your care.
  - In your contact list, include information on the exact type of cancer you have, as well as any treatments you've received and the date each treatment started.
  - Set up a MyChart or health record account if it's available, which will help you track your appointments and communicate with your care team.

## General health tests

Some general health tests are described next.

Tests to plan treatment can be found in

### Guide 2.

#### Guide 2

#### Tests to plan treatment

Biopsy and pathology review

Immunophenotyping with immunohistochemistry (IHC) and flow cytometry (FCM)

Physical exam with special attention to lymph node-bearing areas (including Waldeyer's ring) and to size of liver and spleen

Performance status (PS)

B symptoms (fever, drenching night sweats, and loss of more than 10 percent of body weight over 6 months)

Complete blood count (CBC) with differential, lactate dehydrogenase (LDH), comprehensive metabolic panel (CMP), uric acid, and hepatitis B testing

PET/CT scan (preferred) or CT with contrast of chest, abdomen, and pelvis (C/A/P)

Calculation of International Prognostic Index (IPI), which predicts overall and progression-free survival in DLBCL based on risk factors

Echocardiogram or multigated acquisition (MUGA) scan

Pregnancy test for those of childbearing age if chemotherapy or radiation therapy will be used

Possible:

- Head CT/MRI with contrast or neck CT/MRI with contrast
- HIV testing
- Hepatitis C testing
- Beta-2-microglobulin
- Lumbar puncture for those at risk for central nervous system (CNS) involvement
- Bone marrow biopsy with or without aspirate
- Discussion of fertility preservation

### Medical history

A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter (OTC) medicines, herbals, or supplements you take. Some supplements interact with and affect medicines that your care team may prescribe. Tell your care team about any symptoms you have. A medical history, sometimes called a health history, will help determine which treatment is best for you.

### Family history

Diffuse large B-cell lymphoma (DLBCL) is not inherited from your biological parents. However, some cancers and other diseases can run in families. Your care team will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members on both sides of your family about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. It's important to know the specific type of cancer or where the cancer started, if it is in multiple locations, and if they had genetic testing.

### Physical exam

During a physical exam, your doctor may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your height and weight
- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat

- Feel and apply pressure to parts of your body to see if organs such as your liver and spleen are of normal size, are soft or hard, or cause pain when touched
- Feel for enlarged lymph nodes in your neck, underarm, and groin

## Fertility (all genders)

Treatment such as chemotherapy can affect your fertility, the ability to have children. If you think you want children in the future, ask your care team how cancer and cancer treatment might change your fertility. To preserve your fertility, you may need to take action before starting cancer treatment. Those who want to have children in the future should be referred to a fertility specialist to discuss the options before starting treatment.

Fertility preservation is all about keeping your options open, whether you know you want to have children later in life or aren't sure at the moment. Fertility and reproductive specialists can help you sort through what may be best for your situation.

More information on fertility preservation in adolescents and young adults is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



### Changes in fertility

Treatment might cause your fertility to be temporarily or permanently impaired or interrupted. This loss of fertility is related to your age at time of diagnosis, treatment type(s), treatment dose, and treatment length. Talk to your care team about your concerns and if you are planning a pregnancy.

### Preventing pregnancy during treatment

Cancer and cancer treatment can affect the ovaries and damage sperm. If you become pregnant during chemotherapy, radiation therapy, or other types of systemic therapy, serious birth defects can occur. Speak with your care team about preventing pregnancy while being treated for cancer. Hormonal birth control may or may not be recommended, so ask your doctor about options such as intrauterine devices (IUDs) and barrier methods. Types of barrier methods include condoms, diaphragms, cervical caps, and the contraceptive sponge.

### Those with ovaries

Those who can become pregnant will have a pregnancy test before starting treatment. Cancer treatment can hurt the developing baby if you are or become pregnant during treatment. Therefore, birth control to prevent pregnancy during and after treatment is recommended. If you are pregnant or breastfeeding at the time of your cancer diagnosis, certain treatments will need to be avoided.

Menstruation, menses, menstrual flow, or your period may stop during treatment, but often returns within 2 years after treatment in those 35 years of age and under. It is still possible to become pregnant even though you might not have a period. Therefore, birth control is recommended during and after treatment. Consult your doctor for the best time to plan a pregnancy.

### Those with testicles

Cancer and cancer treatment can damage sperm. Therefore, use contraception (birth control) such as condoms to prevent pregnancy during and immediately after cancer treatment.

## Performance status

Performance status (PS) is a person's general level of fitness and ability to perform daily tasks. Your state of general health will be rated using a PS scale called ECOG (Eastern Cooperative Oncology Group). PS is one factor taken into consideration when choosing a treatment plan. Your preferences about treatment are always important.

The ECOG PS scores range from 0 to 5.

- **PS 0** means the person is fully active.
- **PS 1** means the person is still able to perform light to moderate activity, but with some limitations.
- **PS 2** means the person is limited to the chair or bed less than half of the day and still able to care for self.
- **PS 3** means the person is limited to the chair or bed more than half of the day.
- **PS 4** means the person is totally confined to the bed or chair and completely disabled.
- **PS 5** means the person is not alive.

Good PS is usually PS 0 or PS 1.

## Blood tests

Blood tests check for signs of disease and how well organs are working. They require a sample of your blood, which is removed through a needle placed into your vein. Be prepared to have many blood tests during DLBCL treatment and recovery to check treatment results, blood counts, and the health of organs like your liver and kidneys.

### Complete blood count and differential

A complete blood count (CBC) measures the levels of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs) in your blood. A CBC is a key test that gives a picture of your overall health. A differential counts the number of each type of WBC (neutrophils, lymphocytes, monocytes, eosinophils, and basophils). It also checks if the counts are in balance with each other.

### Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) measures 14 different substances in your blood. It is usually done on the plasma part of your blood. A CMP provides important information about how well your kidneys and liver are working, among other things.

### Creatinine

Creatinine is a waste produced in the muscles. Every person generates a fixed amount of creatinine every day based on how much muscle they have. It is filtered out of the blood by the kidneys. The level of creatinine in the blood tells how well the kidneys are working. Higher levels of creatinine mean the kidneys

aren't working as well as they were when someone had lower levels of creatinine.

### **Electrolytes**

Electrolytes help move nutrients into cells and help move waste out of cells. Electrolytes are ions or particles with electrical charges that help the nerves, muscles, heart, and brain work as they should. Your body needs electrolytes to function properly. Phosphate (PO<sub>4</sub>) is important for strong bones and teeth. Too much phosphate in your blood can be a sign your kidneys aren't working well.

### **Hepatitis B and hepatitis C**

Hepatitis B (HBV) and hepatitis C (HCV) are types of liver disease caused by a virus. A hepatitis blood test will show if you had hepatitis in the past or if you have it today. Some cancer treatments can wake up (or reactivate) the virus. If this happens, it can cause harm to the liver.

### **HIV**

Human immunodeficiency virus (HIV) causes acquired immunodeficiency syndrome (AIDS). An HIV antibody test checks for HIV antibodies in a sample of blood, urine, or saliva. It's important to let your doctor know if you have ever been infected with HIV. Treatment for HIV-positive DLBCL is not covered in this book.

### **HLA typing**

Human leukocyte antigen (HLA) is a protein found on the surface of most cells. It plays an important role in your body's immune response. HLAs are unique to each person. They mark your body's cells. Your body



**Testing takes time. It might take days or weeks for all test results to come in.**

detects these markers to tell which cells are yours. In other words, all your cells have the same set of HLAs. Each person's set of HLAs is called the HLA type or tissue type.

HLA typing is a blood test that detects a person's HLA type. This test is done before a donor (allogeneic) hematopoietic cell transplant (HCT). To find a donor match, your proteins will be compared to the donor's proteins to see how many proteins are the same. A very good match is needed for a transplant to be a treatment option. Otherwise, your body will reject the donor cells or the donor cells will react against your body. Blood or tissue samples from you and your blood relatives will be tested first.

### **Lactate dehydrogenase**

Lactate dehydrogenase (LDH) or lactic acid dehydrogenase is a protein found in most cells. Dying cells release LDH into blood. Fast-growing cells also release LDH and cause levels of this protein to be elevated in the blood.



### Pregnancy test

If planned treatment might affect pregnancy, then those who can become pregnant will be given a pregnancy test before treatment begins.

### SPEP

Serum protein electrophoresis (SPEP) examines specific proteins in the blood called globulins, which may be increased in certain conditions.

### Uric acid

Uric acid is released by cells when DNA breaks down. It is a normal waste product that dissolves in your blood and is filtered by the kidneys where it leaves the body as urine. Too much uric acid in the body is called hyperuricemia. With DLBCL, it can be caused by a fast turnover of lymphoma cells. High uric acid might be a side effect of chemotherapy or

radiation therapy. Very high levels of uric acid in the blood can damage the kidneys.

## Biopsy

A biopsy is the removal of tissue or fluid for testing. It is an important part of an accurate diagnosis of lymphoma. Your sample should be reviewed by a pathologist who is an expert in the diagnosis of lymphoma. The pathologist will note the overall appearance and the size, shape, and type of your cells. This review is often referred to as histology, histopathology, or hematopathology review. Tests will be done on the biopsied cells. Ask questions about your biopsy results and what they mean for your treatment.

**Your preferences about treatment are always important. If you have any religious or personal beliefs about certain kinds of treatment, share them with your care team and make your wishes known.**



Types of possible biopsies include the following:

- **Fine-needle aspiration (FNA)** and core biopsy (CB) use needles of different sizes to remove a sample of tissue or fluid.
- **Incisional biopsy** removes a small amount of tissue through a cut in the skin or body.
- **Excisional biopsy** removes the entire tumor through a cut in the skin or body.
- **Lymph node biopsy** removes tissue from a lymph node.

A biopsy is usually done with other lab methods to accurately diagnose the type of DLBCL. Incisional or excisional biopsies are often preferred for diagnosing DLBCL.

These other lab methods include:

- Immunohistochemistry (IHC)
- Flow cytometry
- Biomarker testing to detect gene rearrangements and karyotype or fluorescence in situ hybridization (FISH) for major translocations

In a gene rearrangement, there is either loss or gain of chromosomal material. A translocation refers to the transfer of genetic material from one chromosome to another.

### Lymph node biopsy

A lymph node biopsy is recommended to diagnose DLBCL. Lymph nodes are usually too small to be seen or felt. Sometimes, lymph nodes can feel swollen, enlarged, hard to the touch, or don't move when pushed (fixed or immobile). A lymph node biopsy can be done using a needle biopsy procedure or as a small surgery to remove (excise) a lymph node.

### Bone marrow tests

Bone marrow tests might be done in certain cases.

There are 2 types of bone marrow tests that are often done at the same time:

- Bone marrow aspirate
- Bone marrow biopsy

Your bone marrow is like a sponge holding liquid and cells. An aspirate takes some of the liquid and cells out of the sponge, and a biopsy takes a piece of the sponge.

For many, this is a painful procedure. Your care team will try to make you as comfortable as possible. The samples are usually taken from the back of the hip bone (pelvis). You will likely lie on your belly or side. For an aspirate, a hollow needle will be pushed through your skin and into the bone. Liquid bone marrow will then be drawn into a syringe. For the biopsy, a wider needle will be used to remove a small piece of bone. You may feel bone pain at your hip for a few days. Your skin may bruise.

## Immunophenotyping

Immunophenotyping is a process that uses antibodies to detect the presence or absence of certain antigens. Antigens are proteins or markers that can be found on the surface of or inside all cells, including white blood cells. Specific groupings of antigens are normal. However, some specific patterns of antigens called the immunophenotype are found on abnormal cells including non-Hodgkin lymphoma (NHL) and DLBCL.

Immunophenotyping can be done using specialized techniques called flow cytometry or immunohistochemistry. These techniques are used to distinguish DLBCL from other types of lymphoma. Immunophenotype can change as cancer progresses.

DLBCL immunophenotype is usually positive for proteins CD20 and CD45, and negative for protein CD3. Immunophenotyping is

used to help support a diagnosis. However, an accurate diagnosis requires a trained pathologist to review the tissue for abnormal cells seen under a microscope. More testing may be needed to establish a subtype.

DLBCL is divided into 2 broad categories:

- Germinal center B-cell (GCB)
- Non-GCB

Immunophenotyping is used to establish diagnosis and GCB versus non-GCB origin.

- GCB is CD10+ or BCL6+ and IRF4/MUM1-.
- Non-GCB is CD10- and IRF4/MUM1+ or BCL6- and IRF4/MUM1-.

Additional markers are used to establish subtype. **See Guide 3.**

### Guide 3

#### Tests to diagnose DLBCL

<b>Needed</b>	<ul style="list-style-type: none"> <li>• Biopsy and hematopathology review</li> <li>• IHC panel: CD20, CD3, CD5, CD10, CD21, CD45, BCL2, BCL6, Ki-67, IRF4/MUM1, and MYC with or without cell surface marker analysis by flow cytometry: kappa/ lambda, CD45, CD3, CD5, CD19, CD10, and CD20</li> <li>• Karyotype or FISH for <i>MYC</i></li> <li>• FISH for <i>BCL2</i> and <i>BCL6</i> rearrangements if <i>MYC</i> positive</li> </ul>
<b>In some cases</b>	<ul style="list-style-type: none"> <li>• Additional IHC studies to determine DLBCL subtype: cyclin D1, kappa/ lambda, CD30, CD138, anaplastic lymphoma kinase (ALK), human herpesvirus-8 (HHV8), and SOX11</li> <li>• Epstein-Barr encoding region in situ hybridization (EBER-ISH)</li> <li>• Karyotype or FISH for <i>IRF4/MUM1</i> rearrangements</li> </ul>

### Flow cytometry

Flow cytometry (FCM) is a laboratory method used to detect, identify, and count specific cells. Flow cytometry involves adding a light-sensitive dye to cells. The dyed cells are passed through a beam of light in a machine. The machine measures the number of cells, things like the size and shape of the cells, and other unique features of cells. Flow cytometry may be used on cells from circulating (peripheral) blood, bone marrow, or a biopsy. The most common use of flow cytometry is in the identification of markers on cells, particularly in the immune system (called immunophenotyping).

The following cell surface markers might be tested using flow cytometry: kappa/lambda, CD45, CD3, CD5, CD19, CD10, and CD20.

### Immunohistochemistry

Immunohistochemistry (IHC) is a special staining process that involves adding a chemical marker to immune cells. The cells are then studied using a microscope. IHC looks for the immunophenotype of cells from a biopsy or tissue sample.

## Biomarker and genetic tests

Biomarker and genetic tests are used to learn more about your type of DLBCL, to guide treatment, and to determine the likely path your cancer will take (prognosis). This genetic testing is different from family history genetic testing or genetic cancer risk testing. This testing looks for changes only in the DLBCL cells that have developed over time, and not changes in the rest of your body's cells. Biomarker testing includes tests of genes or their products (proteins) and identifies the presence or absence of mutations and certain proteins that might suggest the lymphoma subtype. It is sometimes called molecular testing, tumor profiling, gene expression profiling, or genomic testing.

Inside our cells are deoxyribonucleic acid (DNA) molecules. These molecules are tightly packaged into what is called a chromosome. Chromosomes contain most of the genetic information in a cell. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. Each chromosome contains thousands of genes. Genes are coded instructions that determine what proteins are made in your cells. A mutation is when something goes wrong in the genetic code. Proteins are written like this: BCL6. Genes are written with italics like this: *BCL6*. When a gene or protein is found (expressed), it is shown with a plus sign (+) like this: CD10+. When a gene or protein has not been found, it is written with a negative sign (-) like this CD10-.

DLBCL cells sometimes have changes in genes and chromosomes that can be seen under a microscope or found with other tests.

Examples of proteins on the cells:

- BCL2, BCL6, CD3, CD5, CD10, CD20, CD45, IRF4/MUM1, Ki-67, MYC, and others

Examples of genes in the DNA of cells:

- *MYC*, *BCL2*, and *BCL6*

### Beta-2-microglobulin tumor marker test

Beta-2-microglobulin (B2M) is a protein that can be found in the blood, urine, or cerebrospinal fluid (CSF). B2M is a type of tumor marker. Tumor markers are substances made by cancer cells or by normal cells in response to cancer in the body.

### Epstein-Barr virus in situ hybridization

Epstein-Barr encoding region (EBER) in situ hybridization (EBER-ISH) is used to detect the Epstein-Barr virus (EBV) in tissue samples. EBV sometimes can be found in those with DLBCL. This test can help determine the subtype of DLBCL.

### DLBCL mutation testing

A sample of your blood or bone marrow will be used to see if the DLBCL cancer cells have any specific mutations. Some mutations can be targeted with specific therapies. This is separate from the genetic testing for mutations that you may have inherited from your biological parents.

Mutation testing includes tests of genes or their products (proteins). Subtle new drug-

resistant mutations may occur over time.

Mutations can also happen during treatment. Mutation testing is used to look for these new mutations. Some mutations lead to resistance to certain targeted therapies. There are many possible mutations.

### Gene rearrangements

In gene rearrangements, part of a gene has broken off and attached to another gene, creating a new gene. When one cell divides many times, the entire group of cells is called clonal or clonality. In clonal rearrangements, the same gene rearrangements are found in a group of cancer cells.

- *MYC*, *BCL2*, and *BCL6* gene rearrangements are commonly found in DLBCL.

#### *MYC*

The gene for *MYC* (proto-oncogene) is found on chromosome 8. An *MYC* gene rearrangement (*MYC-R*) is often found with a *BCL2* or *BCL6* gene rearrangement.

#### *BCL2*

The gene for *BCL2* (B-cell lymphoma 2) is found on chromosome 18. The transfer of the *BCL2* gene to a different chromosome causes the *BCL2* protein to be made in larger amounts, which may keep cancer cells from dying.

#### *BCL6*

The gene for *BCL6* (B-cell lymphoma 6) is found on chromosome 3. *BCL6* rearrangement is the most frequent chromosomal abnormality found in DLBCL.

### Deletions

When part of a chromosome is missing, it is called a deletion. For example, in del(7q) the q part of chromosome 7 is missing (deleted). Specific chromosomal deletions can be found in some types of diffuse B-cell lymphomas but can also be found in other types of blood cancers and disorders.

### FISH

Fluorescence in situ hybridization (FISH) is a method that involves special dyes called probes that attach to pieces of DNA. Since this test doesn't need growing cells, it can be performed on bone marrow or a blood sample.

FISH can find translocations that are too small to be seen with other methods. A translocation occurs when parts of two chromosomes switch with one another. However, FISH can only be used for known changes. It cannot detect all the possible changes found within the chromosomes and genes. For example, FISH is used to detect *MYC*, *BCL2*, and *BCL6* gene rearrangements.

### Karyotype

A karyotype is a picture of chromosomes. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. A karyotype will show extra, missing (deletion), rearranged, or abnormal pieces of chromosomes. Since a karyotype requires growing cells, a sample of bone marrow or blood must be used.



### Mutations

DLBCL cells can have changes in genes and chromosomes. Mutation testing looks for these changes or abnormalities that are unique to DLBCL cells. Examples of such changes are called deletion, insertion, amplification, translocation (rearrangement), and point mutation.

- ✓ **Amplification** – When part of or a whole chromosome or gene is increased (for example, duplicated)
- ✓ **Deletion** – When part of a chromosome or gene is missing
- ✓ **Insertion** – When a new part of a chromosome or gene is included
- ✓ **Inversion** – Switching of parts within one chromosome
- ✓ **Point mutation** – When part of a gene is changed
- ✓ **Chromosome translocation and gene rearrangement** – Switching of parts between 2 chromosomes. When described at the chromosome level, it is called a translocation. When described at the gene level, it is called rearrangement.

### Translocations

Translocation is a switching of parts between two chromosomes. A translocation between chromosomes 11 and 18 is written as t(11;18). Specific translocations can help distinguish between types of blood cancers and disorders.

### PCR

A polymerase chain reaction (PCR) is a lab process that can make millions or billions of copies of your DNA or RNA (genetic information). PCR is very sensitive. It can find 1 abnormal cell among more than 100,000 normal cells. These copies, called PCR product, might be used for high-throughput sequencing (HTS) or next-generation sequencing (NGS). This is important when testing for treatment response or remission.

### Comparative genomic hybridization

Comparative genomic hybridization (CGH) is a technique that compares DNA samples from normal tissue and tumor tissue. It is used to detect abnormal chromosomes.

### High-throughput sequencing

High-throughput sequencing (HTS) is capable of sequencing hundreds of millions of DNA molecules at a time.

### Next-generation sequencing

Next-generation sequencing (NGS) is a method used to determine a portion of a person's DNA sequence. It shows if a gene has any mutations that might affect how the gene works. NGS looks at the gene in a more detailed way than other methods and can find mutations that other methods might miss.



### Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- ✓ Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- ✓ Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- ✓ Create folders for insurance forms, test types (ie, blood, imaging, pathology, radiology, genetics), treatments, and procedures. Organize items in the folder by date.
- ✓ Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- ✓ Add a section for questions and to take notes.

Bring your medical binder to appointments. You never know when you might need it!

## Genetic cancer risk testing

Genetic cancer risk testing is done using blood or saliva (spitting into a cup). The goal is to look for gene mutations inherited from your biological parents called germline mutations. Some mutations can put you at risk for more than one type of cancer. You can pass these genes on to your children. Also, family members might carry these mutations. Tell your care team if there is a family history of cancer.

## Imaging tests

Imaging tests take pictures of the inside of your body to look for cancer deposits. A radiologist, an expert in interpreting imaging tests, will write a report and send this report to your doctor. While these reports might be available to you through your patient portal or patient access system, please wait to discuss these results with your care team.

### Contrast material

Contrast material is used to improve the pictures of the inside of the body. Contrast materials are not dyes, but substances that help enhance and improve the images of several organs and structures in the body. It is used to make the pictures clearer. The contrast is not permanent and will leave your body in your urine immediately after the test. The types of contrast vary and are different for CT and MRI.

Tell your care team if you have had allergic reactions to contrast in the past. This is important. You might be given medicines to avoid the effects of those allergies. Contrast

might not be used if you have a serious allergy or if your kidneys aren't working well.

### CT scan

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All the images are combined to make one detailed picture. A CT scan of your head, neck, chest abdomen, and pelvis may be one of the tests to look for cancer. In most cases, contrast will be used.

### MRI scan

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. Because of the very strong magnets used in the MRI machine, tell the technologist if you have any metal in your body. During the test, you will likely be asked to hold your breath for 10 to 20 seconds as the technician collects the images. Contrast is often used.

A closed MRI has a capsule-like design where the magnet surrounds you. An open MRI has a magnetic top and bottom, which allows for an opening on each end. Closed MRIs are more common than open MRIs, so if you have claustrophobia (a dread or fear of enclosed spaces), be sure to talk to your care team about it.

### PET scan

A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is a substance injected into a vein to see where cancer cells are in the body and if



they are using sugar produced by your body to grow. Cancer cells show up as bright spots on PET scans. However, not all tumors will appear on a PET scan. Also, not all bright spots are cancer. It is normal for the brain, heart, kidneys, and bladder to be bright on PET. Inflammation or infection can also show up as a bright spot. When a PET scan is combined with CT, it is called a PET/CT scan.

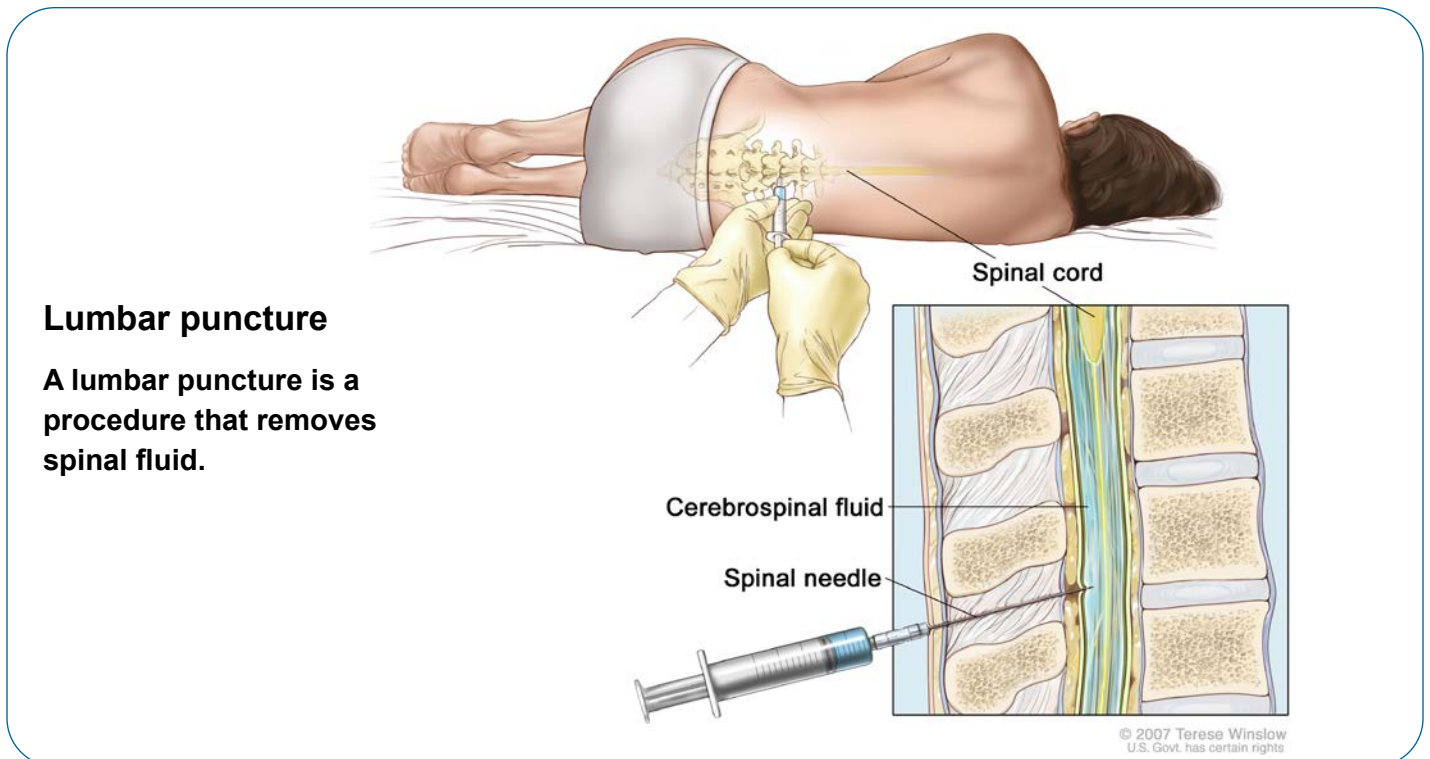
### Scrotal ultrasound

DLBCL can occasionally be found in the testicles. A scrotal ultrasound uses sound waves to make images of the scrotum. The scrotum is the pouch of skin at the base of the penis that contains the testicles.

## Lumbar puncture

Lymphoma can travel to the fluid that surrounds the spine or brain. This may cause symptoms. To know if lymphoma cells are in your spinal fluid, a sample must be taken and tested to rule out a central nervous system (CNS) disease.

A lumbar puncture (LP) is a procedure that removes spinal fluid. It is also called a spinal tap. A lumbar puncture may also be used to inject cancer drugs into spinal fluid. This is called intrathecal (IT) chemotherapy. When systemic therapy and IT therapy are given together to prevent CNS disease, it is called CNS prophylaxis.



# Heart tests

Certain treatments can affect heart (cardiac) function. Heart tests might be used to see how well your heart works. These tests might be used as a baseline and before giving chemotherapy. You might be referred to a heart specialist called a cardiologist.

## Electrocardiogram

An electrocardiogram (ECG or EKG) shows electrical changes in your heart. It reveals information about your heart rate and rhythm. Prolonged corrected QT interval (or QTc) occurs when your heart muscle takes longer than normal to recharge between beats. Often, this electrical disturbance can be seen on an ECG. Certain treatments for DLBCL can cause prolonged QTc. If the QTc becomes too prolonged, it can cause dangerous heart rhythms.

## Echocardiogram

An echocardiogram (or echo) uses sound waves to make pictures. For this test, small patches will be placed on your chest to track your heartbeat. Next, a wand with gel on its tip will be slid across part of your bare chest. A picture of your beating heart will be seen on a screen. The pictures will be recorded for future viewing.

An echocardiogram is one way of measuring ejection fraction, which is the amount of blood pumped out of the left side of your heart every time it beats. In low ejection fraction, the amount of blood pumping from the left side of the heart is lower than normal.

## MUGA

A multigated acquisition (MUGA) scan is used to evaluate the pumping function of your heart. During the test, a small amount of radiotracer is injected into a vein. A special camera, called a gamma camera, will create computer-generated movie images of your beating heart.

MUGA scan might show low ejection fraction. This is when the amount of blood pumping from the left side of the heart is lower than normal.



### **We want your feedback!**

**Our goal is to provide helpful and easy-to-understand information on cancer.**

**Take our survey to let us know what we got right and what we could do better.**

[NCCN.org/patients/feedback](https://www.nccn.org/patients/feedback)

### Key points

- Blood and imaging tests check for signs of disease, how well organs are working, and treatment results.
- A biopsy is the removal of tissue or fluid for testing. It is an important part of an accurate DLBCL diagnosis.
- A sample from your biopsy may undergo lab tests to learn more about your subtype of DLBCL and choose the best treatment for you.
- Immunophenotyping is used to pinpoint the specific subtype of DLBCL.
- *MYC*, *BCL2*, and *BCL6* are gene rearrangements that might be found in DLBCL.
- Imaging tests are used to look for areas of lymphoma involvement and are part of your staging workup.
- A lumbar puncture (LP) may be done to look for DLBCL in spinal and brain fluid.
- Certain treatments can affect heart function. Heart tests might be used to see how well your heart works.
- Online patient portals are a great way to access your test results. Be sure to discuss these results with your care team before drawing any conclusions about what the results might mean.

# 3

## Treating DLBCL

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**There is more than one treatment for diffuse large B-cell lymphomas. This chapter presents an overview of the possible types of treatment and what to expect. Not everyone will receive the same treatment. Treatment options are based on many factors. Together, you and your care team will choose a treatment plan that is best for you.**

DLBCL is highly treatable and curable. The goal of treatment is to achieve a complete response (CR) or complete remission. For many people with DLBCL, treatment is usually a combination of chemotherapy and immunotherapy called chemoimmunotherapy. Radiation therapy might be added. Surgery is not a routine part of treatment for DLBCL. If surgery is needed, find a surgeon with experience in DLBCL.

It is important to have regular talks with your care team about your goals for treatment and your treatment plan.

## Care team

Those with DLBCL should seek treatment at experienced cancer centers.

Treating cancer takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT). An MDT is a team of health care and psychosocial care professionals from different professional backgrounds who have knowledge (expertise) and experience in your type of cancer. This team is united in the planning and implementing of your treatment. Ask who will coordinate your care.

Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and help them get to know you.

Depending on your diagnosis, your team might include the following specialists:

- **A hematologist or hematologic oncologist** is a medical expert in blood diseases and blood cancers. Other types of oncologists include medical, radiation, and surgical oncologists.
- **A medical oncologist** treats cancer using systemic (drug) therapy.
- **A pathologist or hematopathologist** analyzes the cells and tissues removed during a biopsy and provides cancer diagnosis, staging, and information about biomarker testing.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.

- **Oncology pharmacists** are experts in knowing how to use medicines to treat cancer and to manage symptoms and side effects.
- **Palliative care specialists** concentrate on preventing and alleviating suffering and improving quality of life.
- **Nutritionists and dietitians** can provide guidance on what foods are most suitable for your condition.
- **An occupational therapist** helps people with the tasks of daily living.
- **A physical therapist** helps people move with greater comfort and ease.
- **Psychologists and psychiatrists** are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you think and feel.
- **Social workers** help people solve and cope with problems in their everyday lives. Clinical social workers also diagnose and treat mental, behavioral, and emotional issues. The anxiety a person feels when diagnosed with cancer might be managed by a social worker in some cancer centers. They, or other designated professionals, can help navigate the complexities of financial and insurance stresses.
- **Spiritual care specialists** identify and support those with spiritual distress or unmet spiritual needs.



## You know your body better than anyone

Help your care team understand:

- ✓ How you feel
- ✓ What you need
- ✓ What is working and what is not

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

**Get to know your care team and help them get to know you.**

- **A research team** helps to collect research data and coordinate care if you are in a clinical trial. Clinical trials help bring new therapies to patients and advance the treatment for everyone. Consider asking your care team about access to clinical trials.

## Treatment phases

The goal of treatment is remission. Here are some terms you might hear used by your care team.

### Induction

Induction or first-line therapy is the first phase of treatment. The goal of induction is complete response (CR) or complete remission. After induction, you will have tests to look for a response (remission).

### Remission

There are different types of treatment response. When there are no signs of cancer, it is called a complete response (CR) or complete remission. Remission can be short-term (temporary) or long-lasting (permanent). In partial response (PR), cancer is still present, but it has reduced in size.

### Relapse

When DLBCL returns after a period of remission, it is called a relapse. The goal of treatment is to achieve remission again. A relapse is very serious. It is important to ask about your prognosis.

### Refractory

When DLBCL remains and does not respond to treatment, it is called refractory or resistant cancer. This cancer may be resistant at the start of treatment or it may become resistant during treatment. Refractory disease is very serious. It is important to ask about your prognosis.

## Surveillance and monitoring

You will be monitored throughout treatment. Surveillance watches for any changes in your condition after completing treatment. You will have tests during surveillance to check for relapse.

## International Prognostic Index

The International Prognostic Index (IPI) is a scoring system to predict prognosis in those with lymphoma. A prognosis is the likely course your disease will take. IPI is based on age, performance status (PS), the stage of the cancer, lactate dehydrogenase (LDH) results, and if cancer is found in more than one area besides the lymph nodes.

## Systemic therapy

Systemic therapy works throughout the body. Types include chemotherapy, chemoimmunotherapy, immunotherapy, and targeted therapy. Systemic therapy might be used alone or with other therapies. Goals of systemic therapy may be curative or palliative and should be discussed before starting treatment.

The choice of therapy takes into consideration many factors, including age, other serious health issues, and future treatment possibilities like a hematopoietic cell transplant (HCT). Your preferences about treatment are important. If you have any religious or personal beliefs about certain kinds of treatment, now would be the time to share them with your care team.

## Chemotherapy

Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and some normal cells. More than one chemotherapy may be used to treat DLBCL. When only one drug is used, it's called a single agent. A combination or multi-agent regimen is the use of two or more chemotherapy drugs.

Some chemotherapy drugs are liquids that are infused into a vein or injected under the skin with a needle. Other chemotherapy drugs may be given as a pill that is swallowed. The final dose differs between people because it is based on body weight and height. Intrathecal (IT) chemotherapy is injected into spinal or brain fluid.

In most cases, chemotherapy is given in cycles of treatment days followed by days of rest. This allows the body to recover before the next cycle. Cycles vary in length depending on which chemotherapy is used. You will have tests to see how the cancer is responding to treatment. You might spend time in the hospital during treatment.

Here are 2 examples of a chemotherapy drug combination (regimen):

- CVP – Cyclophosphamide, vincristine, and prednisone
- EPOCH – Etoposide (Etopophos), prednisone, vincristine, cyclophosphamide, and doxorubicin

**A biosimilar or substitute might be used in place of rituximab. A biosimilar is an almost identical version of a drug made by another company. It is used in the exact same way and at the same dose as rituximab. Biosimilars for rituximab include: Riabni, Hycela, Ruxience, and Truxima.**

## Chemoimmunotherapy

Chemoimmunotherapy, also called immunochemotherapy, includes chemotherapy and immunotherapy drugs (agents) to treat cancer. There are several chemoimmunotherapy regimens used to treat DLBCL.

Two examples include:

- RCHOP – Rituximab, cyclophosphamide (Cytoxan), doxorubicin, vincristine (Oncovin), and prednisone
- Pola-R-CHP – Polatuzumab vedotin-piiq (Polivy), rituximab, cyclophosphamide, doxorubicin, and prednisone



## Antibody drug conjugate

An antibody drug conjugate (ADC) delivers cell-specific chemotherapy. It attaches to a protein found on the outside of the cancer cell and then enters the cell. Once inside the cell, chemotherapy is released. Loncastuximab tesirine-lpyl (Zynlonta) is an ADC that targets the CD19 protein. Polatuzumab vedotin-piiq targets the CD79b protein and brentuximab vedotin targets the CD30 protein.

## Immunotherapy

Immunotherapy is drug therapy that increases the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells. Immunotherapy can be given alone or with other types of treatment.

### Monoclonal antibody therapy

Antibody therapy uses special proteins normally produced by white blood cells and infection-fighting cells to help the body fight cancer, infection, or other diseases. Monoclonal antibodies (mAbs) used in cancer treatment may kill cancer cells directly or help the immune system recognize and then kill the cancer cells. As with other treatments, there is the potential for complications.

### CD19-targeting monoclonal antibody therapy

Tafasitamab-cxix (Monjuvi) is used to treat DLBCL and high-grade B-cell lymphoma by targeting the CD19 protein.

### CD20-targeting monoclonal antibody therapy

CD20-targeting mAbs (also called anti-CD20 mAbs) such as rituximab (Rituxan) and obinutuzumab (Gazyva) work against the CD20 protein found on the surface of B cells and DLBCL. The drug attaches to the CD20 protein causing direct cell death. It also alerts the immune system to the cancer. This triggers normal immune cells to kill the cancer cells.

### Bispecific monoclonal antibody therapy

Bispecific antibodies (BsAbs) bind to 2 different proteins (CD20 and CD3) at the same time. They treat cancer by engaging T cells. Bispecifics such as epcoritamab-bysp (Epkinyly) and glofitamab-gxbm (Columvi) might be an option after an HCT or CAR T-cell therapy. Bispecifics can cause a side effect called cytokine release syndrome (CRS).

### CD19-targeting CAR T-cell therapy

CAR T-cell therapy is made by removing T cells from your body and then training your own immune cells to fight the lymphoma for you by adding a CAR (chimeric antigen receptor) to the T cells. This programs the T cells to find cancer cells. The programmed T cells will be infused back into your body to find and kill cancer cells. This treatment is not for everyone. There can be severe and sometimes life-threatening reactions to this treatment.

CAR T-cell therapy is one way to target the CD19 protein found on almost all B-cell lymphomas, including DLBCL. CAR T-cell therapy is only used in recurrent lymphoma outside of clinical trials.

CD19-directed CAR T-cell therapy options for DLBCL include axicabtagene ciloleucel (Yescarta), lisocabtagene melaleuca (Breyanzi), and tisagenlecleucel (Kymriah).

More information on CAR T-cell therapy can be found at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.

## Immune modulator

An immunomodulator changes your immune system so it can work more effectively. Lenalidomide (Revlimid) is an example of an immune modulator.

## Targeted therapy

Targeted therapy is drug therapy that focuses on specific or unique features of cancer cells. Targeted therapies seek out how cancer cells grow, divide, and move in the body. These drugs stop or inhibit the action of molecules that help cancer cells grow and/or survive.

Some targeted therapy examples include:

- ▶ Alectinib (Alecensa) and lorlatinib (Lorbrena) target the activity of the ALK protein found in those with an *ALK* gene mutation.
- ▶ Ibrutinib (Imbruvica) is a Bruton tyrosine kinase inhibitor (BTKi). It blocks the BTK protein, which the lymphoma cancer relies on for survival. Since the main signal for DLBCL growth is blocked, the lymphoma cells eventually die off.



### Warnings about supplements and drug interactions

You might be asked to stop taking or avoid certain herbal supplements when on a systemic therapy. Some supplements can affect the ability of a drug to do its job. This is called a drug interaction.

**It is critical to speak with your care team about any supplements you may be taking. Some examples include:**

- ▶ Turmeric
- ▶ Ginkgo biloba
- ▶ Green tea extract
- ▶ St. John's Wort
- ▶ Antioxidants

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart or blood pressure medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy or supportive care medicines given during systemic therapy. Therefore, it is very important to tell your care team about any medicines, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking.

**Bring a list with you to every visit.**

## Radiation therapy

Radiation therapy (RT) uses high-energy radiation from photons, electrons, or protons, and other sources to kill cancer cells and shrink tumors. RT may be used as the main treatment to cure cancer (curative treatment), or as supportive care or palliative care to help ease pain or discomfort caused by cancer.

Radiation is typically delivered from outside the body by a computerized device, which can shape the treatment to closely fit the location and size of the tumor. Treatment is given in small daily doses, on workdays, with weekends off.

You will see your radiation oncologist at least weekly to review your progress and to help with side effects, such as sunburn-like rash. Ask your care team which radiation option(s) are best for your situation, if RT will be combined with chemotherapy, and what side effects to expect. RT puts you at a small risk of developing another cancer in the future.

A four-dimensional (4D) CT scan might be used to plan RT. A 4D-CT records multiple images over time. It allows playback of the scan as a video, so that internal movement can be tracked and observed.

### External beam radiation

External beam radiation therapy (EBRT) uses a machine outside of the body to aim radiation at the tumor(s) or areas of the body.

Common types of EBRT that may be used to treat your cancer include the following:

- ▶ **Three-dimensional conformal radiation therapy (3D-CRT)** uses computer software and CT images to aim beams that match the shape of the tumor.
- ▶ **Intensity-modulated radiation therapy (IMRT)** uses small beams of different strengths to match the shape of the tumor.
- ▶ **Involved-site radiation therapy (ISRT)** treats the cancer site or cancer found in or near lymph nodes (nodal disease).

## Hematopoietic cell transplant

A hematopoietic stem cell is an immature cell that can develop into any type of blood cell. A hematopoietic cell transplant (HCT) replaces hematopoietic stem cells that have been destroyed by high doses of chemotherapy and/or radiation therapy as part of the transplant process. You might hear it called a stem cell transplant (SCT) or a bone marrow transplant (BMT). This book will refer to it as HCT. HCTs are performed in specialized centers.

There are 2 types of HCTs:

- **Autologous** – stem cells come from you.
- **Allogeneic** – stem cells come from a donor who may or may not be related to you.

### Autologous transplant

An autologous transplant is also called HDT/ASCR (high-dose therapy with autologous stem cell rescue) or an autologous HCT. First, your healthy stem cells will be removed. Then, you will receive highly intensified treatment to kill remaining lymphoma cells and your bone marrow cells. Your healthy stem cells will be returned to rescue your marrow.

### Allogeneic transplant

An allogeneic hematopoietic cell transplant (allogeneic HCT) uses healthy stem cells from a donor. The donor may or may not be related to you. Before an HCT, treatment is needed to destroy bone marrow cells. This is called conditioning and it creates room for the healthy donor stem cells. It also weakens the immune

system so your body won't kill the transplanted cells. Chemotherapy is used for conditioning.

After conditioning, you will receive a transfusion of the healthy stem cells from a donor matched to you. A transfusion is a slow injection of blood products into a vein. This can take several hours. The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form. This is called engraftment. It usually takes about 2 to 4 weeks. Until then, you will have little or no immune defense. You may need to stay in a very clean room at the hospital or be given antibiotics to prevent or treat infection. Transfusions are also possible. A red blood cell transfusion is used to prevent bleeding and to treat anemia (below normal red blood cell count). A platelet transfusion is used to treat a low platelet count or bleeding. While waiting for the cells to engraft, you will likely feel tired and weak.

The goal of the transplant is for the new immune system to recognize the lymphoma as foreign and destroy it.

### Possible side effects

Every treatment has side effects. You will be monitored for infections, decreases in your blood counts that require blood transfusions, disease relapse, and graft-versus-host disease (GVHD). In GVHD, the donor cells attack your normal, healthy tissue. There are treatments for GVHD. Ask your care team about the possible side effects or complications of HCT and how this might affect your quality of life.

More information on GVHD can be found at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.

## Surgery

Surgery is an operation or procedure to remove cancer from the body. Surgery is not a routine part of treatment for DLBCL. If surgery is needed, seek the opinion of an experienced surgeon. The surgeon should be an expert in performing your type of surgery in those with DLBCL. Hospitals that perform many surgeries often have better results. You can ask for a referral to a hospital or cancer center that has experience in treating your type of cancer.

## Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of treating 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. Treatment trials are done in phases.

- **Phase I trials** study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase II trials** study how well the drug or approach works against a specific type of cancer.
- **Phase III trials** test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase IV trials** study the long-term safety and benefit of an FDA-approved treatment.

## Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, lab tests, or general health. These requirements 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 group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss with family,

friends, or others whom you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

### Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

### Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

#### 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.

#### Do I have to pay to be in a clinical trial?

It depends on the study, your health insurance, and the state in which you live. In general, procedures, drugs, or tests that are considered standard of care will be billed to you or your insurance, whereas those considered research are covered by the trial sponsor. Your treatment team and the research team can help determine if you are responsible for any costs.



## Finding a clinical trial

### In the United States

#### NCCN Cancer Centers

[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

#### The National Cancer Institute (NCI)

[cancer.gov/about-cancer/treatment/clinical-trials/search](https://www.cancer.gov/about-cancer/treatment/clinical-trials/search)

### Worldwide

#### The U.S. National Library of Medicine (NLM)

[clinicaltrials.gov](https://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](https://www.cancer.gov/contact)

### Supportive care

Supportive care will be specific to your needs. Supportive care is health care given to prevent, reduce, and relieve suffering, and to improve quality of life. Supportive care might include pain relief, palliative care, emotional or spiritual support, financial aid, or family counseling. Tell your care team how you are feeling and about any side effects so they can be managed. Supportive care, best supportive care, and palliative care often mean the same thing.

It is very important to take care of yourself by eating well, drinking plenty of fluids, exercising, and doing things that make you feel energized. Strength is needed to sustain you during treatment.

#### Side effects

All cancer treatments can cause unwanted health issues called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may be harmful to your health. Others may just be unpleasant. Treatment can cause several side effects. Some are very serious.

Ask for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better. There are also ways to prevent some side effects. You will be monitored closely for side effects.

**All cancer treatments can cause unwanted health issues called side effects. It is important to tell your care team about all of your side effects so they can be managed.**

#### Late effects

Late effects are side effects that occur months or years after a disease is diagnosed or after treatment has ended. Late effects may be caused by cancer or cancer treatment. They may include physical, mental, and social problems, and second cancers. The sooner late effects are treated the better. Ask your care team about what late effects could occur. This will help you know what to look for.

#### Survivorship

A person is a cancer survivor from the time of diagnosis until the end of life. After treatment, your health will be monitored for side effects of treatment and the return of cancer. This is part of your survivorship care plan. It is important to keep any follow-up doctor visits and imaging test appointments. Seek good routine medical care, including regular doctor visits for preventive care and cancer screening.

A personalized survivorship care plan will contain a summary of possible long-term effects of treatment called late effects and list follow-up tests. Find out how your primary care provider will coordinate with specialists for your follow-up care.

## Side effects

Some potential side effects are described next. They are not listed in order of importance. Some side effects are very rare.

### Blood clots

Cancer can cause blood clots to form. This can block blood flow and oxygen in the body. Blood clots can break loose and travel to other parts of the body causing stroke or other problems.

### Cytokine release syndrome

Cytokine release syndrome (CRS) is a condition that may occur after treatment with some types of immunotherapy, such as monoclonal antibodies and CAR T cells. It is caused by a large, rapid release of cytokines from immune cells affected by the immunotherapy. Signs and symptoms of CRS include fever, muscle aches, nausea, headache, rash, fast heartbeat, low blood pressure, and trouble breathing.

### Diarrhea

Diarrhea is frequent and watery bowel movements. Your care team will tell you how to manage diarrhea. It is important to drink lots of fluids.

### Distress

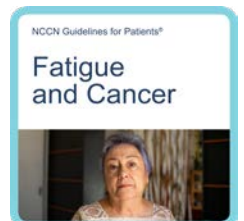
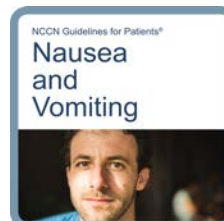
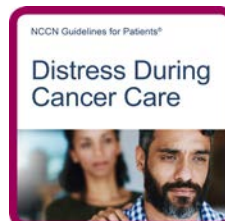
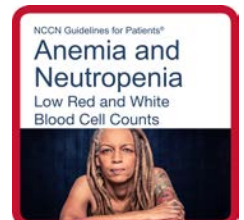
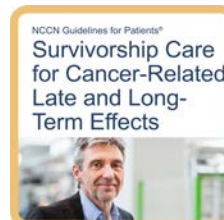
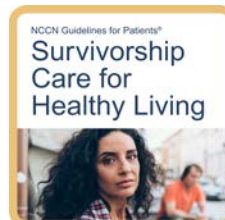
Depression, anxiety, and sleeping issues are common and are a normal part of cancer diagnosis. Talk to your care team and with those whom you feel most comfortable about how you are feeling. There are services, people, and medicines that can help you. Support and counseling services are available.

### Fatigue

Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of treatment. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet, exercise, yoga, acupuncture, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.

## Supportive care resources

More information on supportive care is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.





### **Hair loss**

Chemotherapy may cause hair loss (alopecia) all over your body—not just on your scalp. Some chemotherapy drugs are more likely than others to cause hair loss. Dosage might also affect the amount of hair loss. Most of the time, hair loss from chemotherapy is temporary. Hair often regrows 3 to 6 months after treatment ends. Your hair may be a different shade or texture.

### **Hypersensitivity, allergy, and anaphylaxis**

Certain treatments can cause an unwanted reaction. Hypersensitivity is an exaggerated response by the immune system to a drug or other substance. This can include hives, skin welts, and trouble breathing. An allergy is an immune reaction to a substance that normally is harmless or would not cause an immune response in most people. An allergic response may cause harmful symptoms such as itching or inflammation (swelling). Anaphylaxis or anaphylactic shock is a severe and possible life-threatening allergic reaction.

### **Infections**

Infections occur more frequently and are more severe in those with a weakened immune system. Drug treatment for DLBCL can weaken the body's natural defense against infections. If not treated early, infections can be fatal.

Neutropenia, a low number of white blood cells, can lead to frequent or severe infections. When someone with neutropenia also develops a fever, it is called febrile neutropenia (FN). With FN, your risk of infection may be higher than normal. This is because a low number of white blood cells leads to a reduced ability to fight infections. FN is a side effect of some types of systemic therapy.

### **Loss of appetite**

Sometimes side effects from cancer or its treatment, and the stress of having cancer might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth or difficulty swallowing. Healthy eating is important during treatment. It includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. A registered dietitian who is an expert in nutrition and food can help. Speak to your care team if you have trouble eating or maintaining weight.

### Low blood cell counts

Some cancer treatments can cause low blood cell counts.

- **Anemia** is a condition where your body does not have enough healthy blood cells, resulting in less oxygen being carried to your cells. You might tire easily if you are anemic.
- **Neutropenia** is a decrease in neutrophils, a type of white blood cell. This puts you at risk for infection.
- **Thrombocytopenia** is a condition where there are not enough platelets found in the blood. This puts you at risk for bleeding.

### Lymphedema

Lymphedema is a condition in which lymph fluid builds up in tissues and causes swelling. It may be caused when part of the lymph system is damaged or blocked, such as during surgery to remove lymph nodes, or by radiation therapy. Cancers that block lymph vessels can also cause lymphedema. Swelling usually develops slowly over time. It may develop during treatment, or it may start years after treatment. If you have lymphedema, you may be referred to an expert in lymphedema management. The swelling may be reduced by exercise, massage, compression devices, and other means.

### Nausea and vomiting

Nausea and vomiting are common side effects of treatment. You will be given medicine to prevent nausea and vomiting.

### Neurocognitive or neuropsychological effects

Some treatments can damage the nervous system (neurotoxicity) causing problems with concentration and memory. Survivors are at risk for neurotoxicity and might be recommended for neuropsychological testing. Neuropsychology looks at how the health of your brain affects your thinking and behavior. Neuropsychological testing can identify your limits and doctors can create a plan to help with these limits.

### Neuropathy

Neuropathy is a nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse over time. Neuropathy may be caused by cancer or cancer treatment such as chemotherapy. Most of the time, neuropathy goes away after treatment.

### Neurotoxicity

Some treatments can damage the nervous system (neurotoxicity) causing problems with concentration and memory. Seizures and confusion can occur.

### Organ issues

Treatment might cause your kidneys, liver, and heart to not work as well as they should.

### Pain

Tell your care team about any pain or discomfort. You might meet with a palliative care specialist or with a pain specialist to manage pain.

### Quality of life

Cancer and its treatment can affect your overall well-being or quality of life (QOL). For more information on quality of life, see *NCCN Guidelines for Patients: Palliative Care* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



### Therapy-related toxicity

Many of the drug therapies used to treat diffuse large B-cell lymphomas can be harmful to the body. You will be closely monitored for therapy-related toxicity.

### Tumor lysis syndrome

Cancer treatment causes cell death. In tumor lysis syndrome (TLS), waste released by dead cells builds up in the body causing kidney damage and severe blood electrolyte disturbances. Changes in creatinine, lactic acid, uric acid, phosphorus (Phos), potassium (K), and calcium (Ca) levels can be a sign of TLS. TLS is rare.

### Weight gain

Weight gain is one side effect of high-dose steroids. This can be uncomfortable and cause distress. It is important to maintain muscle mass. Find a physical activity you enjoy. Ask your care team what can be done to help manage weight gain.

### Keep a pain diary

A pain diary is a written record that helps you keep track of when you have pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your pain with your care team. You might be referred to a specialist for pain management.

Include in your pain diary:

- ✓ The time and dose of all medicines
- ✓ When pain starts and ends or lessens
- ✓ Where you feel pain
- ✓ A description of your pain. Is it throbbing, sharp, tingling, shooting, or burning? Is it constant, or does it come and go?
- ✓ Does the pain change at different times of day? When?
- ✓ Does the pain get worse before or after meals? Does certain food or drink make it better?
- ✓ Does the pain get better or worse with activity? What kind of activity?
- ✓ Does the pain keep you from falling asleep at night? Does pain wake you up in the night?
- ✓ A rating of your pain from 0 (no pain) to 10 (worst pain you have ever felt)
- ✓ Does pain get in the way of you doing the things you enjoy?

## Key points

- Diffuse large B-cell lymphoma (DLBCL) is highly treatable and curable. The goal of treatment is to achieve a complete response (CR) or complete remission.
- Treatment can affect fertility in all sexes. Those who want to have children in the future should be referred to a fertility specialist before starting chemotherapy and/or radiation therapy to discuss the options.
- Systemic therapy works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.
- Radiation therapy (RT) uses high-energy radiation from photons, protons, electrons, and other sources to kill cancer cells and shrink tumors.
- A hematopoietic cell transplant (HCT) replaces damaged stem cells with healthy stem cells.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.
- Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. Supportive care is always given.
- Eating a balanced diet, drinking enough fluids, exercise, and doing the things you enjoy can help manage side effects.
- Some side effects, called late effects, may take years to appear. Risk for late effects will depend on the type(s) of cancer treatment you had, and the dose and the length of time you were treated. It is important to keep follow-up appointments.

# 4

## Stages 1, 2, 3, and 4

- 44 Staging
- 45 Stages 1 and 2 non-bulky (limited)
- 46 Stages 1 and 2 bulky (limited)
- 47 Stages 3 and 4
- 48 Follow-up testing
- 48 Key points

**Treatment for DLBCL is based on cancer stage and is often a combination of chemoimmunotherapy and radiation therapy. Together, you and your care team will choose a treatment plan that is best for you.**

Diffuse large B-cell lymphoma (DLBCL) is highly treatable and curable. The goal of treatment is to achieve a complete response (CR) or remission.

## Staging

A PET and/or CT scan will be done to stage DLBCL. In addition, treatment decisions will be based on histology and results of biomarker and genetic tests. Histology is the overall appearance and the size, shape, and type of your cells.

In general, stages for DLBCL are as follows:

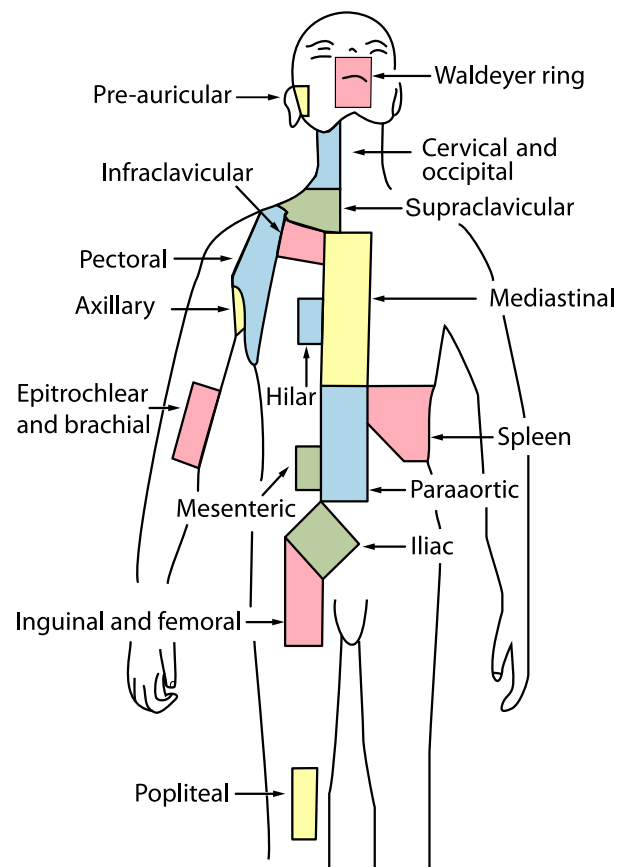
- **Stage 1 (limited)** – Disease found in 1 lymph node or a group of nearby lymph nodes.
- **Stage 2 (limited)** – Disease found in 2 or more lymph node groups on the same side of the diaphragm.
- **Stage 2 bulky** – Bulky disease means there are areas of lymphoma that measure 7.5 centimeters (cm) or larger. Bulky disease can be limited or advanced.

- **Stage 3 (advanced)** – Disease found in lymph nodes above and below the diaphragm on the same side of the body or disease found in nodes above the diaphragm and in the spleen.
- **Stage 4 (advanced)** – Disease has spread outside of the lymphatic system to other parts of the body.

### Lymph node regions

#### Lymph node regions based on the Ann Arbor Staging System

Adapted from: Lymph\_node\_regions.jpg: [https://commons.wikimedia.org/wiki/File:Lymph\\_node\\_regions.svg](https://commons.wikimedia.org/wiki/File:Lymph_node_regions.svg)



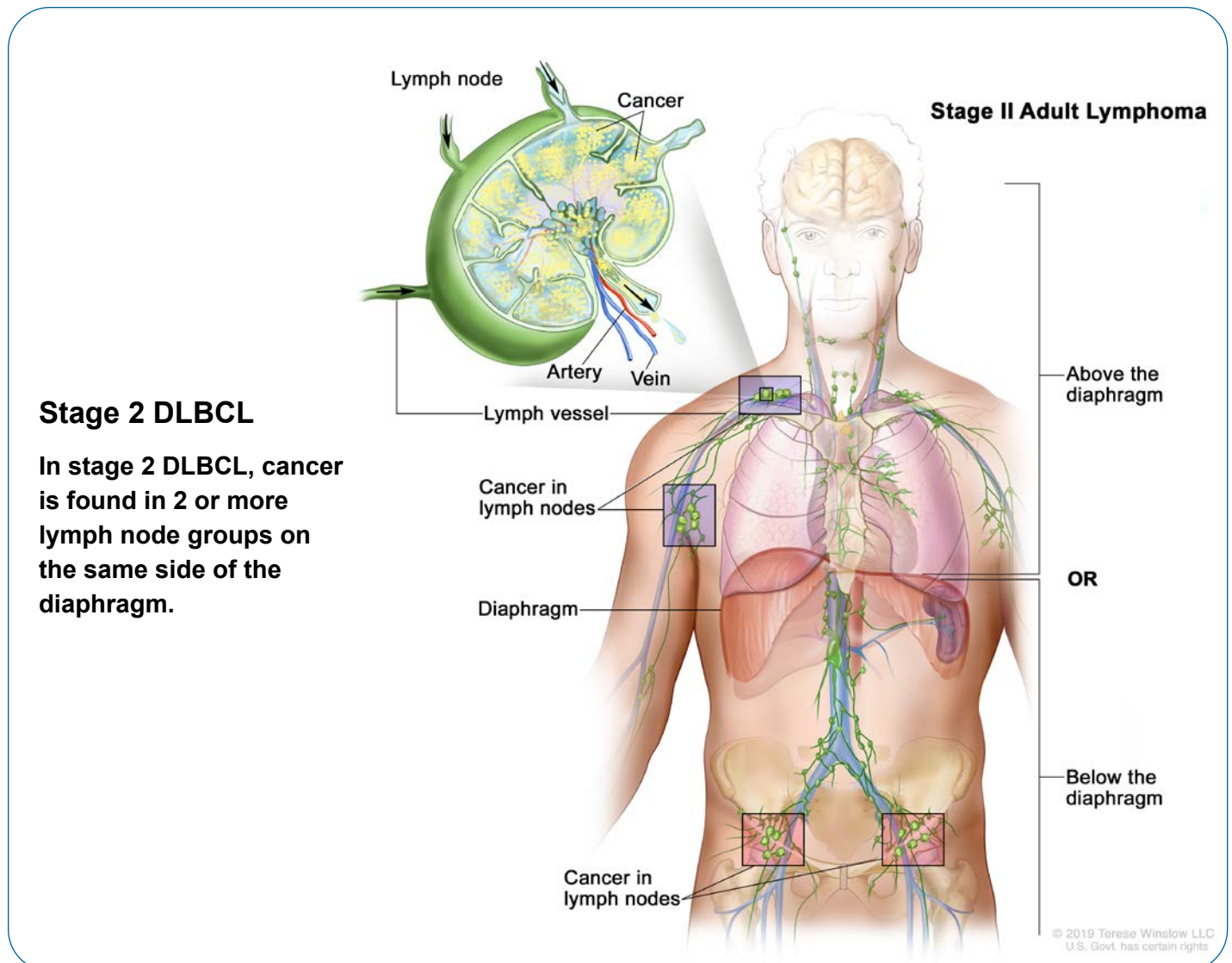
## Stages 1 and 2 non-bulky (limited)

Treatment for non-bulky stage 1 or 2 limited disease is 3 cycles of RCHOP. This is called first-line chemoimmunotherapy. Your cancer will be restaged using PET/CT after 3 cycles of RCHOP and again after the last cycle.

- If a complete response, you will have 1 more cycle of RCHOP for a total of 4 cycles or involved-site radiation therapy

(ISRT). Then, you will enter surveillance and be monitored for relapse.

- If a partial response, you will have 1 to 3 more cycles of RCHOP for a total of 4 to 6 cycles or SRT if PET scan was positive for disease after 3 cycles of RCHOP.
- If disease has progressed, a repeat biopsy will be done, and you will be treated for refractory disease found in *Chapter 5: Relapse and refractory disease*.



## Stages 1 and 2 bulky (limited)

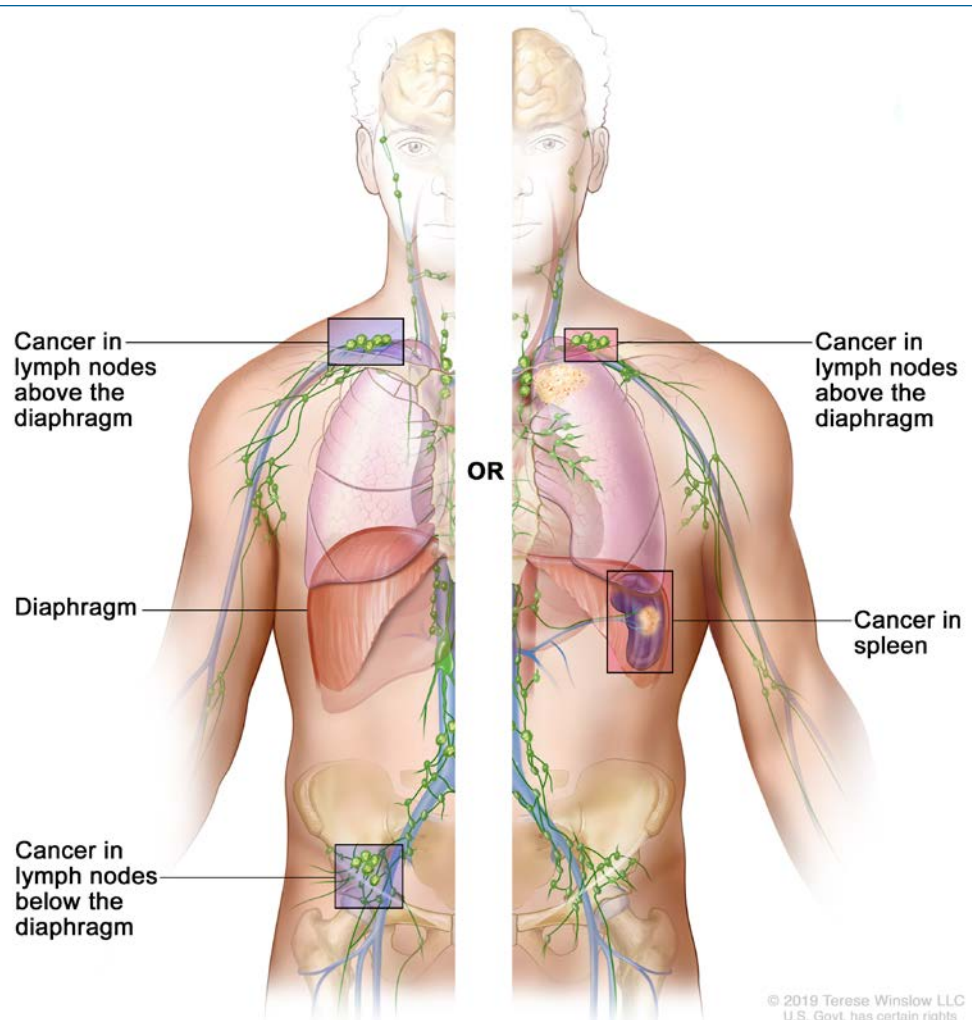
Bulky disease in DLBCL refers to cancer that is 7.5 cm or larger. Treatment for stage 1 or 2 limited, bulky disease is 6 total cycles of RCHOP. This is called first-line chemoimmunotherapy. A type of radiation called involved-site radiation therapy (ISRT) might be added after 3 to 4 cycles of RCHOP.

Your cancer will be restaged using PET/CT after 3 to 4 cycles of RCHOP and again after the last (6th) cycle.

- If a complete response, you will complete the planned course of treatment. If in remission, also called a complete response, then you will enter surveillance and be monitored for relapse.
- If a partial response, you will complete the planned course of treatment.
- If no treatment response or disease has progressed, a repeat biopsy will be done and you will be treated for refractory disease found in *Chapter 5: Relapse and refractory disease*.

### Stage 3 DLBCL

In stage 3 DLBCL, cancer is found in lymph node groups above and below the diaphragm on the same side of the body or cancer is found in lymph nodes above the diaphragm and in the spleen.





## Stages 3 and 4

For stages 3 and 4, chemoimmunotherapy such as RCHOP and Pola-R-CHP are the recommended and preferred options. Other chemotherapy regimens such as DA-EPOCH-R might be used. A CT or PET scan might be done after 2 to 4 cycles to restage

your cancer. For all first-line therapy options, **see Guide 4.**

- If a complete or partial response, you will complete the remaining cycles of RCHOP for a total of 6 cycles. Then, you will enter surveillance and be monitored for relapse.

### Guide 4

#### First-line therapy options

<b>Preferred options</b>	<ul style="list-style-type: none"> <li>• Cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab (RCHOP)</li> <li>• Polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin and prednisone (Pola-R-CHP)</li> </ul>
<b>Other recommended</b>	<ul style="list-style-type: none"> <li>• Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin with rituximab (DA-EPOCH-R)</li> </ul>
<b>For those with heart issues</b>	<ul style="list-style-type: none"> <li>• Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab (DA-EPOCH-R)</li> <li>• Rituximab, cyclophosphamide, liposomal doxorubicin, vincristine, and prednisone (RCDOP)</li> <li>• Rituximab, cyclophosphamide, etoposide, vincristine, and prednisone (RCEOP)</li> <li>• Rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisone (RGCVP)</li> <li>• Rituximab, cyclophosphamide, etoposide, prednisone, and procarbazine (RCEPP)</li> </ul>
<b>For those who are frail or are over 80 years of age with other health issues</b>	<ul style="list-style-type: none"> <li>• Rituximab, cyclophosphamide, liposomal doxorubicin, vincristine, and prednisone (RCDOP)</li> <li>• Rituximab with mini-CHOP (R-mini-CHOP)</li> <li>• Rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisone (RGCVP)</li> <li>• Rituximab, cyclophosphamide, etoposide, prednisone, and procarbazine (RCEPP)</li> </ul>

\*An FDA-approved biosimilar might be used in place of rituximab.

- If no treatment response or disease has progressed, a repeat biopsy will be done and you will be treated for refractory disease found in *Chapter 5: Relapse and refractory disease*.

## Follow-up testing

After completing all cycles of RCHOP, a PET scan will be done. Radiation therapy might be given before entering surveillance to treat any bulky or bone disease sites. Surveillance is a period of testing that begins after remission to monitor for relapse or the return of cancer.

- Surveillance includes physical exam, health history, and blood tests every 3 to 6 months for 5 years. After 5 years, testing will be done once a year or as needed.
- Surveillance imaging may be used for monitoring those without symptoms (asymptomatic). It includes a chest/abdomen/pelvis CT no more than every 6 months for 2 years. After 2 years, imaging testing will be done as needed.

## Key points

- RCHOP is rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.
- Treatment for non-bulky stage 1 or 2 disease is 4 to 6 cycles of RCHOP.
- Bulky disease in DLBCL refers to cancer that is 7.5 cm or larger.
- Treatment for stage 1 or 2 bulky disease is 6 cycles of RCHOP.
- For stages 3 and 4, chemoimmunotherapy such as RCHOP and Pola-R-CHP are the recommended and preferred options. Other chemotherapy regimens such as DA-EPOCH-R might be used.
- A type of radiation called ISRT might be added to treatment. Involved-site radiation therapy (ISRT) treats cancer found in a small region or one area of your body.
- Surveillance is a period of testing that begins after remission to monitor for relapse or the return of cancer.

# 5

## Relapse and refractory disease

- 50 Relapse – Under 12 months
- 52 Relapse – Over 12 months
- 53 Refractory disease
- 54 2 or more relapses
- 54 Follow-up testing
- 55 Key points

**DLBCL returns in less than 1 out of every 2 people in remission. Cancer that returns is called relapse. The goal of treatment is to achieve remission again. When DLBCL progresses despite treatment, it is called refractory. Together, you and your care team will choose a treatment plan that is best for you.**

## Relapse – Under 12 months

Treatment options for relapsed disease are based on the time since your last treatment was completed. If cancer returned and it has been less than 12 months since treatment ended, then treatment will be based on if CAR T-cell therapy is planned.

### CAR T-cell therapy is planned

CAR T-cell therapy is an option for relapse that has occurred less than 12 months since treatment ended. While waiting for CAR T-cell therapy, bridging therapy will be given as needed. **See Guide 5.**

### Guide 5

#### CAR T-cell bridging therapy options

Dexamethasone and cytarabine (DHA) with carboplatin, cisplatin, or oxaliplatin

Gemcitabine, dexamethasone, and cisplatin (GDP) or gemcitabine, dexamethasone, and carboplatin

Gemcitabine and oxaliplatin (GemOx)

Ifosfamide, carboplatin, and etoposide (ICE)

Polatuzumab vedotin-piiq with or without rituximab with or without bendamustine

Involved-site radiation therapy (ISRT)

\*Rituximab might be added to the therapies listed. An FDA-approved biosimilar might be used for rituximab.

### Other options

If CAR T-cell therapy is not planned, then options include as follows:

- Clinical trial
- Second-line therapy, **see Guide 6**
- Palliative involved-site radiation therapy (ISRT)
- Best supportive care to improve quality of life

After a complete response, you will have follow-up testing.

After a partial response, no response, or disease progression, then see treatment for 2 or more relapses on page 54.



**My diagnosis was sudden and unexpected. I am a non-smoker and runner and had just completed a half marathon before diagnosis. My only symptom was a persistent cough. My tumor was causing fluid to back up in my heart and lungs.”**

#### Guide 6

#### Second-line therapy options: HCT planned

<b>Preferred options</b>	<ul style="list-style-type: none"> <li>• Dexamethasone and cytarabine (DHA) with carboplatin, cisplatin, or oxaliplatin</li> <li>• Gemcitabine, dexamethasone, and cisplatin (GDP) or gemcitabine, dexamethasone, and carboplatin</li> <li>• Ifosfamide, carboplatin, and etoposide (ICE)</li> </ul>
<b>Other recommended</b>	<ul style="list-style-type: none"> <li>• Etoposide, methylprednisolone, cytarabine, and cisplatin (ESHAP)</li> <li>• Gemcitabine and oxaliplatin (GemOx)</li> <li>• Mesna, ifosfamide, mitoxantrone, and etoposide (MINE)</li> </ul>

\*Rituximab might be added to any of the therapies listed above. An FDA-approved biosimilar might be used in place of rituximab.

## Relapse – Over 12 months

For cancer that returned after more than 12 months since treatment ended, treatment options are described next.

### HCT is planned

If autologous (self) hematopoietic cell transplant (HCT) is planned, then second-line therapy will be given. **See Guide 6.**

After a complete response, next options include:

- Autologous HCT. ISRT might be added.
- Clinical trial

- In some cases, an allogeneic (donor) hematopoietic cell transplant (HCT)
- Involved-site radiation therapy (ISRT) might be added. ISRT treats lymph nodes where cancer was originally found or cancer located in a small region or one area of your body.

After a partial response, next options include:

- CAR T-cell therapy, **see Guide 8**
- Autologous HCT. ISRT might be added.
- Clinical trial
- In some cases, an allogeneic (donor) HCT. ISRT might be added.

### Guide 7

#### Second-line therapy options: HCT not planned

<b>Preferred options</b>	<ul style="list-style-type: none"> <li>• Lisocabtagene maraleucel (CD19-targeting CAR T-cell therapy)</li> <li>• Polatuzumab vedotin-piiq with or without bendamustine with or without rituximab</li> <li>• Tafasitamab-cxix and lenalidomide</li> </ul>
<b>Other recommended</b>	<ul style="list-style-type: none"> <li>• Cyclophosphamide, etoposide, vincristine, and prednisone (CEOP). Rituximab might be added.</li> <li>• Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin (DA-EPOCH). Rituximab might be added.</li> <li>• Gemcitabine, dexamethasone, and cisplatin (GDP) or gemcitabine, dexamethasone, and carboplatin. Rituximab might be added.</li> <li>• Gemcitabine and oxaliplatin (GemOx). Rituximab might be added.</li> <li>• Rituximab</li> </ul>
<b>Used in some cases</b>	<ul style="list-style-type: none"> <li>• Brentuximab vedotin</li> <li>• Ibrutinib</li> <li>• Lenalidomide with or without rituximab</li> </ul>

\*An FDA-approved biosimilar might be used in place of rituximab.

If no response or disease progression, then see treatment for 2 or more relapses on page 54.

### Other options

If you are not receiving a hematopoietic cell transplant (HCT), then options include:

- › Clinical trial
- › Second-line therapy, **see Guide 7**
- › Palliative ISRT
- › Best supportive care

After a complete response, you will have follow-up testing.

After a partial response, no response, or disease progression, then see treatment for 2 or more relapses on page 54.

## Refractory disease

Refractory disease might be treated with CAR T-cell therapy. While waiting for CAR T-cell therapy, bridging therapy will be given as needed. For bridging therapy, **see Guide 5**.

Other options include:

- › Clinical trial
- › Second-line therapy, **see Guide 6**
- › Palliative ISRT
- › Best supportive care

RT with or without chemoimmunotherapy followed by high-dose therapy with stem cell rescue may be an option in some people with localized disease.

After a complete response, you will have follow-up testing.

After a partial response, no response, or disease progression, then see treatment for 2 or more relapses on page 54.

## 2 or more relapses

For a partial response, second or third relapse, or disease progression, then the treatment options include:

- Third-line therapy, **see Guide 8**
- A systemic therapy not used before
- Clinical trial
- Palliative ISRT
- Best supportive care

For a complete or partial response to treatment, an allogeneic (self) HCT with or without ISRT might be an option in some cases.

## Follow-up testing

After completing treatment, you will have the following tests to monitor for relapse:

- A physical exam, health history, and blood tests every 3 to 6 months for 5 years. After 5 years, these tests will be done once a year or as needed.
- CT of the chest/abdomen/pelvis no more than every 6 months for 2 years. After 2 years, imaging testing will be done as needed.
- It is important to keep any follow-up doctor visits and imaging test appointments. Seek good routine medical care, including regular doctor visits for preventive care and cancer screening.

### Guide 8

#### Third-line and next-line therapy options

<b>Preferred options</b>	CD19-targeting CAR T-cell therapy (preferred if not previously given) <ul style="list-style-type: none"> <li>• Axicabtagene ciloleucel</li> <li>• Lisocabtagene maraleucel</li> <li>• Tisagenlecleucel</li> </ul>
	Bispecific antibody therapy (only after at least two lines of systemic therapy; including those with disease progression after HCT or CAR T-cell therapy) <ul style="list-style-type: none"> <li>• Epcoritamab-bysp</li> <li>• Glofitamab-gxbm</li> </ul>
<b>Other recommended</b>	<ul style="list-style-type: none"> <li>• Loncastuximab tesirine-lpyl</li> <li>• Selinexor (including those with disease progression after HCT or CAR T-cell therapy)</li> </ul>

\*An FDA-approved biosimilar might be used in place of rituximab.



## Key points

- DLBCL returns in less than 1 out of every 2 people in remission.
- Cancer that returns is called relapse.
- Treatment options for relapsed disease are based on the time since your last treatment was completed. The goal of treatment is to achieve remission again.
- If cancer returned and it has been less than 12 months since treatment ended, then treatment will be based on if CAR T-cell therapy is planned.
- If cancer returned after more than 12 months since treatment ended, then treatment will be based on if a hematopoietic cell transplant (HCT) is planned.
- When DLBCL progresses despite treatment, it is called refractory. Refractory disease might be treated with CAR T-cell therapy.
- After completing treatment, you will be monitored for the return of cancer. Keep all follow-up doctor visits and imaging test appointments.

# 6

## ALK-positive large B-cell lymphomas

- 57 Overview
- 57 Treatment
- 58 Key points

**ALK-positive large B-cell lymphoma (ALK+ LBCL) is caused by a mutation in the *ALK* gene. ALK+ LBCL is usually treated with radiation therapy and chemotherapy. Together, you and your care team will choose a treatment plan that is best for you.**

## Overview

ALK-positive large B-cell lymphoma (ALK+ LBCL) is caused by a mutation in the anaplastic lymphoma kinase (*ALK*) gene. *ALK* tells your body how to make proteins that help cells talk to each other. ALK+ LBCL expresses the ALK protein but lacks CD20 (CD20-). The *ALK* mutation makes this lymphoma difficult to treat.

ALK+ LBCL is not related to immune deficiency. Epstein-Barr virus (EBV) and Kaposi sarcoma-associated herpesvirus (HHV8) are negative. A gene fusion called *CLTC::ALK* is common in ALK+ LBCL. It is written as t(2;17)(p23;q23).

Most with ALK+ LBCL have advanced disease with cancer found inside and outside the lymph nodes. Cancer found inside the lymph nodes is called nodal. Cancer found outside the lymph nodes is called extranodal. ALK+ LBCL is more commonly seen in those 40 years of age, assigned male at birth.

## Treatment

Currently, there is no standard of care or agreement on treatment. ALK+ LBCL is usually treated with chemotherapy. Involved-site radiation therapy (ISRT) is preferred when treating localized disease. A clinical trial is recommended if available and it is what you want. Since this cancer is often CD20-, rituximab is not given.

First-line treatment options include:

- Clinical trial (recommended)
- ISRT (preferred for localized disease)
- DA-EPOCH
- CHOEP
- CHOP
- Mini-CHOP
- HyperCVAD
- CODOX-M/IVAC

Treatment options for relapse or refractory disease include:

- Clinical trial (recommended)
- A platinum-based chemotherapy followed by an autologous (self) hematopoietic cell transplant (HCT). Platinum-based chemotherapy includes carboplatin, cisplatin, or oxaliplatin.
- Second-generation ALK inhibitors such as alectinib and lorlatinib followed by an allogeneic (donor) HCT.

## Key points

- ALK-positive large B-cell lymphoma (ALK+ LBCL) is caused by a mutation in the *ALK* gene.
- A gene fusion called *CLTC::ALK* is common in ALK+ LBCL. It is written as t(2;17)(p23;q23).
- Most with ALK+ LBCL have advanced disease with cancer found inside and outside the lymph nodes.
- ALK+ LBCL is usually treated with radiation therapy and chemotherapy.
- A clinical trial is recommended if available and it is what you want.
- Treatment for relapse or refractory disease might be a hematopoietic cell transplant (HCT).

**It is very important to continue to take your medicine as prescribed and not miss or skip any doses.**

# 7

## Primary mediastinal large B-cell lymphoma

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- 62 Relapse or refractory disease
- 62 Key points

**Primary mediastinal large B-cell lymphoma (PMBL) develops in the area behind the breastbone called the mediastinum. Treatment is chemoimmunotherapy. Together, you and your care team will choose a treatment plan that is best for you.**

## Overview

In primary mediastinal large B-cell lymphoma (PMBL), a tumor forms most often behind the breastbone (sternum). This can cause a cough, shortness of breath, or swelling of the head and neck, due to the tumor pressing on the windpipe and the large veins above the heart.

Enlarged lymph nodes in this area can also be found. PMBL can spread to organs and tissues such as the lungs, pericardium (sac around the heart), liver, gastrointestinal (GI) tract, ovaries, adrenal glands, and central nervous system (CNS).

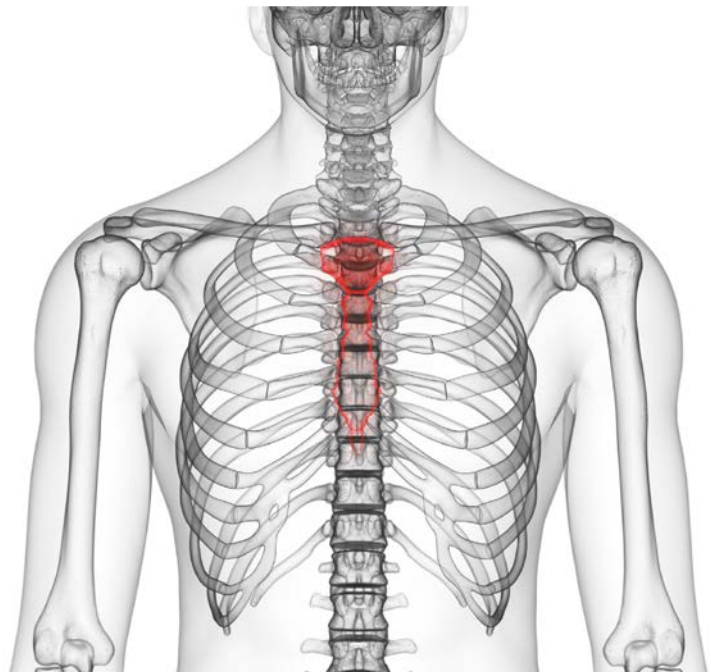
PMBL is more commonly seen in those 30 to 40 years of age, assigned female at birth.

PMBL immunophenotype is CD19+, CD20+, CD22+, CD21, IRF4/MUM1+, and CD23+. BCL2 and BCL6 might be expressed. Abnormal chromosomes are common in PMBL.

An expert hematopathologist review is essential to confirm the diagnosis of PMBL.

### Mediastinum

**Mediastinal lymphomas are growths found in the area of the chest that separates the lungs called the mediastinum. In primary mediastinal large B-cell lymphoma (PMBL), a tumor often forms behind the breastbone.**



## Treatment

Currently, the most used treatment options are:

- 6 cycles of DA-EPOCH-R (dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin with rituximab).
- 6 cycles of RCHOP-21 (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).
- 4 to 6 cycles of RCHOP-14 (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).

A PET/CT scan will be given after treatment to restage your cancer. Some of the tumor tends to remain after treatment and a PET/CT will help find any residual masses. A biopsy might be done.

### After a complete response

- After DA-EPOCH-R, you will enter observation.
- After 6 cycles of RCHOP-14, you will enter observation.
- After 6 cycles of RCHOP-21, you might have involved-site radiation therapy (ISRT) to treat cancer found in a small region or one area of your body.
- After 4 cycles of RCHOP-14, you may have 3 cycles of ifosfamide, carboplatin, and etoposide (ICE). Rituximab might be added (RICE).

### After a partial response or cancer progresses

If there is a partial response or cancer progresses, biopsy will be repeated. If cancer remains, then ISRT might be given or one of the following:

- Pembrolizumab
- Nivolumab with or without brentuximab vedotin
- CAR T-cell therapy
- Or treat as in *Chapter 5: Relapse and refractory disease*

## Follow-up testing

After a complete response (remission), you will be monitored for relapse with the following tests:

- A physical exam, health history, and blood tests every 3 to 6 months for 5 years. After 5 years, these tests will be done once a year or as needed.
- Surveillance imaging is done to monitor those without symptoms (asymptomatic). This includes a CT of the chest/abdomen/pelvis no more than every 6 months for 2 years. After 2 years, imaging testing will be done as needed.

## Relapse or refractory disease

Cancer that returns is called relapse. When cancer progresses despite treatment, it is called refractory.

Treatment options include:

- Pembrolizumab
- Nivolumab with or without brentuximab vedotin
- CAR T-cell therapy
- Autologous HCT
- Clinical trial
- Or treat as in *Chapter 5: Relapse and refractory disease*



**Drug treatment for DLBCL was intense and strong. And, I had unusual side effects. I told my care team right away when I noticed a side effect. This really helped. They were very good at treating it!”**

## Key points

- In primary mediastinal large B-cell lymphoma (PMBL), a tumor forms most often behind the breastbone (sternum).
- Treatment is chemoimmunotherapy.



# 8

## High-grade B-cell lymphomas

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- 66 Relapse and refractory disease
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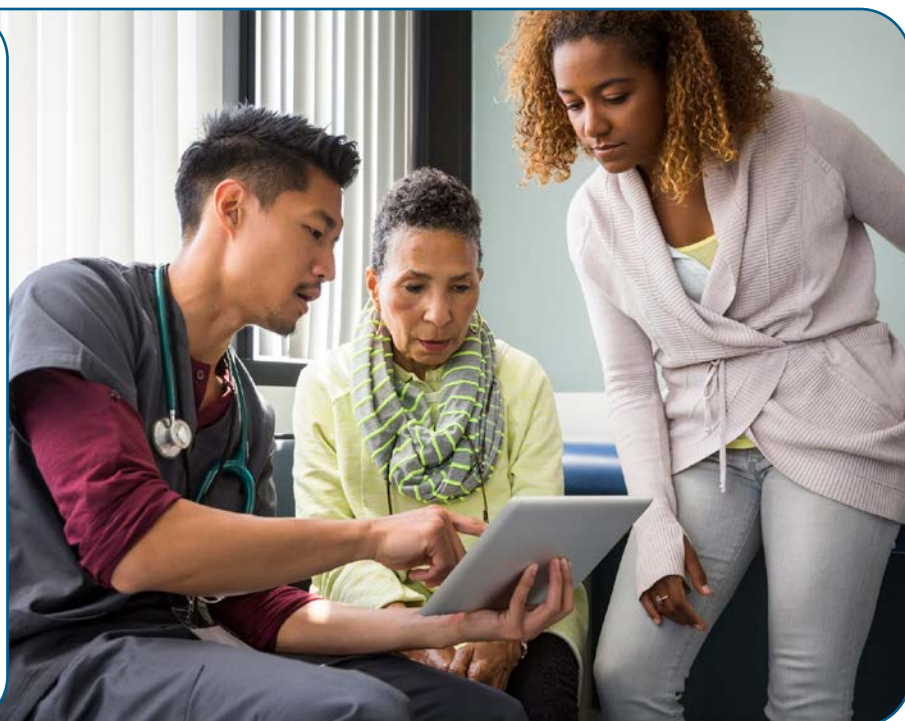
**High-grade B-cell lymphomas (HGBLs) are very aggressive, fast-dividing tumors. This chapter will provide information on HGBL with gene rearrangements and HGBL, not otherwise specified (HGBL, NOS). Together, you and your care team will choose a treatment plan that is best for you.**

## Overview

High-grade B-cell lymphomas have mutations, gene rearrangements such as *MYC*, or other high-risk features that make treatment a challenge. Those with HGBL have an elevated lactate dehydrogenase (LDH), bone marrow and central nervous system (CNS) involvement, and a high International Prognostic Index (IPI) score. Since cancer is often found in the bone marrow and central nervous system, a lumbar puncture might be done. In addition, intrathecal (IT) chemotherapy might be given at the time of a lumbar puncture to prevent CNS disease.

Currently, there is no standard of care or agreement on treatment for HGBLs. Treatment is usually chemoimmunotherapy. Radiation therapy might be given. A clinical trial is recommended, if available and it is what you want.

**Standard of care is the best-known way to treat a particular disease based on past clinical trials. There may be more than one treatment regimen that is considered standard of care. Ask your care team what treatment options are available and if a clinical trial might be right for you.**



## HGBL with *MYC* and *BCL2*

Those with HGBL with gene rearrangements of *MYC* and *BCL2* are treated as follows:

- Clinical trial (recommended)
- ISRT (preferred for localized disease)
- DA-EPOCH-R
- Pola-R-CHP
- RCHOP
- R-mini-CHOP
- R-HyperCVAD
- R-CODOX-M/R-IVAC

## HGBL with *MYC* and *BCL6*

HGBL with gene rearrangements of *MYC* and *BCL6* is often treated with DA-EPOCH-R or other systemic therapies used for DLBCL.

### Chemoimmunotherapy regimens

- ✓ **DA-EPOCH-R** is dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab.
- ✓ **Pola-R-CHP** is polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, and prednisone.
- ✓ **RCHOP** is rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.
- ✓ **R-HyperCVAD** is rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine.
- ✓ **R-CODOX-M/R-IVAC** is rituximab, cyclophosphamide, vincristine, doxorubicin, and methotrexate alternating with rituximab, ifosfamide, etoposide, and cytarabine.

## HGBL, not otherwise specified

HGBL, not otherwise specified (HGBL-NOS) includes tumors that aren't well defined or don't fall into another HGBL category.

Treatment options include:

- Clinical trial (recommended)
- ISRT for localized disease
- DA-EPOCH-R
- RCHOP
- R-mini-CHOP
- R-HyperCVAD
- R-CODOX-M/R-IVAC

## Relapse and refractory disease

For relapse and refractory disease treatment options, see *Chapter 5: Relapse and refractory disease*.

## Key points

- High-grade B-cell lymphomas (HGBLs) are aggressive, fast-dividing tumors.
- Those with HGBL have elevated LDH, bone marrow and CNS involvement, and a high IPI score.
- A clinical trial is recommended for those with HGBL. Treatment options may include radiation therapy for localized disease and chemoimmunotherapy.
- HGBL, not otherwise specified (HGBL-NOS) includes tumors that aren't well defined or don't fall into another HGBL category.

# 9

## Mediastinal gray zone lymphomas

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**Mediastinal gray zone lymphoma (MGZL) has overlapping features of primary mediastinal B-cell lymphoma (PMBL) and Hodgkin lymphoma (HL). Treatment is usually chemotherapy. Together, you and your care team will choose a treatment plan that is best for you.**

## Overview

Gray zone lymphomas have overlapping features of non-Hodgkin primary mediastinal B-cell lymphoma (PMBL) and Hodgkin lymphoma (HL). This means that the cells are large but can vary in size and might look similar to Hodgkin cells (Reed-Sternberg cells). Reed-Sternberg cells are large, abnormal lymphocytes that may contain more than one nucleus.

There are 2 main types of gray zone lymphomas:

- Mediastinal gray zone lymphoma (MGZL)
- Non-mediastinal gray zone lymphomas

## Mediastinal gray zone lymphomas

Mediastinal lymphomas are growths found behind the breastbone (sternum) in the part of the chest that separates the lungs and holds the heart. Mediastinal gray zone lymphoma (MGZL) is different than primary mediastinal large B-cell lymphoma (PMBL). They are treated differently. Primary mediastinal lymphomas are discussed in *Chapter 7*.

MGZLs are more commonly seen in those between 20 to 40 years of age, assigned male at birth. They are characterized by the presence of a large mediastinal mass. Lymph nodes above the collar bone (supraclavicular) may be involved.

MGZL immunophenotype is usually CD45+, PAX5+, BOB.1+, OCT-2+, CD15+, CD20+, CD30+, CD79a+, CD10-, and ALK-. BCL6 might be found and EBV is usually negative. An expert hematopathologist review is essential to confirm the diagnosis of mediastinal gray zone lymphoma.

## Non-mediastinal gray zone lymphomas

Non-mediastinal gray zone lymphomas occur in older persons, have a higher rate of bone marrow involvement, include disease outside the lymph nodes (extranodal disease), and have more advanced-stage disease than mediastinal gray zone lymphomas. However, those with cancer found outside the mediastinum (extra-mediastinal disease) should be diagnosed as having DLBCL, not otherwise specified (DLBCL-NOS).

## Treatment

Since MGZL has features of both classical Hodgkin lymphoma (CHL) and non-Hodgkin PMBL, treatment is a challenge. Currently, there is no standard of care or agreement on treatment. MGZL is usually treated with chemotherapy. If the tumor cells are CD20+, rituximab might be added to chemotherapy. This is called chemoimmunotherapy. Involved-site radiation therapy (ISRT) may be added in those with localized disease.

For possible systemic therapy options, **see Guide 9.**

### Guide 9

#### Systemic therapy options: Mediastinal gray zone lymphomas

##### First-line options

- Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin with rituximab (DA-EPOCH-R)
- Cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab (RCHOP)

##### For those with heart issues

- Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab (DA-EPOCH-R)
- Rituximab, cyclophosphamide, liposomal doxorubicin (Doxil), vincristine, and prednisone (RCDOP)
- Rituximab, cyclophosphamide, etoposide, vincristine, and prednisone (RCEOP)
- Rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisone (RGCVP)
- Rituximab, cyclophosphamide, etoposide, prednisone, and procarbazine (RCEPP)

##### For those who are frail or are over 80 years of age with other health issues

- Rituximab, cyclophosphamide, liposomal doxorubicin (Doxil), vincristine, and prednisone (RCDOP)
- Rituximab with mini-CHOP (R-mini-CHOP)
- Rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisone (RGCVP)
- Rituximab, cyclophosphamide, etoposide, prednisone, and procarbazine (RCEPP)

\*An FDA-approved biosimilar might be used in place of rituximab.

## Key points

- Gray zone lymphomas have overlapping features of primary mediastinal B-cell lymphoma (PMBL) and Hodgkin lymphoma (HL).
- There are 2 main types of gray zone lymphomas: mediastinal gray zone lymphomas and non-mediastinal gray zone lymphomas.
- Mediastinal lymphomas are growths found behind the breastbone (sternum) in the part of the chest that separates the lungs and holds the heart.
- An expert hematopathologist review is essential to confirm the diagnosis of MGZL.
- MGZL is usually treated with chemotherapy. Rituximab might be added to chemotherapy if the tumor cells are CD20+. Involved-site radiation therapy (ISRT) may be added in those with localized disease.

**Mediastinal gray zone lymphoma (MGZL) is different than primary mediastinal large B-cell lymphoma (PMBL). Those with gray zone lymphomas are best managed in cancer centers with experience in treating this type of lymphoma.**



# 10

## Primary cutaneous DLBCL, leg type

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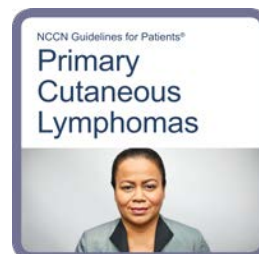
**In primary cutaneous diffuse large B-cell lymphoma (PC-DLBCL), leg type, abnormal B-cell lymphocytes cause skin lesions. Although the skin is involved, the skin cells themselves are not cancerous. Despite its name, PC-DLBCL, leg type can be found anywhere on the body. Treatment options are based on many factors. Together, you and your care team will choose a treatment plan that is best for you.**

## Overview

Primary cutaneous lymphomas (PCLs) or skin lymphomas are a rare group of non-Hodgkin lymphomas (NHLs) that develop in the skin. At the time of diagnosis, PCL is not found in any other areas of the body. Skin lymphoma is not a type of skin cancer. Skin cancer develops from skin cells. PCL develops from abnormal lymphocytes.

Primary cutaneous diffuse large B-cell lymphoma (PC-DLBCL), leg type consists of large, transformed B cells that typically appear as red or bluish-red tumors on the skin. Despite its name, the disease can involve the torso, arms, legs, buttocks, or anywhere on the body. PC-DLBCL, leg type can also spread to areas other than the skin. An expert hematopathologist review is essential to confirm the diagnosis of primary cutaneous DLBCL, leg type. A skin biopsy is done to distinguish between PC-DLBCL, leg type and other types of primary cutaneous lymphomas.

More information on skin lymphomas can be found in the *NCCN Guidelines for Patients: Primary Cutaneous Lymphomas*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



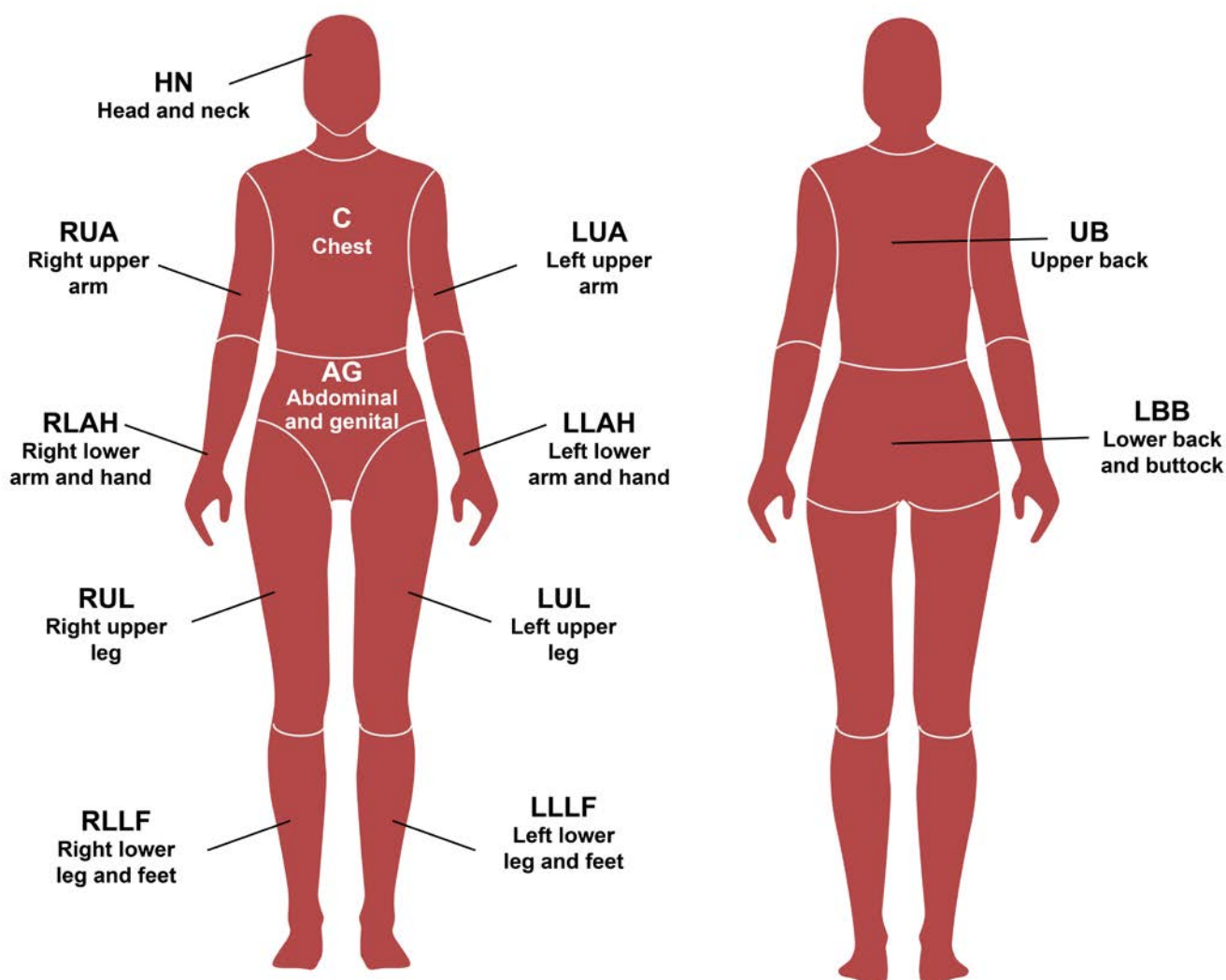
## Treatment

Treatment is based on the number of skin lesions and their location. This is called staging. Skin lesions/tumors (T) will be measured by their depth, height, size, and region of the body. Lesions are often measured in centimeters (cm). Body regions are based on regional lymph node drainage patterns. Body regions include head/neck, chest, upper

arm, lower arm and hand, abdomen and genitals, upper leg, lower leg and feet, upper back, and lower back and buttocks.

Disease may be solitary, regional, generalized skin only, or outside the skin (extracutaneous). At the end of treatment, imaging tests are needed to assess response.

### Body regions are based on regional lymph node drainage patterns.



## Solitary or regional disease

A solitary lesion is one lesion (T1). Regional lesions can be multiple lesions limited to one body region or two adjoining regions (T2). Disease area will be measured.

Options include:

- RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) with local involved-site radiation therapy (ISRT)
- Local ISRT
- Clinical trial

After a complete response (CR), you will have follow-up testing to monitor for relapse.

For a relapse, if not given before, you might be treated with RCHOP or local involved-site radiation therapy (ISRT).

## Generalized skin-only disease

Generalized skin-only disease covers a larger area of the body than regional disease. There are multiple lesions that involve 2 or more body regions (T3) not next to one another. Disease is not found in lymph nodes, blood, or other organs. Treatment works inside the body to target the skin lesions. Involved-site radiation therapy (ISRT) might be used to target a specific area of skin.

## First treatment

First-line therapy is the first treatment given. Skin-only disease is initially treated with RCHOP. RCHOP is rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. ISRT might be added to treat the skin lesions. A clinical trial is also an option.

After a complete response, you will have imaging tests and be monitored for relapse with follow-up testing.

For a relapse, if not given before, you might be treated with RCHOP or local radiation therapy (ISRT). Other treatment options are based on if relapse occurred less than 12 months or more than 12 months since your initial treatment ended. For more information, see *Chapter 5: Relapse and refractory disease*.

## Next treatment or relapse

If there was no response, a partial response, or a relapse, then treatment will be:

- A different chemoimmunotherapy
- Palliative ISRT

## Extracutaneous disease

Extracutaneous disease is found outside the skin. This is cancer that might be found in the lymph nodes, blood, or organs. Treatment will be based on the stage of diffuse large B-cell lymphoma (DLBCL) found in *Chapter 4: Stages 1, 2, 3, and 4*.

## Follow-up testing

After a complete response (CR), you will be monitored for relapse with the following tests:

- A physical exam, health history, and blood tests every 3 to 6 months for 5 years. After 5 years, these tests will be done once a year or as needed.
- CT of the chest/abdomen/pelvis no more than every 6 months for 2 years. After 2 years, imaging testing will be done as needed.

## Relapse and refractory disease

Treatment options are based on if relapse occurred less than 12 months or more than 12 months since your initial treatment ended. For more information, see *Chapter 5: Relapse and refractory disease*.

## Key points

- Primary cutaneous diffuse large B-cell lymphoma (PC-DLBCL), leg type consists of large, transformed B cells that typically appear as red or bluish-red tumors on the skin. It is not skin cancer.
- Despite its name, PC-DLBCL, leg type can be found anywhere on the body.
- Treatment is based on the number of skin lesions and their location. This is called staging.
- Disease may be solitary, regional, generalized skin only, or outside the skin (extracutaneous).
- A solitary lesion is one lesion (T1).
- Regional lesions can be multiple lesions limited to one body region or two adjoining regions (T2).
- Generalized skin-only disease covers a larger area of the body than regional disease. There are multiple lesions that involve 2 or more body regions (T3) not next to one another.
- Extracutaneous disease is disease that might be found in the lymph nodes, blood, or organs.

# 11

## Making treatment decisions

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**It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.**

## It's your choice

In shared decision-making, you and your care team share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your care team.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your

care team. If you take the time to build a relationship with your care team, it will help you feel supported when considering options and making treatment decisions.

## Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

## Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

## Questions to ask

Possible questions to ask your care team are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.







## Questions about options

1. What will happen if I do nothing?
2. How do my age, overall health, and other factors affect my options?
3. Which option is proven to work best for my cancer, age, overall health, and other factors?
4. What if I am pregnant or am planning to get pregnant soon?
5. What are the possible complications and side effects? Are any life-threatening?
6. What can be done to prevent or relieve the side effects of treatment?
7. Am I a candidate for a clinical trial? Can I join a clinical trial at any time?
8. What decisions must be made today?
9. Is there a social worker or someone who can help me decide about treatment?
10. Is there a hospital or treatment center you can recommend for treatment?

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## Resources

### **Be the Match**

[bethematch.org/one-on-one](https://bethematch.org/one-on-one)

### **Blood & Marrow Transplant Information Network**

[bmtinfonet.org](https://bmtinfonet.org)

### **Cancer Hope Network**

[cancerhopenetwork.org](https://cancerhopenetwork.org)

### **Lymphoma Research Foundation**

[lymphoma.org](https://lymphoma.org)

### **MedlinePlus**

[medlineplus.gov](https://medlineplus.gov)

### **National Bone Marrow Transplant Link (nbmtLINK)**

[nbmtlink.org](https://nbmtlink.org)

### **National Cancer Institute (NCI)**

[cancer.gov/types/lymphoma/patient/adult-nhl-treatment-pdq](https://cancer.gov/types/lymphoma/patient/adult-nhl-treatment-pdq)

### **National Coalition for Cancer Survivorship**

[canceradvocacy.org](https://canceradvocacy.org)

### **The Leukemia & Lymphoma Society**

[LLS.org/PatientSupport](https://LLS.org/PatientSupport)

### **Triage Cancer**

[triagecancer.org](https://triagecancer.org)

**Need help paying for medicine or treatment?**

**Ask your care team what options are available.**



# Words to know

## **allogeneic hematopoietic cell transplant (allogenic HCT)**

A cancer treatment that replaces abnormal blood stem cells with healthy donor cells.

## **autologous hematopoietic cell transplant (autologous HCT)**

A cancer 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). The high-dose therapy is used to eradicate the disease and stem cell rescue is needed because of the toxic effects of the treatment.

## **best supportive care**

Treatment to improve quality of life and relieve discomfort.

## **biomarker testing**

A lab test of any molecule in your body that can be measured to assess your health. Also called molecular testing.

## **biopsy**

A procedure that removes fluid or tissue samples to be tested for a disease.

## **biosimilar**

A drug that is almost an identical drug made by another company. It has been approved by the U.S. Food and Drug Administration (FDA) and must be used in the exact same way and at the same dose as the other drug.

## **bone marrow**

The sponge-like tissue in the center of most bones.

## **bone marrow aspiration**

A procedure that removes a liquid bone marrow sample to test for a disease.

## **bone marrow biopsy**

A procedure that removes bone and solid bone marrow samples to test for a disease.

## **chemotherapy**

Cancer drugs that stop the cell life cycle so that cells don't increase in number.

## **chromosome**

The structures within cells that contain coded instructions for cell behavior.

## **clinical trial**

A type of research that assesses health tests or treatments.

## **complete response (CR)**

No signs of lymphoma are found. Also called complete remission.

## **computed tomography (CT)**

A test that uses x-rays from many angles to make a picture of the insides of the body.

## **contrast**

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

## **deoxyribonucleic acid (DNA)**

A chain of chemicals in cells that contains coded instructions for making and controlling cells.

## **flow cytometry (FCM)**

A lab test of substances on the surface of cells to identify the type of cells present.

## **fluorescence in situ hybridization (FISH)**

A lab test that uses special dyes to look for abnormal chromosomes and genes.

**gene**

A set of coded instructions in cells for making new cells and controlling how cells behave.

**hematopathologist**

A doctor who specializes in the study of blood diseases and cancers using a microscope.

**hematopoietic cell transplant (HCT)**

A cancer treatment that replaces abnormal blood stem cells with healthy cells. Also called stem cell transplant (SCT) or bone marrow transplant (BMT).

**high-grade B-cell lymphoma (HGBL)**

A type of lymphoma that grows and spreads quickly and has severe symptoms.

**histology**

The study of tissues and cells under a microscope.

**human leukocyte antigen (HLA)**

A cell protein by which your body knows its own cells from foreign cells.

**imaging test**

A test that makes pictures (images) of the insides of the body.

**immune system**

The body's natural defense against infection and disease.

**immunohistochemistry (IHC)**

A lab test of cancer cells to find specific cell traits involved in abnormal cell growth.

**immunophenotyping**

A lab test that detects the type of cells present based on the cells' surface proteins.

**induction**

The first treatment that is given to greatly reduce the amount of cancer.

**in situ hybridization (ISH)**

A lab test of the number of a gene.

**involved-site radiation therapy (ISRT)**

Uses radiation therapy to treat cancer located in a small region or one area of your body.

**karyotype**

Lab test that makes a map of chromosomes to find defects.

**lactate dehydrogenase (LDH)**

A protein in blood that helps to make energy in cells.

**lymph**

A clear fluid containing white blood cells.

**lymph node**

A small, bean-shaped disease-fighting structure.

**lymphadenopathy**

Lymph nodes that are abnormal in size or consistency.

**lymphatic system**

Germ-fighting network of tissues and organs that includes the bone marrow, spleen, thymus, lymph nodes, and lymphatic vessels. Part of the immune system.

**lymphocyte**

A type of white blood cell that is part of the immune system.

**magnetic resonance imaging (MRI)**

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

**mediastinal gray zone lymphoma (MGZL)**

A type lymphoma with overlapping features of Hodgkin lymphoma (HL) and primary mediastinal large B-cell lymphoma (PMBL) found in the mediastinum (the area behind the breastbone).

**monitoring**

A period of testing for changes in cancer status.

**mutation**

An abnormal change in the instructions within cells for making and controlling cells.

**partial response (PR)**

Lymphoma is still present but has reduced in size.

**pathologist**

A doctor who's an expert in testing cells and tissue to find disease.

**peripheral blood (PB)**

Blood that circulates throughout the body.

**platelet (PLT)**

A type of blood cell that helps control bleeding. Also called thrombocyte.

**polymerase chain reaction (PCR)**

A lab process in which copies of a DNA part are made.

**positron emission tomography (PET)**

A test that uses radioactive material to see the shape and function of body parts.

**primary mediastinal large B-cell lymphoma (PMBL)**

A fast-growing type of lymphoma that develops from B cells in the mediastinum (the area behind the breastbone).

**prognosis**

The likely course a disease will take.

**radiation therapy (RT)**

A treatment that uses high-energy rays.

**recovery**

A period of time without treatment to allow blood cell counts to return to normal.

**recurrence**

The return of cancer after a cancer-free period.

**red blood cell (RBC)**

A type of blood cell that carries oxygen from the lungs to the rest of the body. Also called an erythrocyte.

**refractory cancer**

A cancer that does not improve with treatment.

**relapse**

The return or worsening of cancer after a period of improvement.

**remission**

Minor or no signs of disease.

**side effect**

An unhealthy or unpleasant physical or emotional response to treatment.

**supportive care**

Treatment for the symptoms or health conditions caused by cancer or cancer treatment. Also sometimes called palliative care or best supportive care.

**translocation**

A switching of parts between two chromosomes.

**tumor lysis syndrome (TLS)**

A rare condition caused when waste released by dead cells is not quickly cleared out of your body.

**white blood cell (WBC)**

A type of blood cell that helps fight infections in the body. Also called a leukocyte.

# NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas, Version 1.2024. 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  
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800.789.7366 • [pennmedicine.org/cancer](http://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](http://uhhospitals.org/services/cancer-services)  
CC Taussig Cancer Institute  
866.223.8100 • [my.clevelandclinic.org/departments/cancer](http://my.clevelandclinic.org/departments/cancer)  
Case CCC  
216.844.8797 • [case.edu/cancer](http://case.edu/cancer)

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800.826.4673 • [cityofhope.org](http://cityofhope.org)

**Dana-Farber/Brigham and Women's Cancer Center |  
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**Fred & Pamela Buffett Cancer Center**  
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402.559.5600 • [unmc.edu/cancercenter](http://unmc.edu/cancercenter)

**Fred Hutchinson Cancer Center**  
Seattle, Washington  
206.667.5000 • [fredhutch.org](http://fredhutch.org)

**Huntsman Cancer Institute at the University of Utah**  
Salt Lake City, Utah  
800.824.2073 • [healthcare.utah.edu/huntsmancancerinstitute](http://healthcare.utah.edu/huntsmancancerinstitute)

**Indiana University Melvin and Bren Simon  
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888.600.4822 • [www.cancer.iu.edu](http://www.cancer.iu.edu)

**Mayo Clinic Comprehensive Cancer Center**  
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Rochester, Minnesota  
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904.953.0853 • Florida  
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[mayoclinic.org/cancercenter](http://mayoclinic.org/cancercenter)

**Memorial Sloan Kettering Cancer Center**  
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**Robert H. Lurie Comprehensive Cancer Center  
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**Roswell Park Comprehensive Cancer Center**  
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**Siteman Cancer Center at Barnes-Jewish Hospital  
and Washington University School of Medicine**  
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901.448.5500 • [uthsc.edu](http://uthsc.edu)

**Stanford Cancer Institute**  
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877.668.7535 • [cancer.stanford.edu](http://cancer.stanford.edu)

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800.293.5066 • [cancer.osu.edu](http://cancer.osu.edu)

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410.955.8964  
[www.hopkinskimmelcancercenter.org](http://www.hopkinskimmelcancercenter.org)

**The UChicago Medicine Comprehensive Cancer Center**  
Chicago, Illinois  
773.702.1000 • [uchicagomedicine.org/cancer](http://uchicagomedicine.org/cancer)

**The University of Texas MD Anderson Cancer Center**  
Houston, Texas  
844.269.5922 • [mdanderson.org](http://mdanderson.org)

**UC Davis Comprehensive Cancer Center**  
Sacramento, California  
916.734.5959 • 800.770.9261  
[health.ucdavis.edu/cancer](http://health.ucdavis.edu/cancer)



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858.822.6100 • [cancer.ucsd.edu](http://cancer.ucsd.edu)

UCLA Jonsson Comprehensive Cancer Center  
Los Angeles, California  
310.825.5268 • [cancer.ucla.edu](http://cancer.ucla.edu)

UCSF Helen Diller Family  
Comprehensive Cancer Center  
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800.689.8273 • [cancer.ucsf.edu](http://cancer.ucsf.edu)

University of Colorado Cancer Center  
Aurora, Colorado  
720.848.0300 • [coloradocancercenter.org](http://coloradocancercenter.org)

University of Michigan Rogel Cancer Center  
Ann Arbor, Michigan  
800.865.1125 • [rogelcancercenter.org](http://rogelcancercenter.org)

University of Wisconsin Carbone Cancer Center  
Madison, Wisconsin  
608.265.1700 • [uwhealth.org/cancer](http://uwhealth.org/cancer)

UT Southwestern Simmons  
Comprehensive Cancer Center  
Dallas, Texas  
214.648.3111 • [utsouthwestern.edu/simmons](http://utsouthwestern.edu/simmons)

Vanderbilt-Ingram Cancer Center  
Nashville, Tennessee  
877.936.8422 • [vicc.org](http://vicc.org)

Yale Cancer Center/Smilow Cancer Hospital  
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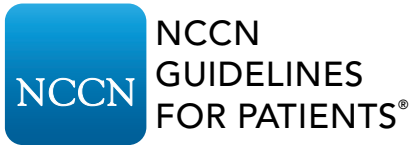
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