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✓ Step-by-step guides to the cancer care options likely to have the best results
✓ Based on treatment guidelines used by health care providers worldwide
✓ Designed to help you discuss cancer treatment with your doctors
These NCCN Guidelines for Patients are based on the NCCN Guidelines® for B-Cell Lymphomas, Version 5.2022 – July 12, 2022

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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 start in 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

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 help fight infection and disease.

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 the immune system that starts in lymphocytes. A lymphocyte is a type of immune cell that is also a type of white blood cell. White blood cells fight infection. Lymphocytes are found in both blood and lymph tissue. 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 a 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 kill tumor cells and infected cells directly in a targeted and specific way. T cells help control immune responses and form specific immune memory.
- **Natural killer (NK) cells** can kill tumor cells or virus-infected cells.

NHL can be formed from either B-cell, T-cell, or NK-cell lymphocytes. Diffuse large B-cell lymphoma starts in mature B cells. B cells produce antibodies that are used to attack invading bacteria, viruses, and toxins. The antibody molecules latch onto and destroy invading viruses or bacteria.

DLBCL

Diffuse large B-cell lymphoma (DLBCL) is the most common type of NHL. It accounts for about 3 out of every 10 NHLs. Large-celled, fast-growing tumors 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.

**DLBCL subtypes**

There are many subtypes of DLBCL. If you have DLBCL along with another lymphoma, it will likely be treated as DLBCL. For DLBCL subtypes covered in this book, see Guide 1.

---

I had none of the typical DLBCL symptoms. Nothing about my experience was typical. I was young, in my 20s, and had DLBCL in a bone in my foot.”
**Guide 1**

**DLBCL subtypes**

DLBCL, not otherwise specified (NOS) (includes germinal center and nongermininal center)
- Germinal center (or follicle center) is not the same as follicular lymphoma (FL) and can occur in DLBCL and Burkitt lymphoma.

- DLBCL with follicular lymphoma (FL) of any grade
- DLBCL with gastric mucosa-associated lymphoid tissue (MALT) lymphoma
- DLBCL with nongastric MALT lymphoma
- Intravascular large B-cell lymphoma
- DLBCL associated with chronic inflammation
- ALK-positive large B-cell lymphoma
- Epstein-Barr virus-positive (EBV-positive) DLBCL, NOS
- T-cell/histiocyte-rich large B-cell lymphoma
- Fibrin-associated DLBCL (FA-DLBCL)
- Large B-cell lymphoma with IRF4 rearrangement
- Double-expressor DLBCL
- Primary mediastinal large B-cell lymphoma (PMBL)
- Gray zone lymphoma (also known as B-cell lymphoma, unclassifiable with features intermediate between DLBCL and Hodgkin lymphoma)
- High-grade B-cell lymphomas with translocations of MYC and BCL2 and/or BCL6 (double- or triple-hit lymphoma)
- High-grade B-cell lymphomas, NOS
- Primary cutaneous DLBCL, leg type
Information on subtypes not covered in this book:

- Primary cutaneous marginal zone lymphoma (PCMZL) and primary cutaneous follicle center lymphoma (PCFCL) - For more information, read the NCCN Guidelines for Patients: Primary Cutaneous Lymphomas and NCCN Guidelines for Patients: B-Cell Lymphomas - Follicular Lymphoma, available at NCCN.org/patientguidelines.

- Primary DLBCL of the central nervous system (CNS) - For more information, read the NCCN Guidelines for Patients: Central Nervous System Cancers - Primary Central Nervous System Lymphoma, available at NCCN.org/patientguidelines.

- DLBCL arising from chronic lymphocytic leukemia (CLL) called Richter’s transformation - For more information, read the NCCN Guidelines for Patients: Chronic Lymphocytic Leukemia, available at NCCN.org/patientguidelines.
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 lymphomas (NHLs) start in lymphocytes, a type of immune and white blood cell. White blood cells fight infection.

- Diffuse large B-cell lymphoma (DLBCL) is the most common type of NHL.

- Large-celled, fast-growing tumors are commonly found in lymph nodes, spleen, liver, bone marrow, or other tissues and organs. Symptoms include fever, night sweats, and weight loss.

- There are many subtypes of DLBCL.

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
# 2 Testing for DLBCL

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NCCN Guidelines for Patients®
Diffuse Large B-Cell Lymphomas, 2022
Accurate testing is essential to diagnose and treat DLBCL. This chapter presents an overview of possible tests you might receive and what to expect.

Test results

Results from imaging studies and biopsies will be used to determine your treatment plan. 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.

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

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, medical records, and tests results. You can do the same on your computer.
• Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
• Organize your binder in a way that works for you. Add a section for questions and to take notes.
• Bring your medical binder to appointments. You never know when you might need it!
access it in an emergency. Keep your primary care physician (PCP) informed of changes to this list. You are encouraged to keep your PCP. They are great partners in care.

- Include in your contact list information on your exact subtype of DLBCL, as well as any treatment and the date it started.

General health tests

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 medicines, herbals, or supplements you take. Some supplements interact and affect prescriptions that your doctor may give you. Tell your doctor about any symptoms you have. A medical history, sometimes called a health history, will help determine which treatment is best for you.

Family history
Some cancers and other diseases can run in families. Your doctor 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 is important to know the specific type of cancer, or where the cancer started, and if it is in multiple locations.

Physical exam
During a physical exam, your health care provider 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 are of normal size, are soft or hard, or cause pain when touched. Tell your doctor if you feel pain.
- Feel for enlarged lymph nodes in your neck, underarm, and groin area. Tell your doctor if you have felt any lumps or have any pain.

For possible tests, see Guide 2.
### Guide 2
Testing for DLBCL

**Biopsy, histology grading, and pathology review**

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

**Physical exam with attention to 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), and uric acid**

**PET/CT scan (including neck) and/or chest/abdomen/pelvis CT with contrast**

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

**Hepatitis B testing**

**Echocardiogram or multigated acquisition (MUGA) scan if certain treatments will be used**

**Pregnancy test if chemotherapy or radiation therapy will be used**

**Possible:**
- Head CT/MRI with contrast or neck CT/MRI with contrast
- Discussion of fertility issues and sperm banking
- 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; bone marrow biopsy is not necessary if PET/CT scan demonstrates bone disease
Fertility (all sexes)

Treatment such as chemotherapy can affect your fertility, the ability to have children. If you think you want children in the future, ask your doctor how cancer and cancer treatment might change your fertility. In order 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 really 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 can be found in the NCCN Guidelines for Patients: Adolescents and Young Adults with Cancer, available at NCCN.org/patientguidelines.

Impaired fertility

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

Preventing pregnancy

Preventing pregnancy during treatment is important. Cancer and cancer treatment can affect the ovaries and damage sperm. 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 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 40 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 time and still able to care for self.
- PS 3 means the person is limited to the chair or bed more than half of the time.
- PS 4 means the person is totally confined to bed or chair and completely disabled.
- PS 5 means the person is not alive.

Good PS is usually PS 0 or PS 1.

International Prognostic Index

The International Prognostic Index (IPI) is a scoring system for prognosis in those with lymphoma. A prognosis is the likely course your disease will take. IPI is based on age, performance status (PS), cancer stage, lactate dehydrogenase (LDH) results, and if cancer is found in the bone marrow, central nervous system (CNS), liver, gastrointestinal tract, or lung.
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. You might have blood tests as often as every 6 to 48 hours during DLBCL treatment and recovery to check treatment results, blood counts, and the health of organs like your liver and kidneys.

Some possible tests described next are listed alphabetically and not in order of importance.

**CMV Ab**
Cytomegalovirus (CMV) antibody (Ab) testing looks for antibodies to CMV, a virus in the herpes family. CMV is very common. Most people do not even know they have it.

**Complete blood count**
A complete blood count (CBC) measures the levels of red blood cells (RBCs), white blood cells (WBCs), and platelets in your blood. Your doctor will want to know if you have enough RBCs to carry oxygen throughout your body, WBCs to fight infection, and platelets to control bleeding.

**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.

**Differential**
There are 5 types of WBCs: neutrophils, lymphocytes, monocytes, eosinophils, and basophils. A differential counts the number of each type of WBC. It also checks if the counts are in balance with each other.

**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.

**Hepatitis B and C**
Hepatitis is a virus that causes inflammation of the liver. Hepatitis B (HBV) and hepatitis C (HCV) are spread by contact with blood and other bodily fluids. A blood test will show if you had hepatitis in the past or if you have it today. Some treatments might cause HBV to reactivate, which can cause liver damage.

**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. Treatment for HIV-positive DLBCL is not covered in this book.

**HLA typing**
Human leukocyte antigens (HLAs) are proteins found on the surface of most cells. They play an important role in your body’s immune response. HLAs are unique to each person. They mark your body’s cells. Your body 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) stem cell transplant. 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 tissues 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.

**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 and can impair kidney function.
Biopsy

A biopsy is the removal of a sample tissue or fluid for testing. It is an important part of an accurate diagnosis. Your sample should be reviewed by a pathologist who is an expert in the diagnosis of DLBCL. 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 it means for your treatment.

Types of possible biopsies include:

- **Fine-needle aspiration (FNA) or core biopsy (CB)** uses needles of different sizes to remove a sample of tissue or fluid.
- **Excisional biopsy** removes a small amount of tissue 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 in order to accurately diagnose the type of DLBCL.

These 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

Samples of bone and marrow are removed in a biopsy.
Testing for DLBCL Biopsy

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 core 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.

The samples are usually taken from the back of the hip bone (pelvis). You will likely lie on your belly or side. Your doctors will first clean and give sedation or numb your skin and outer surface of your bone. 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 core sample. You may feel bone pain at your hip for a few days. Your skin may bruise.

What is your family health history?

Some cancers and other diseases run in families—those who are related to you through genes passed down from parent to child. This information is called a family health history. You can ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. For relatives who have died, ask about the cause and age of death.

Start by asking your parents, siblings, and children. Next, talk to half-siblings, aunts and uncles, nieces and nephews, grandparents, and grandchildren.

Write down what you learn about your family health history and share this information with your health care provider.

Some of the questions to ask include:

- Do you have any chronic diseases, such as heart disease or diabetes, or health conditions such as high blood pressure or high cholesterol?
- Have you had any other diseases, such as cancer or stroke?
- How old were you when each of these diseases and health conditions was diagnosed?
- What is our family’s ancestry—from what countries did our ancestors originate?
Genetic testing

Genetic 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 doctor if there is a family history of cancer.

There are 3 major types of genetic testing:

- **Cytogenetic** - to examine whole chromosomes
- **Biochemical** - to measure proteins produced by genes
- **Molecular** - to look for small DNA or gene mutations

While it can be confusing, just know that testing done to look for an inherited gene mutation or an inherited risk of cancer is different than genetic testing done on cancer cells or testing to look for proteins produced by cancer cells. This book refers to tests done on cancer cells or to look for evidence of cancer as biomarker tests.

Biomarker tests

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 for the proteins your cells make. A mutation is when something goes wrong in the genetic code.

A sample from your biopsy will undergo lab tests to look for specific DNA mutations/alterations, protein levels, or other molecular features. This information is used to learn more about your type of DLBCL and to choose the best treatment for you. It is sometimes called molecular testing, tumor profiling, gene expression profiling, or genomic testing.

Biomarker testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins that might suggest treatment. Proteins are written like this: BCL6. Genes are written with italics like this: BCL6. When a gene or protein is found, 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-.

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 (B2M) 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.

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 either a bone marrow or 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 with a karyotype. For example, FISH is used to detect MYC, BCL2, and BCL6 gene rearrangements.

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

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

- **Double-hit B-cell lymphoma** is a group of tumors with gene rearrangements involving at least 2 genes, including **MYC, BCL2, BCL6, or other genes.**

**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 diffuse large B-cell lymphoma (DLBCL).
Testing for DLBCL Immunophenotyping

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, rearranged, or abnormal pieces of chromosomes. Since a karyotype requires growing cells, a sample of bone marrow must be used.

Mutation testing
A sample of your lymphoma cells may 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 parents.

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

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 high-throughput method used to determine a portion of a person’s DNA sequence.

PCR
A polymerase chain reaction (PCR) is a lab process that can make millions or billions of copies of your DNA (genetic information) in just a few hours, but results can take days. 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 HTS or NGS.

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 white blood cells. Specific groupings of antigens are normal. However, some specific patterns of antigens are found on abnormal cells.

Immunophenotyping can be done using flow cytometry or immunohistochemistry. It is used to pinpoint the specific subtype of DLBCL. Immunophenotype can change as cancer progresses.

Diffuse large B-cell lymphoma 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-.

DLBCL immunophenotype is usually CD20+, CD45+, and CD3-. Additional markers are used to establish subtype. See Guide 3.

**Flow cytometry**

Flow cytometry 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 proteins on the surface of thousands 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).

**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.

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<th>Tests to diagnose DLBCL subtype</th>
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| Needed  | • IHC panel: CD20, CD3, CD5, CD10, 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  
  • FISH for *BCL2, BCL6* rearrangements if *MYC* positive |
| In some cases  | • IHC panel: cyclin D1, kappa/lambda, CD30, CD138, ALK, HHV8, and SOX11  
  • Epstein-Barr encoding region in situ hybridization (EBER-ISH) |
Imaging tests

Imaging tests take pictures of the inside of your body. Imaging tests look for cancer deposits in different parts of the body. A radiologist, an expert in interpreting imaging tests, will write a report and send this report to your doctor. Your doctor will discuss the results with you.

The following imaging tests are listed in alphabetical order and not in order of importance.

**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 chest, abdomen, and/or pelvis may be one of the tests to look for cancer. In most cases, contrast will be used.

**Contrast**
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 the body in your urine after the test. The types of contrast vary and are different for CT and MRI.

Tell your doctors if you have had allergic reactions to contrast in the past—especially to iodine or shellfish like shrimp. 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.

**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. Tell the technician if you have any metal in your body.

**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. When a PET scan is combined with CT, it is called a PET/CT scan. It may be done with one or two machines depending on the cancer center.

**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

A lumbar puncture (LP) or spinal tap is a procedure that removes spinal fluid. It is also used to inject chemotherapy into the spinal fluid. This is called intrathecal (IT) chemotherapy.

At the time of IT, a sample of your spinal fluid will be taken and tested. DLBCL can travel to the cerebrospinal fluid (CSF) that surrounds the spine or brain. This is called central nervous system (CNS) disease. When systemic therapy and IT therapy are given together to prevent CNS disease, it is called CNS prophylaxis.

“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.”
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 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 medicines 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.

Cardiac nuclear medicine scan
A nuclear heart scan is an imaging test that uses special cameras and a radioactive substance called a tracer to create pictures of your heart. The tracer is injected into your blood and travels to your heart. This test can also be used to measure the ejection fraction.

Testing takes time. It might take days or weeks for all test results to come in.
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 a sample tissue or fluid for testing. It is an important part of an accurate DLBCL diagnosis.

- Immunophenotyping is used to pinpoint the subtype of DLBCL.

- A sample from your biopsy will undergo lab tests to look for specific DNA (deoxyribonucleic acid) mutations/alterations, protein levels, or other molecular features. This information is used to learn more about your subtype of DLBCL and to choose the best treatment for you.

- Biomarker testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins that might suggest treatment.

- $\textit{MYC}$, $\textit{BCL2}$, and $\textit{BCL6}$ are gene rearrangements found in DLBCL.

- Imaging tests are used to look for areas of lymphoma involvement and are part of your staging workup.

- A lumbar puncture 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.
## Treatment overview

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There is more than one treatment for DLBCL. 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 right for you.

DLBCL is treatable and curable. Treatment for DLBCL 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.

**Treatment team**

Treating DLBCL takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT). An MDT is a team of doctors, health care workers, and social care professionals from different professional backgrounds who have knowledge (expertise) and experience with 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:

- **A hematologist or hematologic oncologist** is a medical expert in blood diseases and blood cancers.
- **A pathologist or hematopathologist** analyzes the cells and tissues removed during a biopsy and provides cancer diagnosis, staging, and information about biomarker testing.
- **A diagnostic radiologist** interprets the results of x-rays and other imaging tests.
- **An interventional radiologist** performs needle biopsies and places ports for treatment.
- **A medical oncologist** treats cancer in adults using systemic therapy.
- **A radiation oncologist** prescribes and plans radiation therapy to treat cancer.
- **An anesthesiologist** gives anesthesia, a medicine so you do not feel pain during surgery or procedures.
- **Residents and fellows** are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- **Nurse practitioners and physician assistants** are health care providers. Some of your clinic visits may be done by a nurse practitioner or physician assistant.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
Sometimes, these experts are called nurse navigators.

- **Oncology pharmacists** provide medicines used to treat cancer and to manage symptoms and side effects.

- **Palliative care nurses, advanced practice providers, and physicians** help provide an extra layer of support with your cancer-related symptoms.

- **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.

- **A certified lymphedema therapist** gives a type of massage called manual lymph drainage.

- **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 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 workers, can help navigate the complexities of financial and insurance stresses.

- **A research team** helps to collect research data and coordinate care if you are in a clinical trial.

Your physical, mental, and emotional well-being are important. You know yourself better than anyone. Help other team members 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 who to contact with questions or concerns.
3 Treatment overview

Treatment phases

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 remission. During and at the end of induction, you will have tests to look for a response (remission).

**Consolidation**
For those in remission, consolidation may occur after induction. It is used to kill any cancer cells that might be left in the body after induction. This is to prevent cancer from returning. Sometimes, this treatment is called post-remission therapy, which might be a combination of consolidation and maintenance therapy. Not everyone will receive consolidation therapy.

**Maintenance**
Maintenance can be the third phase of treatment. It is treatment to prevent cancer from returning. It may be given for a long time and occur over years. Maintenance is also called post-consolidation therapy because it is treatment after (post) consolidation. Not everyone will receive maintenance therapy. Maintenance may be recommended depending on your type of disease, consolidation, and risk of relapse.

**Remission**
There are different types of treatment responses. 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, 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 has not gone away and does not respond to treatment, it is called refractory or resistant cancer. The 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**
You will be monitored throughout treatment. Surveillance watches for any changes in your condition after remission or a hematopoietic cell transplant. You will have tests during surveillance to check for relapse.
Preventing pregnancy during treatment

If you become pregnant during chemotherapy, radiation therapy, or other types of systemic therapy, serious birth defects can occur. Speak to your care team about preventing pregnancy while being treated for cancer. Those who want to become pregnant in the future should be referred to a fertility specialist to discuss the options before starting chemotherapy and/or radiation therapy.

Systemic therapy

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

Warnings!
You might be asked to stop taking or avoid certain food or herbal supplements when on a systemic therapy. Some supplements and food 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
- Gingko biloba
- Green tea extract
- St. John’s Wort

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy. This is why it is important to tell your doctor about any medications, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you take. Bring a list with you to every visit.

You should not become pregnant during treatment with systemic therapy or radiation therapy.
Chemotherapy

Chemotherapy kills fast-growing 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 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 well treatment is working. You might spend time in the hospital during treatment.

This is an example of a chemotherapy drug combination (regimen):

- EPOCH is etoposide (Etopophos), prednisone, vincristine, cyclophosphamide, and doxorubicin.

Chemoimmunotherapy

Chemoimmunotherapy, also called immunochemotherapy, includes chemotherapy and immunotherapy drugs to treat cancer.

Some examples include:

- RCHOP is rituximab, cyclophosphamide (Cytoxan), doxorubicin, vincristine (Oncovin), and prednisone.
- RCDOP is rituximab, cyclophosphamide, liposomal doxorubicin (Doxil), vincristine, and prednisone.
- RCEOP is rituximab, cyclophosphamide, etoposide, vincristine, and prednisone.
- RCEPP is rituximab, cyclophosphamide, etoposide, prednisone, and procarbazine (Matulane).
- RGCVP is rituximab, gemcitabine (Gemzar or Infugem), cyclophosphamide, vincristine, and prednisone.

“During chemo, I made sure to eat even when I wasn’t hungry, and to drink plenty of water.”
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 antibodies to help the body fight cancer, infection, or other diseases. Antibodies are proteins made by the immune system that bind to specific markers on cells or tissues. Monoclonal antibodies (mAbs) used in cancer treatment may kill cancer cells directly, block development of tumor blood vessels, or help the immune system kill cancer cells. As with other treatments, there is the potential for complications.

- Rituximab (Rituxan) works against the protein CD20 found on the surface of B cells. When it binds to this protein it triggers cell death. A biosimilar or substitute might be used in place of rituximab. A biosimilar is almost an identical drug made by another company. It must be used in the exact same way and at the same dose as rituximab. Biosimilars include: Riabni, Hycela, Ruxience, and Truxima.
- Other mAb therapy examples include brentuximab vedotin (Adcetris), nivolumab (Opdivo), pembrolizumab (Keytruda), polatuzumab vedotin-piiq (Polivy), loncastuximab tesirine, and tafasitamab-cxix (Monjuvi).

CD19-targeting CAR T-cell therapy

CD19-directed genetically modified autologous T-cell immunotherapy (CD19-targeting CAR T-cell therapy) or anti-CD19 CAR T-cell therapy is made from your own T cells. T cells will be removed from your body, and in the lab, a CAR (chimeric antigen receptor) will be added to them. This programs the T cells to find the 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 and is only offered in certified centers. There can be severe and sometimes life-threatening reactions.

CAR T-cell therapy is only used in recurrent lymphoma outside of clinical trials.

- Axicabtagene ciloleucel (Yescarta)
- Lisocabtagene melaleuca (Breyanzi)
- Tisagenlecleucel (Kymria)

More information on CAR T-cell therapy can be found in "NCCN Guidelines for Patients: Immunotherapy Side Effects," available at NCCN.org/patientguidelines.
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 the action of molecules that help cancer cells grow and/or survive. Ibrutinib (Imbruvica) is one such example.

Radiation therapy

Radiation therapy (RT) uses high-energy radiation from photons, electrons, or protons, and other sources to kill cancer cells and shrink tumors. It is given over a certain period of time. Radiation therapy can be given alone or with certain systemic therapies. When used as supportive care to help ease pain or discomfort caused by cancer, it is called palliative RT.

- RT given to prevent cancer in the central nervous system or testicles is called prophylaxis or prophylactic RT.
- Those with cancer in the central nervous system at diagnosis may receive radiation to the brain area.
- Those with testicular disease at diagnosis may receive radiation to the testes.

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.

EBRT

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 cancer found in or near lymph nodes (nodal disease).

Cranial irradiation

In cranial irradiation, the areas of the brain targeted for DLBCL radiation treatment are different from areas targeted for brain metastases of solid tumors. Cranial irradiation might be given to prevent DLBCL from spreading to the brain. This is called prophylaxis.

Total body irradiation

Total body irradiation (TBI) is radiation of the whole body given before bone marrow transplant.

Whole brain irradiation

Whole brain irradiation is radiation of the whole brain and is a type treatment for lymphoma involving the central nervous system.
Hematopoietic cell transplant

A hematopoietic cell transplant (HCT) replaces damaged hematopoietic stem cells. A hematopoietic stem cell is an immature cell that can develop into any type of blood cell. 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 autoHCT. 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 transplant uses healthy stem cells from a donor. The donor may or may not be related to you. An allogeneic HCT (alloHCT) is sometimes used to treat a relapse.

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.

Radiation therapy may also be given as part of conditioning treatment.

After conditioning, you will receive the healthy stem cells through a transfusion. 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.

**Possible side effects**

Every treatment has side effects. You will be monitored for infections, 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 doctor 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 in *NCCN Guidelines for Patients: Graft-Versus-Host Disease*, available at NCCN.org/patientguidelines.
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 fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA). Clinical trials don’t always include experimental agents. Sometimes, they study a new way to deliver an existing treatment or a new biomarker to help assign an appropriate treatment.

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.

Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

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

Worldwide

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

Need help finding a clinical trial?
NCI’s Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact
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, 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.

Are clinical trials free?
There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.
Supportive care

Supportive care is health care given during all cancer stages. It aims 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. Best supportive care, supportive care, and palliative care are often used interchangeably.

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.

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

Anemia, neutropenia, and thrombocytopenia

Some cancer treatments can cause low blood cell counts.

- **Anemia** is a condition where your body does not make 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, the most common 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.

For more information on anemia, neutropenia, and thrombocytopenia, see *NCCN Guidelines for Patients: Anemia and Neutropenia*, available at [NCCN.org/patientguidelines](http://NCCN.org/patientguidelines).

Distress

Depression, anxiety, and sleeping problems are common in cancer. Talk to your doctor and with those whom you feel most comfortable about how you are feeling. There are services, people, and medicine that can help you. Support and counseling services are available.

For more information, see *NCCN Guidelines for Patients: Distress During Cancer Care*, available at [NCCN.org/patientguidelines](http://NCCN.org/patientguidelines).
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, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.

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.

Scalp cooling
Scalp cooling (or scalp hypothermia) might help lessen hair loss in those receiving certain types of chemotherapy. Some people find scalp cooling uncomfortable and have headaches as a side effect from the cold. You may experience hair loss even with scalp cooling treatment.

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 that is commonly seen with rituximab.

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. Infections can be caused by viruses, fungus, or bacteria. Antibiotics can treat bacterial infections. Antifungal medicines can treat fungal infections. You may be given antiviral drugs to prevent viral infections.

Lymphedema
Lymphedema is a condition in which extra 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 sleeves, and other means. Ask your care team about the ways to treat lymphedema.
Nausea and vomiting
Nausea and vomiting are a common side effect of treatment. You will be given medicine to prevent and treat nausea and vomiting.

For more information, see NCCN Guidelines for Patients: Nausea and Vomiting, available at NCCN.org/patientguidelines.

Neurocognitive 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.

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.

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
- Describe 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?
- Rate 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?
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. DLBCL treatment can cause a number of 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.

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.

Therapy-related toxicity
Many of the drug therapies used to treat DLBCL can be harmful to the body. You will be closely monitored for therapy-related toxicity.

Trouble eating
Sometimes side effects from surgery, cancer, or other treatments might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth. 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 your weight.

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 sign of TLS. TLS can be life-threatening.

“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!”
Survivorship

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.

You should discuss a personalized survivorship care plan with your care team. It 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.

For more information on survivorship, see the NCCN Guidelines for Patients: Survivorship series at NCCN.org/patientguidelines.
Key points

- Treatment decisions should involve a multidisciplinary team (MDT) from different fields of medicine who have knowledge (expertise) and experience with your type of cancer.
- DLBCL is treatable and curable. The goal of treatment is to achieve a complete response (CR) or remission.
- 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.
- Chemotherapy kills fast-growing cells throughout the body, including cancer cells and some normal cells.
- Immunotherapy is drug therapy that increases the activity of your immune system.
- Targeted therapies can block the ways cancer cells grow, divide, and move in the body.
- 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.
- A hematopoietic cell transplant (HCT) replaces damaged bone marrow stem cells with healthy stem cells. You might hear it called a stem cell transplant (SCT) or bone marrow transplant (BMT).
- Clinical trials study how safe and helpful tests and cancer treatments are for people.
- Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. Supportive care is always given.
- All cancer treatments can cause unwanted health issues called side effects. It is important for you to tell your care team about all your side effects so they can be managed.
- Eating a balanced diet, drinking enough fluids, exercise, yoga, and massage therapy 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

48 Staging
49 Treatment
50 Stages 1 and 2 non-bulky (limited)
51 Stages 1 and 2 bulky (limited)
52 Stage 2 with mesenteric disease or stages 3 and 4
53 Follow-up testing
53 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 right for you.

**Staging**

A PET and/or CT scan will be done to stage DLBCL. In addition, treatment decisions are based on histology and results of genetic and biomarker 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** – Disease found in 1 lymph node or a group of nearby lymph nodes.
- **Stage 2** – 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.
- **Stage 3** – 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** – Disease has spread outside of the lymphatic system to other parts of the body.
**Treatment**

DLBCL is treated with RCHOP first. Radiation therapy might follow. Involved-site radiation therapy (ISRT) treats cancer found in or near lymph nodes (nodal disease).

RCHOP consists of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. For all first-line options, see Guide 4.

---

**Guide 4**

**First-line therapy options**

<table>
<thead>
<tr>
<th>Preferred</th>
<th>• Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (RCHOP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other recommended</td>
<td>• Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab (DA-EPOCH-R)</td>
</tr>
</tbody>
</table>
| 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, cyclophosphamide, etoposide, prednisone, and procarbazine (RCEPP)  
• Rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisone (RGCVP) |
| For those who are frail or are over 80 years of age with other health issues | • Rituximab, cyclophosphamide, etoposide, prednisone, and procarbazine (RCEPP)  
• Rituximab, cyclophosphamide, liposomal doxorubicin (Doxil), vincristine, and prednisone (RCDOP)  
• Rituximab with mini-CHOP (R-mini-CHOP)  
• Rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisone (RGCVP) |

*Note: An FDA-approved biosimilar might be used for rituximab.*
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 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 radiation therapy (ISRT) 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.

Stage 2 DLBCL

In stage 2 DLBCL, cancer is found in 2 or more lymph node groups on the same side of the diaphragm.
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 cycles of RCHOP. This is called first-line chemoimmunotherapy. A type of radiation called ISRT might be added.

If ISRT planned
After end of first-line chemoimmunotherapy, your will have a PET/CT before starting radiation therapy (ISRT).

- If a complete response, you will complete the planned course of treatment with a first dose of radiation therapy (ISRT).
- If a partial response, you will complete the planned course of treatment with a higher ISRT dose or enter a clinical trial. You might be treated for refractory disease found in Chapter 5: Relapse and refractory disease.
- 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.

If ISRT not planned
After 3 or 4 cycles, your cancer will be restaged using PET/CT. A repeat biopsy might also be done.

- If in remission, also called a complete 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.
- If a partial response, you might have radiation therapy (ISRT) or be treated for refractory disease found in Chapter 5: Relapse and refractory disease.
- 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.

It is very important to continue to take your medicine as prescribed and not miss or skip any doses.
Stage 2 with mesenteric disease or stages 3 and 4

The mesentery is a fold of membrane that attaches the intestine to the abdominal wall and holds it in place. For stage 2 cancer with mesenteric disease or stages 3 and 4, then a clinical trial or RCHOP are the recommended and preferred options. Other chemotherapy regimens might be used. A CT scan might be done after 2 to 4 cycles to restage your cancer.

- 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.
- 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.
Follow-up testing

After completing all 6 cycles of RCHOP, a PET scan will be done. ISRT might be done 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 is used for monitoring those without symptoms (asymptomatic). It includes a chest/abdominal/pelvic 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 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 stage 2 cancer with mesenteric disease or stages 3 and 4, a clinical trial or RCHOP are the recommended options. The mesentery is a membrane that attaches the intestine to the abdominal wall and holds it in place.
- A type of radiation called ISRT might be added to treatment. Involved-site radiation therapy (ISRT) treats cancer found in or near lymph nodes (nodal disease).
- After completing all 6 cycles of RCHOP, a PET scan will be done. ISRT might be done 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.
5

Relapse and refractory disease

55 Relapse – Under 12 months
56 Relapse – Over 12 months
56 Refractory disease
58 2 or more relapses
58 Follow-up testing
58 Key points
Relapse and refractory disease

Relapse – Under 12 months

DLBCL returns in about half of those in remission. Cancer that returns is called relapse. When DLBCL progresses despite treatment, it is called refractory. The goal of treatment is to achieve remission again. Together, you and your care team will choose a treatment plan that is right 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.

Other options

If you are not receiving CAR T-cell therapy, then options include:

- Clinical trial
- Second-line therapy, see Guide 6
- Palliative involved-site radiation therapy (ISRT)
- Best supportive care

Best supportive care improves quality of life and relieves discomfort.

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

If you have a partial response, no response, or disease progression, then see treatment for 2 or more relapses.

Guide 5

CAR T-cell therapy 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

*Note: Rituximab might be added to any of the therapies listed. An FDA-approved biosimilar might be used for rituximab.
Relapse – Over 12 months

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

**Stem cell transplant is planned**
If autologous stem cell transplant therapy is planned, then second-line therapy will be given. See Guide 7.

After a complete response, next options include:

- Autologous (self) hematopoietic cell transplant (autoHCT). ISRT might be added.
- Clinical trial
- In some cases, an allogeneic (donor) hematopoietic cell transplant (alloHCT). Involved-site radiation therapy (ISRT) might be added. ISRT treats lymph nodes where cancer was originally found.

After a partial response, next options include:

- Anti-CD19 CAR T-cell therapy
- Autologous (self) stem cell transplant (autoSCT). ISRT might be added.
- Clinical trial
- In some cases, an allogeneic (donor) stem cell transplant (alloSCT). ISRT might be added.

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

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

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.
Guide 6
Second-line therapy options

<table>
<thead>
<tr>
<th>Preferred options</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Gemcitabine and oxaliplatin (GemOx)</td>
</tr>
<tr>
<td>• Polatuzumab vedotin-piiq. Bendamustine and/or rituximab might be added.</td>
</tr>
<tr>
<td>• Tafasitamab-cxix and lenalidomide</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cyclophosphamide, etoposide, vincristine, and prednisone (CEOP). Rituximab might be added.</td>
</tr>
<tr>
<td>• Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin (DA-EPOCH). Rituximab might be added.</td>
</tr>
<tr>
<td>• Gemcitabine, dexamethasone, and cisplatin (GDP) or gemcitabine, dexamethasone, and carboplatin. Rituximab might be added.</td>
</tr>
<tr>
<td>• Rituximab</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Used in some cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Brentuximab vedotin for CD30+ disease</td>
</tr>
<tr>
<td>• Bendamustine with or without rituximab</td>
</tr>
<tr>
<td>• Ibrutinib (non-GCB DLBCL)</td>
</tr>
<tr>
<td>• Lenalidomide with or without rituximab (non-GCB DLBCL)</td>
</tr>
<tr>
<td>• Axicabtagene ciloucleucel or lisocabtagene maraleucel</td>
</tr>
</tbody>
</table>

*Note: An FDA-approved biosimilar might be used for rituximab.

Guide 7
Second-line therapy options if hematopoietic cell transplant (HCT) planned

<table>
<thead>
<tr>
<th>Preferred options</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dexamethasone and cytarabine (DHA) with carboplatin, cisplatin, or oxaliplatin</td>
</tr>
<tr>
<td>• Gemcitabine, dexamethasone, and cisplatin (GDP) or gemcitabine, dexamethasone, and carboplatin</td>
</tr>
<tr>
<td>• Ifosfamide, carboplatin, and etoposide (ICE)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Etoposide, methylprednisolone, cytarabine, and cisplatin (ESHAP)</td>
</tr>
<tr>
<td>• Gemcitabine and oxaliplatin (GemOx)</td>
</tr>
<tr>
<td>• Mesna, ifosfamide, mitoxantrone, and etoposide (MINE)</td>
</tr>
</tbody>
</table>

*Note: Rituximab might be added to any of the therapies listed. An FDA-approved biosimilar might be used for rituximab.
2 or more relapses

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

- Anti-CD19 CAR T-cell therapy (if not given before) such as axicabtagene ciloleucel, lisocabtagene maraleucel, or tisagenlecleucel.
- A systemic therapy not used before
- Clinical trial
- Palliative ISRT
- Best supportive care

For a complete or partial response to treatment, an allogeneic stem cell transplant (alloSCT) 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.

Key points

- DLBCL returns in about half of those in remission.
- Cancer that returns is called relapse.
- When DLBCL progresses despite treatment, it is called refractory.
- 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 stem cell transplant is planned.
- After completing treatment, you will be monitored for the return of cancer. Keep all follow-up doctor visits and imaging test appointments.
Primary cutaneous DLBCL, leg type

60 Overview
60 Treatment
61 Solitary or regional disease
62 Generalized skin-only disease
62 Extracutaneous disease
62 Follow-up testing
63 Key points
Primary cutaneous diffuse large B-cell lymphoma (PC-DLBCL), leg type is a rare aggressive form of lymphoma. In PC-DLBCL, leg type, abnormal B-cell lymphocytes cause skin lesions. Although the skin is involved, the skin cells themselves are not cancerous. Treatment options are based on many factors. Together, you and your care team will choose a treatment plan that is right 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.

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.
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 with local ISRT
- Local ISRT
- Clinical trial

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 dependent 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.
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. 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.

Other chemoimmunotherapy regimens might be used if you have heart issues. These might include:

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

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

- A different chemoimmunotherapy
- Palliative ISRT
- Ibritumomab tiuxetan

Other treatment options are dependent 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.

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, 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.
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, the disease can involve the torso, arms, legs, buttocks, or 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.

Let us know what you think!

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

NCCN.org/patients/response
7 Gray zone lymphomas

- Overview
- Types
- Treatment
- Key points
Gray zone lymphomas have overlapping features of classical Hodgkin lymphoma (CHL) and diffuse large B-cell lymphoma (DLBCL). Treatment is usually the same systemic therapy options used for those with DLBCL. Together, you and your care team will choose a treatment plan that is right for you.

Overview

Gray zone lymphomas have overlapping features of DLBCL and classic Hodgkin lymphoma (CHL). 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.

Gray zone lymphomas are sometimes also called:

- B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and CHL
- Large B-cell lymphoma with Hodgkin features

In general, CD45 is often positive, and CD15, CD20, CD30, and CD79 are also frequently positive. CD10 and ALK are usually negative. B-cell transcription factors such as PAX5, BOB.1, and OCT-2 are often positive; BCL6 is variably expressed and EBV is more often negative.

An expert hematopathologist review is essential to confirm the diagnosis of gray zone lymphoma.

Types

There are 2 main types:

- Mediastinal gray zone lymphomas
- Non-mediastinal gray zone lymphomas

Mediastinal lymphomas are growths found in the area of the chest that separates the lungs. Mediastinal gray zone lymphomas are different than primary mediastinal large B-cell lymphoma (PMBL). There have been rare cases of mediastinal gray zone lymphomas with combined features of PMBL and CHL.

Mediastinal gray zone lymphomas

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

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.
Treatment

Since gray zone lymphomas have features of both classical Hodgkin lymphoma and non-Hodgkin DLBCL, treatment is a challenge. Currently, there is no standard of care or agreement on treatment. Gray zone lymphomas are usually treated with the same chemoimmunotherapy options (RCHOP or DA-EPOCH-R) used for those with DLBCL. If the tumor cells are CD20+, rituximab might be added to chemotherapy. A clinical trial is an option. Radiation therapy (ISRT) should be strongly considered for those with limited stage disease.

- DA-EPOCH-R is dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin, with rituximab.
- RCHOP is rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Those with gray zone lymphomas are best managed in cancer centers with experience in treating this type of lymphoma.

Key points

- Gray zone lymphomas have overlapping features of diffuse large B-cell lymphoma (DLBCL) and classic Hodgkin lymphoma (CHL).
- There are 2 main types of gray zone lymphomas: mediastinal gray zone lymphomas and non-mediastinal gray zone lymphomas.
- Mediastinal lymphomas are growths found in the area of the chest that separates the lungs.
- An expert hematopathologist review is essential to confirm the diagnosis of gray zone lymphoma.
- Those with gray zone lymphomas are best managed in cancer centers with experience in treating this type of lymphoma.
- Gray zone lymphomas are usually treated with the same chemoimmunotherapy options (RCHOP or DA-EPOCH-R) used for those with DLBCL.
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Primary mediastinal large B-cell lymphoma

- Overview
- Treatment
- Follow-up testing
- Relapse or refractory disease
- Key points
Primary mediastinal large B-cell lymphoma (PMBL) is a type of diffuse large B-cell lymphoma (DLBCL) that develops in the area behind the breastbone called the mediastinum. Under the microscope, PMBL looks similar to both DLBCL and Hodgkin lymphoma (HL). Treatment is the same systemic therapy options used for DLBCL. Together, you and your care team will choose a treatment plan that is right for you.

Overview

Primary mediastinal large B-cell lymphoma (PMBL) is a type of diffuse large B-cell lymphoma (DLBCL) marked by the overgrowth of fibrous (scar-like) lymph tissue. A tumor often forms behind the breastbone (sternum) causing 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 tract, ovaries, adrenal glands, and central nervous system.

PMBL is CD19+, CD20+, CD22+, CD21, IRF4/MUM1+, and CD23+ with a variable expression of BCL2 and BCL6. Abnormal chromosomes are common in PMBL.

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

Treatment

Treatment options include:

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

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 R-CHOP, ISRT is preferred. Involved-site radiation therapy (ISRT) treats cancer found in or near lymph nodes.
- After 4 cycles of RCHOP, you may have consolidation with 3 cycles of ifosfamide, carboplatin, and etoposide (ICE). Rituximab might be added.

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
- 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 chest/abdomen/pelvic CT 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 DLBCL progresses despite treatment, it is called refractory.

Treatment options include:

- Pembrolizumab (after 2 or more prior lines of therapy)
- Nivolumab with or without brentuximab vedotin
- Or treat as in Chapter 5: Relapse and refractory disease.
- CAR T-cell therapy with axicabtagene ciloleucel or lisocabtagene maraleucel (after 2 or more lines of prior systemic therapy)
- Tisagenlecleucel is not FDA-approved for relapsed or refractory primary mediastinal large B-cell lymphoma.

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.
Key points

- Primary mediastinal large B-cell lymphoma (PMBL) is a type of diffuse large B-cell lymphoma.
- Mediastinal lymphomas are growths found in the area of the chest that separates the lungs called the mediastinum.
- In PMBL, overgrowth of a scar-like lymph tissue forms a tumor most often behind the breastbone (sternum).
- Treatment is a combination of systemic therapies commonly used in DLBCL.

If you have any religious or personal beliefs about certain kinds of treatment, share them with your care team.
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High-grade B-cell lymphomas

- With translocations of MYC and BCL2 and/or BCL6
- Not otherwise specified
- Key points
High-grade B-cell lymphomas (HGBLs) are very aggressive, fast-growing tumors. This chapter will provide information on HGBL with MYC and BCL2 and/or BCL6 rearrangements (HGBL, R) and HGBL, not otherwise specified (HGBL, NOS). Together, you and your care team will choose a treatment plan that is right for you.

There are currently 2 types of HGBLs:

- HGBL with MYC and BCL2 and/or BCL6 rearrangements (HGBL, R)
- HGBL, not otherwise specified (HGBL, NOS)

With translocations of MYC and BCL2 and/or BCL6

HGBL with translocations of MYC and BCL2 or BCL6 is called double-hit lymphoma (HGBL, DH).

HGBL with translocations of MYC, BCL2, and BCL6 is called triple-hit lymphoma (HGBL, TH).

Treatment options include:

- Clinical trial (recommended)
- ISRT (preferred for localized disease)
- RCHOP
- DA-EPOCH-R

The following are potentially toxic regimens. Your performance status (PS) and other health issues will be taken into consideration before prescribing these:

- R-HyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine)
- R-CODOX-M/R-IVAC (rituximab, cyclophosphamide, vincristine, doxorubicin, and methotrexate alternating with rituximab, ifosfamide, etoposide, and cytarabine)

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

Not otherwise specified

HGBL, not otherwise specified (or HGBL, NOS) lack MYC and BCL2 and/or BCL6 gene rearrangements. This includes tumors that cannot be classified as other well-defined DLBCL subtypes.

Treatment options include:

- Clinical trial (recommended)
- ISRT for early-stage disease
- RCHOP
- DA-EPOCH-R
The following are potentially toxic regimens. Your PS and other health issues will be taken into consideration before prescribing these:

- R-HyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine)
- R-CODOX-M/R-IVAC (rituximab, cyclophosphamide, vincristine, doxorubicin, and methotrexate alternating with rituximab, ifosfamide, etoposide, and cytarabine)

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-growing tumors.
- HGBL with translocations of MYC and BCL2 or BCL6 is called double-hit lymphoma (HGBL, DH).
- HGBL with translocations of MYC, BCL2, and BCL6 is called triple-hit lymphoma (HGBL, TH).
- HGBL, not otherwise specified (HGBL, NOS) lacks an MYC and BCL2 and/or BCL6 rearrangement.
- A clinical trial is recommended for these types of diffuse large B-cell lymphomas. Other systemic therapy options are available.

Need help paying for medicine or treatment?

Ask your care team what options are available.
10 Making treatment decisions

- 75 It’s your choice
- 75 Questions to ask
- 85 Resources
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 like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- 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 doctor. 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 doctors 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 to ask about testing and diagnosis

1. What subtype of DLBCL do I have? What does this mean in terms of my prognosis and treatment options?

2. What tests do I need? What other tests do you recommend?

3. How soon will I know the results and who will explain them to me?

4. Where will the tests take place? How long will the tests take?

5. Is there a cancer center or hospital nearby that specializes in my subtype of DLBCL?

6. How do I prepare for testing?

7. Would you give me a copy of the pathology report and other test results?

8. Who will talk with me about the next steps? When?

9. Will I start treatment before the test results are in?

10. Will I have a biopsy? What type? What will be done to make me comfortable?

11. How often will I have blood tests?

12. How long will it take to get these test results?
Questions to ask your care team about their experience

1. What is your experience treating DLBCL?

2. What is the experience of those on your team?

3. Do you only treat DLBCL? What else do you treat?

4. I would like a second opinion. Is there someone you can recommend? Who can help me gather all of my records for a second opinion?

5. I would like another pathologist or hematopathologist to review my blood samples. Is there someone you recommend?

6. How many patients like me (of the same age, gender, race) have you treated?

7. Will you be consulting with experts to discuss my care? Whom will you consult?

8. How many procedures like the one you’re suggesting have you done?

9. Is this treatment a major part of your practice?

10. How often is a complication expected? What are the complications?

11. Who will manage my day-to-day care?
Questions to ask about options

1. What will happen if I do nothing?

2. How do my age, overall health, and other factors affect my options?

3. What if I am pregnant? What if I’m planning to get pregnant in the near future?

4. Am I a candidate for a hematopoietic cell transplant (HCT)?

5. Am I a candidate for a clinical trial? Can I join a clinical trial at any time?

6. Which option is proven to work best for my cancer, age, and other risk factors?

7. What are the possible complications and side effects?

8. Does any option offer long-term cancer control? Are the chances any better for one option than another? Less time-consuming? Less expensive?

9. What decisions must be made today? How long do I have to decide about treatment?

10. Is there a social worker or someone who can help me decide?

11. Is there a hospital or treatment center you can recommend for treatment? Can I go to one hospital for radiation therapy and a different center for systemic therapy?
Questions to ask about treatment

1. What are my treatment choices? What are the benefits and risks? Which treatment do you recommend and why?

2. Does the order of treatment matter?

3. Will I have to go to the hospital or elsewhere for treatment? How often? How long is each visit? Will I have to stay overnight in the hospital or make travel plans?

4. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment? Should I bring someone with me?

5. Can I stop treatment at any time? What will happen if I stop treatment?

6. How much will this treatment cost me? How much will my insurance pay for this treatment? Are there any programs to help me pay for treatment?

7. Will I miss work or school? Will I be able to drive? When will I be able to return to my normal activities?

8. How do you know if the treatment worked? How will I know?

9. What can be done to prevent or relieve the side effects of this treatment?

10. Are there any life-threatening side effects of this treatment? How will I be monitored?

11. What are the chances my cancer will return after this treatment? How will it be treated if it returns?

12. What are my chances of developing a different cancer later in life?
Questions to ask about radiation therapy

1. What type of radiation therapy (RT) will I have?

2. What will you target?

3. What is the goal of this RT?

4. How many treatment sessions will I require? Can you do a shorter course of RT?

5. Do you offer this type of RT here? If not, can you refer me to someone who does?

6. What side effects can I expect from RT?

7. Should I eat or drink before RT?

8. Will I be given medicine to help me relax during RT?

9. What should I wear?
Questions to ask about surgery

1. What will be removed during surgery? What will this mean in terms of my recovery?

2. What kind of surgery will I have? Will I have more than one surgery?

3. Does my cancer involve any veins or arteries? How might this affect surgery?

4. How long will it take me to recover from surgery? When will I be able to return to work?

5. How much pain will I be in? What will be done to manage my pain?

6. What is the chance that this surgery will shorten my life?

7. What other side effects can I expect from surgery? What complications can occur from this surgery?

8. What treatment will I have before, during, or after surgery? What does this treatment do?
Questions to ask about side effects

1. What are the side effects of treatment?

2. What are the side effects of DLBCL?

3. How long will these side effects last? Do any side effects lessen or worsen in severity over time?

4. What side effects should I watch for? What side effects are expected and which are life threatening?

5. When should I call the doctor? Can I text? What should I do on weekends and during non-office hours?

6. What emergency department or ER should I go to? Will my treatment team be able to communicate with the ER team?

7. What medicines can I take to prevent or relieve side effects?

8. Will you stop treatment or change treatment if there are side effects? What do you look for?

9. What can I do to lessen or prevent side effects? What will you do?

10. What medicines may worsen side effects of treatment?

11. What are some of the likely permanent side effects that I might have from the treatment?
Questions to ask about clinical trials

1. What clinical trials are available for my type of cancer?

2. What are the treatments used in the clinical trial?

3. What does the treatment do?

4. Has the treatment been used before? Has it been used for other types of lymphoma?

5. What are the risks and benefits of this treatment?

6. What side effects should I expect? How will the side effects be controlled?

7. How long will I be in the clinical trial?

8. Will I be able to get other treatments if this doesn’t work?

9. How will you know the treatment is working?

10. Will the clinical trial cost me anything? If so, how much?

11. How do I find out about clinical trials that I can participate in? Are there online sources that I can search?
Questions to ask about hematopoietic cell transplants

1. Which type of transplant is an option for me?
2. What do I need to do to prepare?
3. What will you do to prepare?
4. What are the risks to myself and/or the donor?
5. How will the transplant affect my prognosis?
6. How will a transplant affect the quality and length of my life?
7. What should I expect from a transplant?
8. How long should I expect to be in the hospital?
9. How will I feel before, during, and after the transplant?
10. How many transplants has this center done for my subtype of DLBCL?
11. What is my risk of developing graft-versus-host disease?
## Resources

**American Association for Cancer Research (AACR)**  
aacr.org

**American Cancer Society (ACS)**  

**Be The Match®**  
bethematch.org

**Blood & Marrow Transplant Information Network (BMT InfoNet)**  
bmtinfonet.org

**CancerCare**  
cancercare.org/diagnosis/lymphoma

**Cancer Support Community**  
cancersupportcommunity.org/living-cancer

**Chemocare**  
chemocare.com

**Leukemia & Lymphoma Society**  
lls.org/PatientSupport

**Lymphoma Research Foundation**  
lymphoma.org/aboutlymphoma/nhl/dlbcl

**MedlinePlus**  
medlineplus.gov

**MyHealthTeam**  
mylymphomateam.com

**My Survival Story**  
mysurvivalstory.org

**National Bone Marrow Transplant Link**  
bmbtlink.org

**National Cancer Institute (NCI)**  
cancer.gov/types/lymphoma/patient/adult-nhl-treatment-pdq

**National Coalition for Cancer Survivorship**  
canceradvocacy.org/toolbox

**National Financial Resource Directory - Patient Advocate Foundation**  
patientadvocate.org/explore-our-resources/national-financial-resource-directory

**National Hospice and Palliative Care Organization**  
nhpco.org/patients-and-caregivers

**OncoLink**  
oncolink.org

**Patient Access Network Foundation**  
panfoundation.org

**Radiological Society of North America**  
radiologyinfo.org

**Testing.com**  
testing.com
Words to know

**allogeneic hematopoietic cell transplant (alloHCT)**
A cancer treatment that replaces abnormal blood stem cells with healthy donor cells.

**autologous hematopoietic cell transplant (autoHCT)**
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).

**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 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 blood count (CBC)**
A lab test that includes the number of blood cells.

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

**comprehensive metabolic panel (CMP)**
Tests up to 14 chemicals in your blood.

**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.

**core needle biopsy**
A procedure that removes tissue samples with a hollow needle. Also called core biopsy.

**cytogenetics**
The study of chromosomes using a microscope.

**deoxyribonucleic acid (DNA)**
A chain of chemicals in cells that contains coded instructions for making and controlling cells.

**differential**
A lab test of the number of white blood cells for each type.
**Words to know**

**double-hit lymphomas**
High-grade B-cell lymphomas with translocations of MYC and BCL2 or BCL6.

**fine-needle aspiration (FNA)**
A procedure that removes tissue samples with a very thin needle.

**flow cytometry**
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.

**gray zone lymphomas**
A type of diffuse large B-cell lymphoma (DLBCL) with overlapping features of classical Hodgkin lymphoma (CHL) and DLBCL.

**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 lymphoma**
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 found in or near lymph nodes (nodal disease).

**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.

**lumbar puncture (LP)**
A procedure that removes spinal fluid with a needle. Also called a spinal tap.

**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.

**lymphedema**
Swelling in the body due to a buildup of fluid called lymph.

**magnetic resonance imaging (MRI)**
A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

**monitoring**
A period of testing for changes in cancer status.

**morphology**
The science of the form and structure of organisms.

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

**partial response**
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**
Blood that circulates throughout the body.

**platelet**
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 DLBCL that develops from B cells in the mediastinum (the area behind the breastbone).

**prognosis**
The pattern and outcome of a disease.

**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.

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

**recurrence**
The return of cancer after a cancer-free period.

**refractory cancer**
A cancer that does not improve with treatment.

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

**side effect**
An unhealthy or unpleasant physical or emotional response to treatment.

**stem cell transplant (SCT)**
A cancer treatment that replaces abnormal blood stem cells with healthy cells. Also called hematopoietic cell transplant (HCT) or bone marrow transplant (BMT).
**supportive care**
Treatment for the symptoms or health conditions caused by cancer or cancer treatment. Also, sometimes called palliative care or best supportive care.

**triple-hit lymphomas**
High-grade B-cell lymphomas with translocations of MYC, BCL2, and BCL6.

**tumor lysis syndrome (TLS)**
A condition caused when waste released by dead cells is not quickly cleared out of your body.

**white blood cell**
A type of blood cell that helps fight infections in the body. Also called a leukocyte.
This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas, Version 4.2022. It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

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

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

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

Dana-Farber/Brigham and Women’s Cancer Center | Massachusetts General Hospital Cancer Center
Boston, Massachusetts
617.732.5500 • youhaveus.org
617.726.5130 massgeneral.org/cancer-center

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

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

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

Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance
Seattle, Washington
206.606.7222 • seattlecc.org
206.667.5000 • fredhutch.org

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah
800.824.2073 • huntsmancancer.org

Indiana University Melvin and Bren Simon Comprehensive Cancer Center
Indianapolis, Indiana
888.800.4822 • www.cancer.iu.edu

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

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

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

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

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

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

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

St. Jude Children’s Research Hospital/
The University of Tennessee Health Science Center
Memphis, Tennessee
866.278.5833 • sjude.org
901.448.5500 • uthealth.edu

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

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

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

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

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

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Los Angeles, California
310.825.5268 • cancer.ucla.edu

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720.848.0300 • coloradocancercenter.org

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

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

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

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

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

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