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FOR PATIENTS®

2024

Follicular Lymphoma



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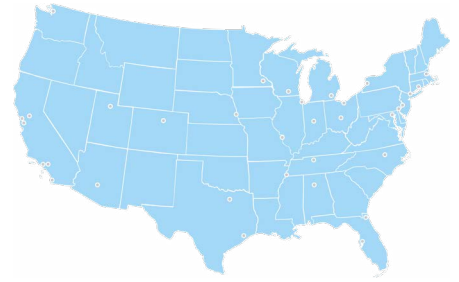


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Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The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

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas Version 2.2024 – April 30, 2024.

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Lymphoma basics

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Follicular lymphoma (FL) is a slow-growing (indolent) non-Hodgkin lymphoma (NHL). NHLs develop from B lymphocytes, a type of white blood cell. In FL, excess amounts of abnormal B lymphocytes form clusters (follicles) in the lymph nodes and sometimes other tissues.

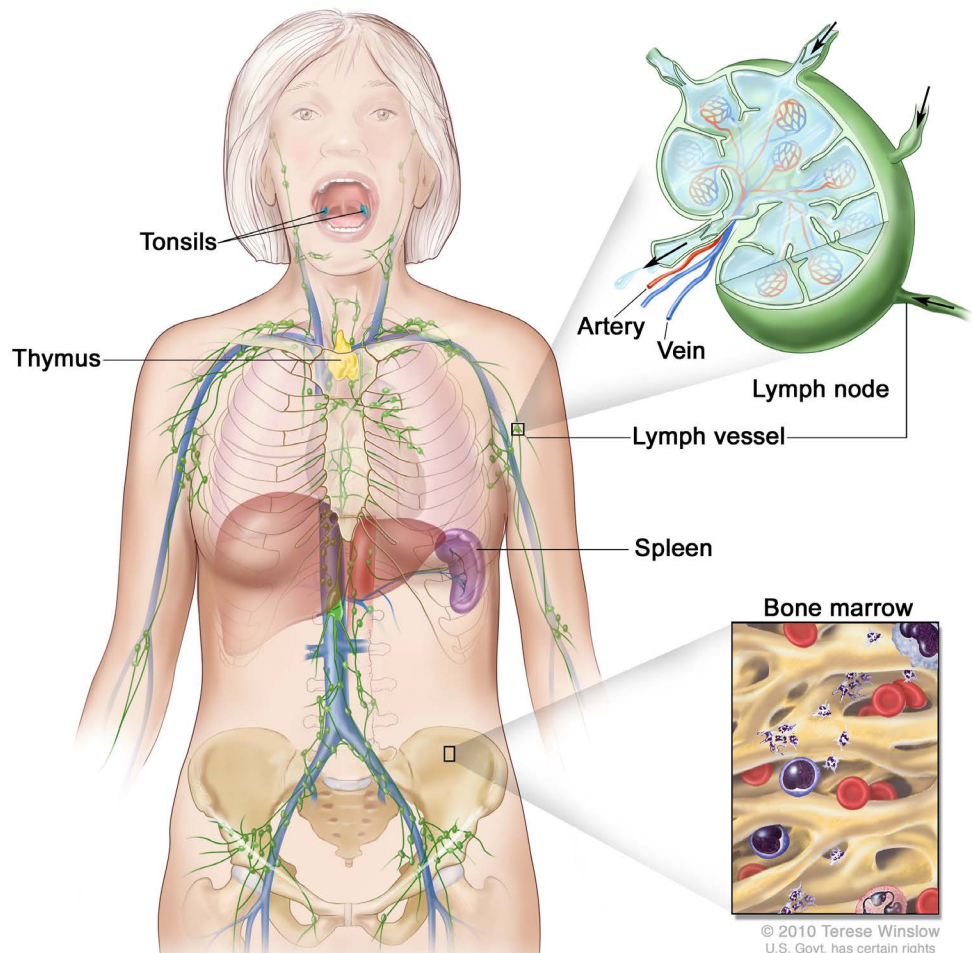
Lymphatic system

Non-Hodgkin lymphoma (NHL) begins in the lymphatic system. The lymphatic or lymph system is a major part of the body's immune system. It is a germ- and cancer-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. White blood cells, such as lymphocytes cells, help fight infection and other diseases.

Lymphatic system

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



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

Lymphocytes

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

There are 3 main types of lymphocytes:

- **B lymphocytes or B cells** make antibodies. An antibody is a protein that specifically targets infections or cancer cells and recruits other parts of the immune system.
- **T lymphocytes or T cells** help fight infections, cancer, and control immune responses.
- **Natural killer (NK) cells** can kill tumor cells or virus-infected cells.

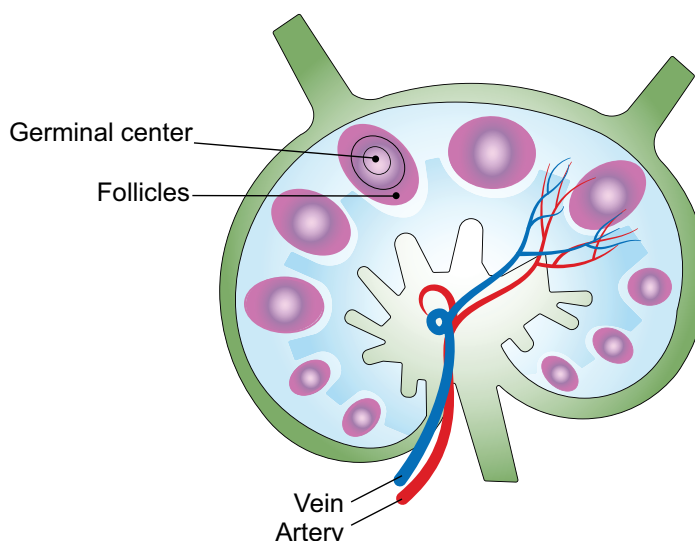
Follicular lymphoma starts in mature B cells.

Follicular lymphoma

Follicular lymphoma (FL) is a common type of non-Hodgkin lymphoma (NHL). It is a slow-dividing, slow-growing B-cell lymphoma that typically forms tumors in lymph nodes. However, FL can form tumors in other parts

Germinal centers

Follicular lymphoma (FL) starts in the temporary germinal centers (GCs) of lymph nodes. These germinal centers are short-lived structures that form in response to infection or inflammation. When B cells within germinal centers grow out of control, it can form FL.



of the body such as the bone marrow. This is called extranodal (outside of the lymph node) disease. Not everyone with FL needs treatment right away.

How does FL develop?

In lymph nodes, temporary germinal centers (GCs) form in response to an immune stressor such as infection or inflammation. This is normal. But, when cells within germinal centers grow without proper regulation, it can develop into FL. In FL, excess amounts of abnormal B lymphocytes group together to form clusters (follicles) in the lymph nodes. It might be helpful to know that these short-lived germinal centers are different than those found in some subtypes of Burkitt lymphoma (BL) and diffuse large B-cell lymphoma (DLBCL).

There are 2 zones in the germinal center: light and dark.

- **B cells in the light zone are called centrocytes.** They are smaller, less in number, and divide less than B cells in the dark zone.
- **B cells within the dark zone are called centroblasts.** They are larger than the cells in the light zone and reproduce (divide) more.

The types of cells found in your FL help determine the grade, which then determines the stage. The stage tells if your cancer should be treated as classic FL, diffuse large B-cell lymphoma, transformed FL, or individualized.

Grading

The types of cells found in your FL help determine the grade. Grades include 1, 2, 3A, and 3B. Grade 3B contains only centroblasts (large cells), while the other grades contain mixtures of centrocytes (small cells) and centroblasts (large cells). The more centroblasts, the higher the grade. The grade helps tell how your lymphoma should be treated.

Two different organizations categorize FL based on grade. In the 2022 World Health Organization classification (WHO5), follicular lymphoma grades 1, 2, and 3A are termed classic FL (cFL). International Consensus classification (ICC) groups grades 1 and 2 as cFL. This book follows the ICC classification system.

- FL grade 1 and 2 are treated as classic FL according to the ICC.
- Grade 3A might be treated as classic FL or DLBCL depending on the cancer center and the types of cells found with testing.
- FL grade 3B (FL3B) called follicular large B cell lymphoma in the WHO5 is rare. It is treated as DLBCL.

Types of FL

The following types of FL are described in this book.

Classic FL

As mentioned on the previous page, classic FL (cFL) is grade 1 or 2. Almost everyone with FL has a t(14;18)(q32;q21) chromosome translocation or has excess levels of the BCL2 protein (BCL2+) in their tumor. A chromosome translocation is the switching of part of one chromosome with another chromosome within the lymphoma cells.

Uncommon FL

When FL has uncommon pathologic (disease) features or is t(14;18)-negative, it might be called uncommon FL (uFL). It is treated as classic FL in this book.

Pediatric-type FL

Pediatric-type FL (PTFL) usually occurs in children but can also occur in adults. Usually, only one lymph node is enlarged in the head and neck region and there might be no symptoms.

Transformed FL

FL can transform into a more aggressive lymphoma called diffuse large B-cell lymphoma (DLBCL). This means your slow-growing FL has turned into a large-cell, fast-growing lymphoma. Transformed FL can occur before, during, or after treatment. In DLBCL, tumors are commonly found in lymph nodes, spleen, liver, bone marrow, or other tissues and organs.

Key points

- The lymphatic or lymph system is a network of tissues and organs that helps your body fight infections and disease. It is part of the immune system.
- Non-Hodgkin lymphoma (NHL) is a cancer that develops from lymphocytes, a type of white blood cell.
- Lymphocytes normally grow in response to infection or inflammation. When they grow on their own without proper regulation, they can develop into lymphoma.
- Follicular lymphoma (FL) is a slow-growing (indolent) lymphoma that typically forms tumors in the lymph nodes. However, FL can be found in other parts of the body.
- In FL, excess amounts of abnormal B lymphocytes form clusters (follicles) in the germinal centers of lymph nodes.
- Not everyone with FL needs treatment right away.

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Testing for FL

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Accurate testing is essential to diagnose and treat follicular lymphoma (FL). This chapter presents an overview of possible tests you might receive and what to expect.

Follicular lymphoma (FL) might be found because of swollen lymph nodes or an enlarged spleen. Swollen lymph nodes can occur anywhere in the body but are most often in the neck, armpit, and groin area and in the chest, abdomen, and pelvis on imaging scans. FL symptoms can include fever, night sweats, fatigue, and weight loss. These symptoms are referred to as B symptoms. Not everyone has the same symptoms.

Test results

Accurate testing is needed to diagnose and treat FL. Results from blood tests, bone marrow aspirate and biopsy, and imaging studies will be used to guide your treatment plan. It is important you understand what these tests mean. Ask questions about your test results. Online patient portals are one way to access your test results, but may also contain communication between members of your health care team and other information that might need explaining. Please wait to discuss all test results with your doctor or health care team so you have a complete and accurate understanding of the results.

Keep these things in mind:

- It's beneficial to have a support system in place during diagnosis and treatment. Enlist the help of friends, family members, or peers who can provide transportation, meals, and emotional support. These can be different people for different tasks or change over time.
- Consider bringing someone with you to doctor visits if possible, or have someone on the phone or join you for telehealth visits.
- Don't hesitate to ask questions and take notes during appointments. Write down questions and ask a friend or family member to take notes. Caregivers should ask questions, too.
- Organize your medical documents, including insurance forms, medical records, and test results. Keep a list of contact information for your care team and update your primary care physician (PCP) regarding any changes. Include details about the specific type of cancer, treatment, and dates in your contact list.
- Set up a MyChart or health record account if it's available, which can help you track your appointments and communicate with your care team. In many places the MyChart or portal messages are not immediately seen by a nurse or physician, so ask your care team how best to communicate with them, especially in an emergency.

For possible tests and procedures, **see Guide 1.**

General health tests

Some general health tests are described next.

Medical history

A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new

medicines and any over-the-counter (OTC) medicines, herbals, or supplements you take. Some supplements interact with and affect medicines that your care team may prescribe. Tell your care team about any symptoms you have. A medical history, sometimes called a health history, will help determine which treatment is best for you.

Guide 1

Tests to plan treatment

Biopsy and pathology review

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

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

Performance status (PS)

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

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

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

Bone marrow biopsy and aspirate

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

Possible:

- Echocardiogram or multigated acquisition (MUGA) scan
- Neck CT with contrast
- PET/CT scan
- Beta-2-microglobulin
- Uric acid
- Quantitative immunoglobulins and other blood tests
- Hepatitis C testing
- Discussion of fertility preservation

Family history

Some cancers and other diseases can run in families. Your care team will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members on both sides of your family about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. It's important to know the specific type of cancer or where the cancer started, if it is in multiple locations, and if they had genetic testing.

Physical exam

During a physical exam, your health care provider may:

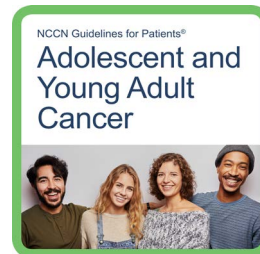
- Check your temperature, blood pressure, pulse, and breathing rate
- Check your height and weight
- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs such as your spleen and liver are of normal size, are soft or hard, or cause pain when touched.
- Feel for enlarged lymph nodes in your neck, underarm, and groin.

Fertility (all genders)

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

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

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



Changes in fertility

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

Preventing pregnancy during treatment

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

Those with ovaries

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

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

Those with testicles

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

Performance status

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

The ECOG PS scores are as follows:

- **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 the bed or chair and completely disabled.

Good PS is usually PS 0 or PS 1.

Blood tests

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

Complete blood count and differential

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

Comprehensive metabolic panel

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

Creatinine

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

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

Electrolytes

Electrolytes help move nutrients into cells and help move waste out of cells. Electrolytes are ions or particles with electrical charges that help the nerves, muscles, heart, and brain work as they should. Your body needs electrolytes such as phosphate (PO₄), potassium (K), and calcium (Ca) to function properly.

Hepatitis B and hepatitis C

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

HLA typing

Human leukocyte antigen (HLA) is a protein found on the surface of most cells. It plays an important role in your body's immune response. HLAs are unique to each person. They mark your body's cells. Your body detects these markers to tell which cells are yours. In other words, all your cells have the same set of HLAs. Each person's set of HLAs is called the HLA type or tissue type.

HLA typing is a blood test that detects a person's HLA type. This test is done before a donor (allogeneic) hematopoietic cell transplant. To find a donor match, your proteins will be compared to the donor's white

blood cells 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 samples from you and your blood relatives will be tested first.

Quantitative immunoglobulins

The quantitative immunoglobulin blood test measures abnormal levels of immunoglobulins, also known as antibodies, in your blood. Antibodies are proteins made by the immune system. An immunoglobulin (Ig) test usually measures 3 specific types (classes) of immunoglobulins called IgG, IgM, and IgA. These immunoglobulins may be abnormally high due to your lymphoma or abnormally low due to prior and current lymphoma treatment.

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

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.

Liver function tests

Liver function tests (LFTs) look at the health of your liver by measuring chemicals that are made or processed by the liver. Levels that are too high or low signal that the liver is not working well.

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

Pregnancy test

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

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. High uric acid might be a side effect of chemotherapy or radiation therapy. Very high levels of uric acid in the blood can damage the kidneys.

Biopsy

A biopsy is the removal of a sample of tissue or fluid for testing. It is an important part of an accurate diagnosis of lymphoma. Your sample should be reviewed by a pathologist who is an expert in the diagnosis of FL. 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. Request a copy of the pathology report. Ask questions about your biopsy results and what it means for your treatment.

A biopsy is usually done with other lab methods to accurately diagnose FL. These other lab methods include:

- Immunohistochemistry (IHC)
- Flow cytometry (FCM)

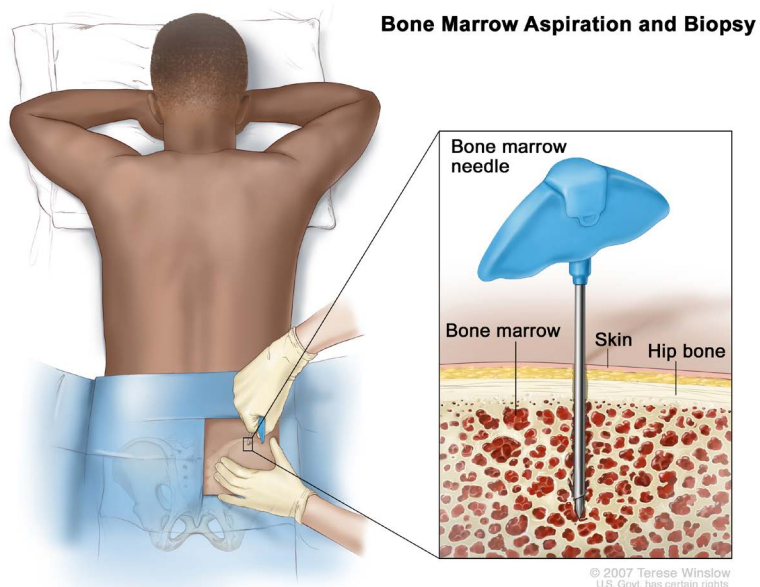
- FL genetic testing to detect chromosome translocations or mutations, which may include karyotype, fluorescence in situ hybridization (FISH), or sequencing studies.

Lymph node biopsy

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

Bone marrow aspirate and biopsy

Samples of bone and marrow are removed in a biopsy



A lymph node biopsy can be done in the following ways:

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

A core or excisional biopsy are preferred.

Bone marrow tests

Bone marrow tests might be done depending on your situation. 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.

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

Immunophenotyping

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

Immunophenotyping can be done using specialized techniques called flow cytometry or immunohistochemistry. These techniques are used to distinguish FL from other types of lymphoma such as diffuse large B-cell lymphoma (DLBCL). Immunophenotype can change as cancer progresses. FL immunophenotype is usually CD10+, BCL2+, CD23+/-, CD43-, CD5-, CD20+, and BCL6+. Rare cases of FL may be CD10- or BCL2-. For more information on tests to diagnose FL, **see Guide 2.**

Flow cytometry

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

The following cell surface markers might be tested using flow cytometry: kappa/lambda, CD19, CD20, CD5, CD23, and CD10.

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.

Testing for FL biomarker and genetic changes

Biomarker and genetic tests are used to learn more about your type of FL, to guide treatment, and to determine the likely path your cancer will take (prognosis). This genetic testing is different from family history genetic testing or genetic cancer risk testing. This

testing looks for changes only in the FL cells that have developed over time, and not changes in the rest of your body’s cells.

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. Proteins are written like this: BCL6. Genes are written with italics like this: *BCL6*. When a gene or protein is found (expressed), it is shown with a plus sign (+) like this: CD10+. When a gene or protein has not been found, it is written with a negative sign (-) like this CD10-.

Guide 2 Tests to diagnose FL	
Needed	<ul style="list-style-type: none">• Biopsy and hematopathology review• IHC panel: CD20, CD3, CD5, CD10, BCL2, BCL6, CD21, or CD23 with or without cell surface marker analysis by flow cytometry: kappa/lambda, CD19, CD20, CD5, CD23, and CD10
In some cases	<ul style="list-style-type: none">• Biomarker testing to detect: immunoglobulin (Ig) gene rearrangements <i>BCL2</i> and <i>BCL6</i> rearrangements, 1p36, and <i>IRF4/MUM1</i> rearrangements• IHC panel: Ki-67; IRF4/MUM1, and cyclin D1• Next-generation sequencing (NGS) panel including <i>EZH2</i>, <i>TNFRSF14</i>, and <i>STAT6</i> mutation

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

Examples of proteins on the cells:

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

Examples of genes in the DNA of cells:

- *BCL6*, *IRF4/MUM1*, *EZH2*, and others

Beta-2-microglobulin tumor marker test

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

FL mutation testing

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

FL cells can have changes in genes and chromosomes. Mutation testing using methods such as karyotype, fluorescence in situ hybridization (FISH), polymerase chain reaction (PCR), and next-generation sequencing (NGS) are used to look for these changes or abnormalities. Some mutations may determine the type of treatment given. Subtle new drug-resistant mutations may occur

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

FISH

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

Karyotype

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

Translocations

Translocation is a switching of parts between two chromosomes. A translocation between chromosome 14 and 18 is written as t(14;18). Specific translocations can help distinguish between types of blood cancers and disorders.

Gene rearrangements

Normal B cells and T cells break their DNA in certain ways to create diversity within your immune system. In a tumor, all cancer cells derive from the same original cell. In FL that cell is a B cell. When that one B cell divides many times, the entire group of B cells is called clonal or the tumor is described as having clonality. In clonal cells, the same gene rearrangement are found in a group of cancer cells. Pathologists have tests they can use to determine if a group of cells are clonal or not.

PCR

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

Next-generation sequencing

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

FL genetic changes

FL cells can have changes in genes and chromosomes. Mutation testing looks for these changes or abnormalities that are unique to FL cells. Examples of such changes are called deletion, insertion, amplification, translocation (rearrangement), and point mutation. Most follicular lymphomas will test positive for t(14;18) or BCL2.

- ✓ **Amplification** – When part or a whole chromosome or gene is increased (for example, duplicated)
- ✓ **Deletion** – When part of a chromosome or gene is missing
- ✓ **Insertion** – When a new part of a chromosome or gene is included
- ✓ **Inversion** – Switching of parts within one chromosome
- ✓ **Point mutation** – When part of a gene is changed
- ✓ **Chromosome translocation and gene rearrangement** – Switching of parts between 2 chromosomes. When described at the chromosome level, it is called a translocation. When described at the gene level, it is called rearrangement. For example, the chromosome translocation is written as t(14;18)(q32;q21) and its gene rearrangement is written as *IGH::BCL2*.

Imaging tests

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

Contrast material

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

Tell your care team if you have had allergic reactions to contrast in the past. This is important. You might be given medicines to avoid the effects of those allergies. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

CT scan

A CT or CAT (computed tomography) 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 pelvis may be one of the tests to look for cancer. In most cases, contrast will be used.

MRI scan

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

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

MRI is most commonly used to evaluate the brain and the spinal cord.

PET scan

A PET (positron emission tomography) 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 how much sugar is being taken up by the cancer cells. This gives an idea about how fast the cancer cells are growing. Cancer cells show up as bright spots on PET scans. However, not all tumors will appear on a PET scan. Also, not all bright spots are cancer. It is normal for the brain, heart, kidneys, and bladder to be bright on PET. Inflammation or infection can also show up as a bright spot. When a PET scan is combined with CT, it is called a PET/CT scan.

Heart tests

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

- An electrocardiogram (ECG or EKG) shows electrical activity in your heart.
- An echocardiogram (or echo) uses sound waves to make pictures of your heart.
- A multigated acquisition (MUGA) scan is another way to evaluate the pumping function of your heart. It uses a small amount of radiotracer injected into a vein and a special camera creates computer-generated movie images of your beating heart.



Create a medical binder

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

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

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

Key points

- Blood and imaging tests check for signs of disease, how well organs are working, and assess treatment results.
- A biopsy is the removal of a sample tissue or fluid for testing. It is an important part of an accurate FL diagnosis.
- Immunophenotyping is used to distinguish FL from other types of lymphoma.
- A sample from your biopsy may undergo lab tests to learn more about your FL and 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.
- Certain treatments can affect heart function. Heart tests might be used to see how well your heart works.
- Online patient portals are one way to access your test results. Be sure to discuss these results with your care team before drawing any conclusions about what the results might mean.



We want your feedback!

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

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

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

3

Treating FL

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

Care team

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

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

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

- **A hematologist or hematologic oncologist** is a medical expert in blood diseases and blood cancers. Other types of oncologists include medical, radiation, and surgical oncologists.
- **A radiation oncologist** treats cancer using radiation therapy.
- **A pathologist or hematopathologist** analyzes the cells and tissues removed during a biopsy and provides cancer diagnosis, staging, and information about biomarker testing.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **An advanced practice nurse (APN) or a physician assistant (PA)** help provide an extra layer of support with your cancer-related symptoms.
- **Oncology pharmacists** are experts in knowing how to use medicines to treat cancer and to manage symptoms and side effects.
- **Palliative care specialists** concentrate on preventing and alleviating suffering and improving quality of life.
- **Nutritionists and dietitians** can provide guidance on what foods are most suitable for your condition.
- **An occupational therapist** helps people with the tasks of daily living.
- **A physical therapist** helps people move with greater comfort and ease.

- **Psychologists and psychiatrists** are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you think and feel.
- **Social workers** help people solve and cope with problems in their everyday lives. Clinical social workers also diagnose and treat mental, behavioral, and emotional issues. The anxiety a person feels when diagnosed with cancer might be managed by a social worker in some cancer centers. They, or other designated professionals, can help navigate the complexities of financial and insurance stresses.
- **Spiritual care specialists** identify and support those with spiritual distress or unmet spiritual needs.
- **A research team** helps to collect research data and coordinate care if you are in a clinical trial. Clinical trials help bring new therapies to patients and advance the treatment for everyone. Consider asking your care team about access to clinical trials.

Treatment overview

Follicular lymphoma (FL) is highly treatable and may be curable in certain circumstances. Often, treatment for FL can wait until you have symptoms. However, most people with FL do not have symptoms when starting treatment. This is because you might not have symptoms even though the cancer in your lymph nodes has grown or progressed (called progressive lymphadenopathy).

Treatment for FL usually consists of systemic therapy and sometimes radiation therapy. Systemic therapy is drug therapy that works throughout the body. Some types include chemotherapy, targeted therapy, and immunotherapy. The choice of therapy takes into consideration many factors, including age, other serious health issues, and future treatment possibilities like a hematopoietic cell transplant (HCT) or cellular therapy. 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. It is important to have regular talks with your care team about your goals for treatment and your treatment plan.

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. A follicular lymphoma IPI (FLIPI-1) is based on age, Ann Arbor cancer stage, hemoglobin (Hgb) and lactate dehydrogenase (LDH) results, and the number of lymph node sites with cancer.

GELF criteria

The Groupe d'Etude des Lymphomes Folliculaires (GELF) Criteria measures tumor burden or the amount of cancer in the body. It helps your care team decide if treatment should start right way.

According to GELF criteria, there is high tumor burden with any of the following:

- Cancer 3 centimeters (cm) or larger in 3 or more lymph node areas
- A tumor mass 7 cm or larger (bulky disease) found anywhere in the body
- B symptoms (such as fever, night sweats, fatigue, and weight loss)
- Enlarged spleen (splenomegaly)
- Fluid build-up around the lungs (pleural effusion) or in the abdomen (peritoneal ascites)

- Low white blood cell (leukopenia) and/or platelet (thrombocytopenia) counts
- Leukemia

Remission

The goal of treatment is remission. There are different types of treatment response. When there are no signs of cancer on imaging and a bone marrow biopsy, it is called a complete response (CR) or complete remission. Remission can be short-term (temporary) or long-lasting (permanent). In partial response (PR), cancer is still present, but it has reduced in size. Follicular lymphoma can go through long periods of remission followed by relapse. FL can also regress or get smaller on its own without treatment. This is not completely understood but it is common for the size of your FL to fluctuate in size.

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



Relapse

FL might relapse more than once. When FL returns after a period of remission, it is called a relapse. The goal of treatment is to achieve remission again. But, depending on the pace of tumor growth and the location and size of the tumor, you may or may not need immediate treatment. A relapse may or may not be serious. It is important to ask about your prognosis.

Refractory

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

Surveillance and monitoring

You will be monitored throughout treatment. Surveillance watches for any changes in your condition. You will have tests during surveillance to check for relapse. You might hear it called active surveillance or observation.

Observation without treatment

Some slow-growing (indolent) lymphomas do not require immediate treatment, including FL. Observation is sometimes called active surveillance or watch and wait. During observation, your care team will monitor for changes in your health or signs that your lymphoma has grown or progressed.

Chemotherapy

Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and some normal cells. More than one chemotherapy may be used to treat FL. 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 the cancer is responding to treatment. You might spend time in the hospital during treatment.

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.

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. A monoclonal antibody is made from a unique white blood cell, such as B or T cell. 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.

CD20-targeting monoclonal antibody therapy

CD20-targeting mAbs (also called anti-CD20 mAbs) such as rituximab (Rituxan) and obinutuzumab (Gazyva) work against the protein CD20 found on the surface of B cells. The drug binds to the CD20 protein causing cell death.

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

Bispecific antibody therapy

Bispecific antibodies (BsABs) bind to 2 different proteins (CD20 and CD3 antigen) at the same time. It treats cancer by engaging and activating T cells, and redirecting them to the site of the lymphoma. Bispecific examples include epcoritamab-bysp (Epkinly), mosunetuzumab-axgb (Lunsumio), and glofitamab-gxbm (Columvi).

CD19-targeting monoclonal antibody therapy

Tafasitamab-cxix (Monjuvi) is used to treat transformed FL or high-grade B-cell lymphomas by targeting the CD19 protein.

Chemoimmunotherapy

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

CD19-targeting CAR T-cell therapy

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

CAR T-cell therapy is one way to target CD19. CD19-directed CAR T-cell therapy options for FL include axicabtagene ciloleucel (Yescarta), lisocabtagene maraleucel (Breyanzi), and tisagenlecleucel (Kymriah).

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



Targeted therapy

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

Other systemic therapies

Antibody drug conjugate

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

Enzyme inhibitor

A methyltransferase inhibitor blocks enzymes involved in gene expression and cell division. Tazemetostat (Tazverik) is a methyltransferase inhibitor that might be used for relapsed or refractory disease.

Immune modulator

An immunomodulator changes your immune system so it can work more effectively especially when combined with monoclonal antibodies. Lenalidomide (Revlimid) is an example of an immune modulator that is used commonly with rituximab, obinutuzumab or tafasitamab.

Radiation therapy

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

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

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

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

External beam radiation

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

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

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

Total body irradiation

Total body irradiation (TBI) is radiation of the whole body given before hematopoietic cell transplant (HCT).

Hematopoietic cell transplant

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

There are 2 types of HCTs:

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

HCTs are only given in very specific cases for follicular lymphoma. Ask your care team why.

Autologous transplant

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

Allogeneic transplant

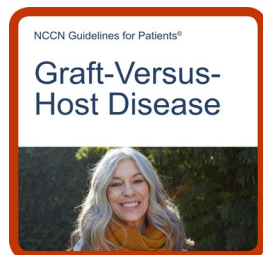
An allogeneic hematopoietic cell transplant (allogeneic HCT) uses healthy stem cells from a donor. The donor may or may not be related to you. Before an HCT, treatment is needed to destroy bone marrow cells. This is called conditioning and it creates room for the healthy donor stem cells. It also weakens the immune system so your body won't kill the transplanted cells. Chemotherapy is used for conditioning. Radiation therapy may also be given as part of conditioning treatment.

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

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 care team about the possible side effects or complications of HCT and how this might affect your quality of life.

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



Warnings about supplements and drug interactions

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

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

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

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

Bring a list with you to every visit.

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of treating cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

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

Phases

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

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



Finding a clinical trial

In the United States

NCCN Cancer Centers

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

The National Cancer Institute (NCI)

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

Worldwide

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

clinicaltrials.gov/

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)

1.800.4.CANCER (1.800.422.6237)

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

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, lab tests, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss with family, friends, or others whom you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

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

Frequently asked questions

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

Will I get a placebo?

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

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

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

General supportive care

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

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

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, the person and what other illnesses they may have, and medicines they may be taking. Some side effects may be harmful to your health. Others may just be unpleasant. Treatment can cause several side effects. Some are very serious.

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

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

Late effects

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

Survivorship

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

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

Side effects

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

Blood clots

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

Cytokine release syndrome

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

Diarrhea

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

Distress

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

people, and medicines that can help you. Support and counseling services are available.

Fatigue

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

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.

Hand-foot syndrome

Hand-foot syndrome is a common side effect of chemotherapy. Small amounts of chemotherapy leak out of very small blood vessels called capillaries in the palms of the hands and soles of the feet. It causes redness, swelling, and pain. Sometimes blisters appear. You will want to protect your hands and feet by applying moisturizer or lotion.

Hypersensitivity, allergy, and anaphylaxis

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

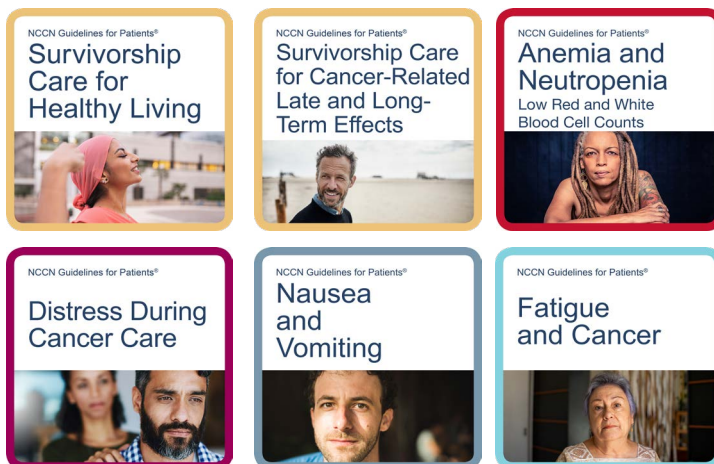
Infections

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

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

Supportive care resources

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



Loss of appetite

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

Low blood cell counts

Some cancer treatments can cause low blood cell counts.

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

Lymphedema

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

Nausea and vomiting

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

Neurocognitive or neuropsychological effects

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

Neuropathy

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

Neurotoxicity

Some treatments can damage the nervous system (neurotoxicity) causing problems with concentration and memory. Seizures and confusion can occur. If treatment includes methotrexate (MTX), then you will be monitored for methotrexate neurotoxicity. Neurotoxicity, such as seizures and confusion, can be seen with immunotherapy, as well.

Organ issues

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

Pain

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

Quality of life

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

Therapy-related toxicity

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

Tumor lysis syndrome

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

Weight gain

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

Seek out support groups at your local hospital, through social media, or from those listed in the back of this book. Look to friends, relatives, neighbors, and coworkers for social support.



Key points

- Follicular lymphoma (FL) is highly treatable and may be curable in certain circumstances. Often, treatment for FL can wait until you have symptoms. However, most people with FL do not have symptoms when starting treatment.
- Treatment for FL usually consists of systemic therapy. Radiation therapy might be given. 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.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.
- Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. Supportive care is always given.
- 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.



You know your body better than anyone

Help your care team understand:

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

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

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

4

Classic FL

- 43 Cancer staging
- 44 Stages 1 and 2 (limited)
- 46 Stages 3 and 4 (advanced)
- 48 Follow-up care
- 49 Relapse or disease progression
- 49 Key points

Treatment for classic follicular lymphoma (cFL) is based on cancer stage. Often, treatment can wait until you have symptoms. Together, you and your care team will choose a treatment plan that is best for you.

Cancer staging

Cancer staging is used to reflect prognosis and help guide treatment decisions. Prognosis is the likely course your cancer will take. In follicular lymphoma (FL), your age, the number and location of lymph nodes affected by cancer, blood test results, and other factors play a role in prognosis. In addition, treatment decisions will be based on histology and results of FL biomarker and genetic tests. Histology is the overall appearance and the size, shape, and type of your cells.

There are different kinds of staging systems. The Lugano Modification of Ann Arbor Staging System is used for FL. Your care team may explain your cancer stage in different ways than described next. In general, stages for FL are as follows:

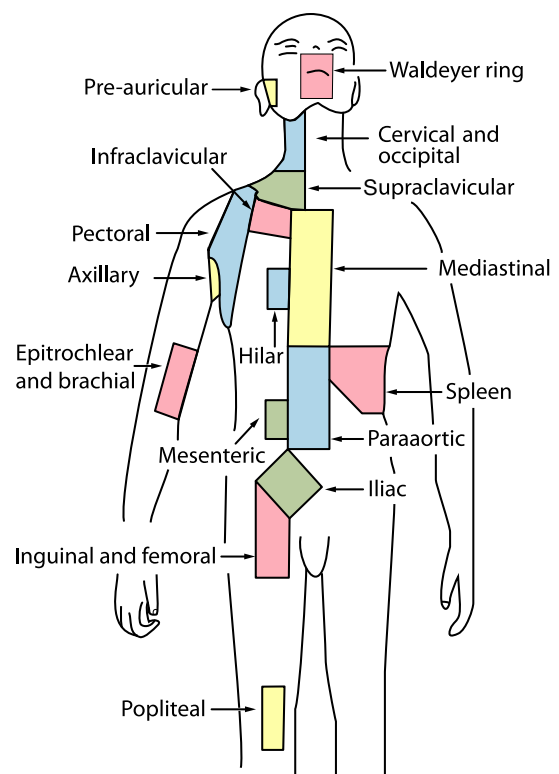
- **Stage 1 (limited)** – Disease found in 1 lymph node or a group of nearby lymph nodes.
- **Stage 2 (limited)** – Disease found in 2 or more lymph node groups on the same side of the diaphragm.

- **Stage 2 bulky** – Bulky disease means there are areas of lymphoma that measure 7.5 centimeters (cm) or larger. Bulky disease can be limited or advanced.
- **Stage 3 (advanced)** – Disease found in lymph nodes above and below the diaphragm on the same side of the body or disease found in nodes above the diaphragm and in the spleen.
- **Stage 4 (advanced)** – Disease has spread outside of the lymphatic system to other parts of the body.

Lymph node regions

Lymph node regions based on the Ann Arbor Staging System

Adapted from: Lymph_node_regions.jpg: https://commons.wikimedia.org/wiki/File:Lymph_node_regions.svg



Stages 1 and 2 (limited)

Stage 1 or contiguous stage 2

In stage 1, cancer is found in one lymph node. In contiguous stage 2, cancer is found in lymph node groups next to one another.

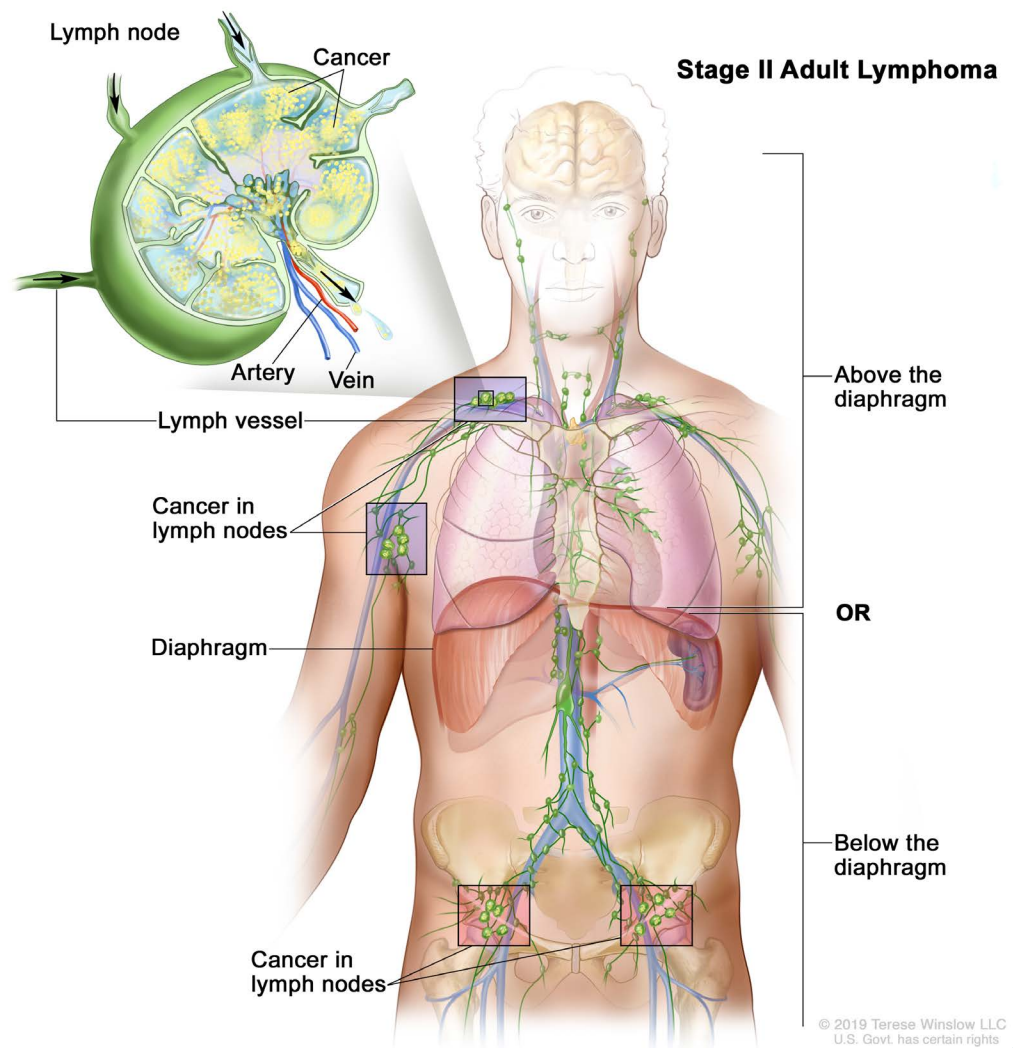
For stage 1 or contiguous stage 2 disease, treatment options include:

- Involved-site radiation therapy (ISRT) (preferred)

- ISRT with CD20-targeting monoclonal antibody (mAb) therapy. Other systemic therapy might be added as found in **Guide 3**.
- CD20-targeting monoclonal antibody therapy (rituximab or obinutuzumab) with or without systemic therapy. Obinutuzumab is not used by itself as a single agent. For systemic therapy options, **see Guide 3**.

Stage 2 FL

In stage 2 FL, cancer is found in 2 or more lymph node groups on the same side of the diaphragm.



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Non-contiguous stage 2

In non-contiguous stage 2, disease is found in two or more lymph node groups on the same side of the diaphragm. Treatment options include CD20-targeting monoclonal antibody (mAb) therapy. Other systemic therapy and/or radiation therapy (ISRT) might be added. Observation might be an option in some cases. For systemic therapy options, **see Guide 3**.

Treatment response

For a complete response (CR) or partial response (PR), observation and follow-up care is recommended.

For no response or disease progression, see treatment for stages 3 and 4 (advanced) in the next section.

Information on treatment for FL that has transformed into diffuse large B-cell lymphoma can be found in Chapter 6: Transformed FL.

Guide 3

First-line systemic therapy options

Preferred options

- Bendamustine with obinutuzumab or rituximab (not recommended if you had bendamustine before)
- Cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) with obinutuzumab or rituximab
- Cyclophosphamide, vincristine, and prednisone (CVP) with obinutuzumab or rituximab
- Lenalidomide with rituximab
- Rituximab

Other recommended

- Lenalidomide with obinutuzumab

For those who are older or unwell:

- Chlorambucil with or without rituximab
- Cyclophosphamide with or without rituximab

Note: An FDA-approved biosimilar might be used in place of rituximab. Extended (maintenance) therapy might be rituximab or obinutuzumab. A hematopoietic cell transplant (HCT) might be an option in very select cases.

Stages 3 and 4 (advanced)

In stage 3, disease is found in lymph nodes on both sides of the diaphragm or in lymph nodes above the diaphragm and in the spleen.

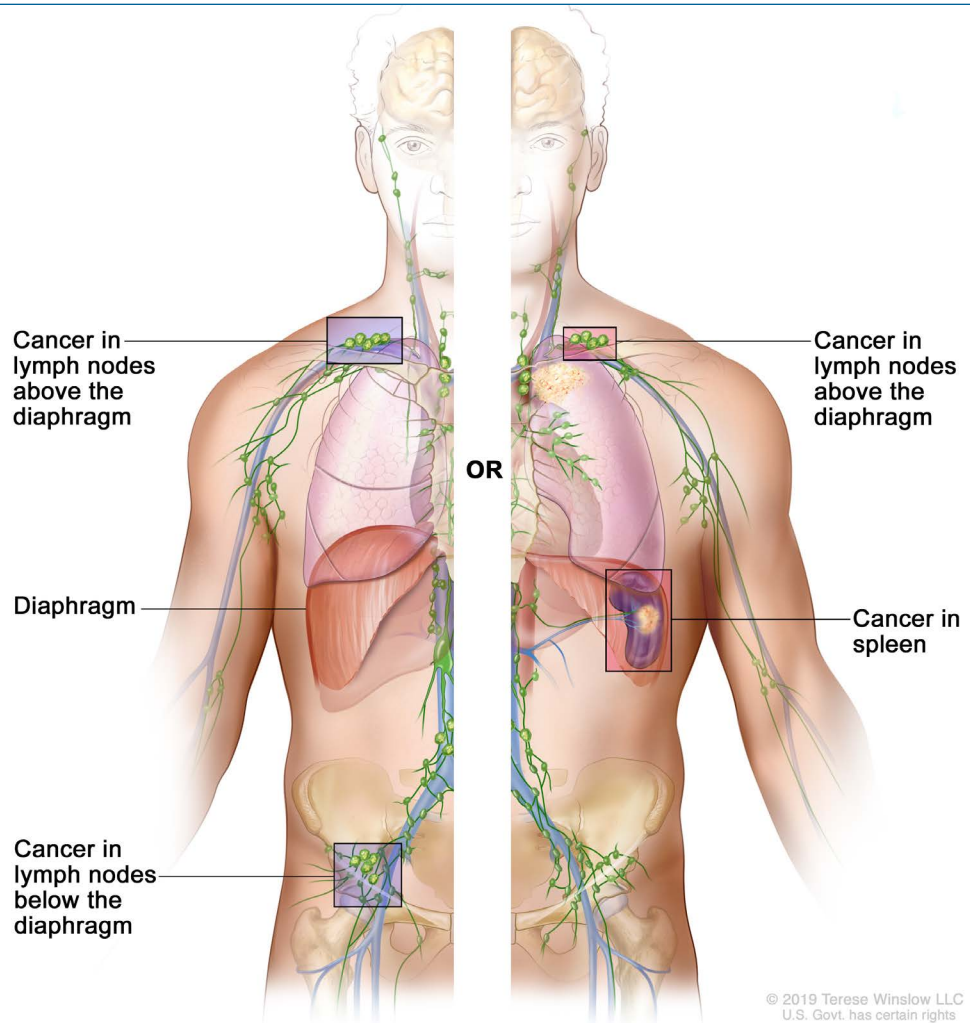
In stage 4, disease is found in various areas outside of the lymph nodes. This is called extranodal disease.

Observation

Your care team might wait until certain signs or symptoms appear before starting treatment. This is called observation. You might hear it called active surveillance or watch and wait. During this time, you will have a physical exam and lab tests every 3 to 6 months for 5 years and then every year afterward. You will also have CT imaging scans with contrast no more than every 6 months. After 2 years, you will have a CT no more than once a year. Surveillance imaging is used for monitoring those without symptoms. It looks for changes in your lymphoma.

Stage 3 FL

In stage 3 FL, 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.



When to begin treatment

Most people with FL do not have symptoms when starting treatment. Treatment will likely start for any of the following:

- Candidate for a clinical trial
- B symptoms (such as fever, night sweats, fatigue, and weight loss)
- Threatened end-organ function (refers to damage occurring in major organs fed by the circulatory system such as the heart, kidneys, brain, and eyes)
- Low red blood cell count (cytopenia) not related to FL.
- If there is bulky disease or high tumor burden as defined by GELF criteria.

- Steady or rapid disease progression
- You want to start treatment
- Cancer in lymph nodes is growing called progressive lymphadenopathy

Treatment may include systemic therapy, a clinical trial, or involved-site radiation therapy (ISRT). ISRT treats cancer found in a small region or one area of your body.

First-line therapy

First-line systemic therapy is the first set of drug treatment given. For a list of first-line therapy options, **see Guide 3**.

Guide 4

Second-line systemic therapy options

Preferred options	<ul style="list-style-type: none"> • Bendamustine with obinutuzumab or rituximab (not recommended if you had bendamustine before) • CHOP with obinutuzumab or rituximab • CVP with obinutuzumab or rituximab • Lenalidomide with rituximab
Other recommended	<ul style="list-style-type: none"> • Lenalidomide (if not candidate for CD2-targeting mAb therapy) • Lenalidomide with obinutuzumab • Obinutuzumab • Rituximab <p>For those who are older or unwell:</p> <ul style="list-style-type: none"> • Rituximab • Tazemetostat • Cyclophosphamide with or without rituximab

Note: An FDA-approved biosimilar might be used in place of rituximab. Extended (maintenance) therapy might be rituximab or obinutuzumab. A hematopoietic cell transplant (HCT) might be an option in very select cases.

Second-line therapy

Second-line therapy is the next set of drug treatment given. **See Guide 4.**

Third-line therapy

If cancer returns or does not respond to treatment, a different second-line systemic therapy will be given. After multiple lines of systemic therapy, bispecific antibody therapy or CAR T-cell therapy might be given.

Bispecific monoclonal antibody therapy options include:

- Epcoritamab-bysp (Epkinly)
- Mosunetuzumab-axgb (Lunsumio)

CAR T-cell therapy options include the following:

- Axicabtagene ciloleucel (Yescarta)
- Lisocabtagene maraleucel (Breyanzi)
- Tisagenlecleucel (Kymriah)

Other options include:

- Tazemetostat
- Zanubrutinib with obinutuzumab
- A hematopoietic cell transplant (HCT) in very select cases

Treatment response

Imaging tests such as PET/CT (preferred) or CT scan with contrast will be done to look at how the cancer responded to treatment and where any cancer might remain.

- **For a complete response (CR)**, you will likely enter observation with follow-up care. You might have extended (maintenance) therapy.
- **For a partial response (PR)**, you might continue with your current therapy or switch to a different one.
- **For no response or disease progression**, you may have another biopsy and another round of systemic therapy with different agents (drugs) or a clinical trial could be considered. If you have had 3 or more lines systemic therapy, then bispecific antibody therapy or CAR T-cell therapy might be given.
- Information on treatment for FL that has transformed into diffuse large B-cell lymphoma can be found in *Chapter 6: Transformed FL*.

Follow-up care

After treatment, you will be monitored for signs and symptoms that cancer has returned. During this time, you will have a physical exam and lab tests every 3 to 6 months for 5 years and then every year afterward or as needed. You will also have CT scans with contrast no more than every 6 months. After 2 years, you will have a CT no more than once a year. Surveillance imaging is used for monitoring those without symptoms. It looks for changes in your lymphoma.

Relapse or disease progression

Most people with FL do not have symptoms when starting treatment. Treatment will likely start for any of the following:

- Candidate for a clinical trial
- B symptoms (such as fever, night sweats, fatigue, and weight loss)
- Threatened end-organ function (refers to damage occurring in major organs fed by the circulatory system such as the heart, kidneys, brain, and eyes)
- Low red blood cell count (cytopenia) not related to FL.
- If there is bulky disease or high tumor burden as defined by Groupe d'Etude des Lymphomes Folliculaires (GELF) criteria.
- Steady or rapid disease progression
- You want to start treatment
- Cancer in lymph nodes is growing, called progressive lymphadenopathy

A PET/CT scan might be done before starting treatment. Treatment options include systemic therapy, clinical trial, or involved-site radiation therapy (ISRT). ISRT treats cancer found in a small region or one area of your body. The goal of treatment is to achieve another remission.

Key points

- Follicular lymphoma (FL) forms in and is mostly limited to the lymph nodes. However, FL can be found outside of the lymph nodes in areas such as the bone marrow or blood.
- Treatment options include radiation therapy, systemic (drug) therapy, or a clinical trial. The goal of treatment is remission.
- Since FL is often a slow-growing disease, your care team might wait until symptoms appear before starting treatment. This is called observation, active surveillance, or watch and wait. However, most people with FL do not have symptoms when starting treatment.
- FL often goes through periods of remission and relapse. When FL relapses or progresses, a different systemic therapy will be given.

5

Adult pediatric-type FL

51 Testing and staging

51 Treatment

51 Key points

Pediatric-type follicular lymphoma (PTFL) usually occurs in children but can also occur in adults. PTFL is stage 1 or 2. If it is stage 3 or 4, then it is not PTFL. Together, you and your care team will choose a treatment plan that is best for you.

Testing and staging

Pediatric-type FL (PTFL) usually occurs in children but can also occur in adults. PTFL is stage 1 or 2 and is often found in lymph nodes in the head and neck region or sometimes the groin area. If your tumor is stage 3 or 4, then it is not PTFL. Tumor testing will look for certain PTFL biomarkers and genetic changes. A PET/CT scan and bone marrow biopsy might be done before starting treatment.

The Lugano Modification of Ann Arbor Staging System is used for FL. In general, stages 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 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

PTFL has an excellent prognosis and sometimes requires no treatment other than a biopsy. Excision is the preferred treatment for PTFL. Excision is surgery to remove tumor. Other options include radiation therapy to the tumor area or RCHOP chemoimmunotherapy.

RCHOP is rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. After treatment you will enter observation and follow-up care to monitor for return of cancer.

Key points

- Pediatric-type FL (PTFL) usually occurs in children but can also occur in adults. It is stage 1 or 2. If it is stage 3 or 4, then it is not PTFL.
- In stage 1, disease is found in 1 lymph node or a group of nearby lymph nodes.
- In stage 2, disease is found in 2 or more lymph node groups on the same side of the diaphragm.
- Treatment options include surgery to remove the tumor (preferred), radiation therapy, or chemoimmunotherapy.

6

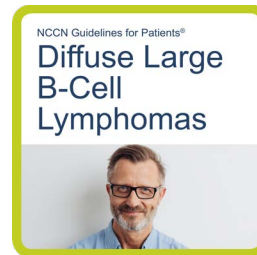
Transformed FL

- 53 Overview
- 53 After little or no therapy
- 55 After multiple lines of therapy
- 58 Key points

Follicular lymphoma (FL) can transform into a more aggressive lymphoma called diffuse large B-cell lymphoma (DLBCL). This means your slow-growing FL has turned into a large-cell, fast-growing lymphoma. Together, you and your care team will choose a treatment plan that is best for you.

- High-grade B-cell lymphomas (HGBLs) have mutations, gene rearrangements such as MYC, or other high-risk features.

For more information on DLBCL and treatment for HGBLs, read the *NCCN Guidelines for Patients: Diffuse Large B-Cell Lymphomas*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Overview

Follicular lymphoma (FL) can transform into diffuse large B-cell lymphoma (DLBCL). This can occur before, during, or after treatment. In DLBCL, large-cell, fast-dividing tumors are commonly found in lymph nodes, spleen, liver, bone marrow, or other tissues and organs. The risk of transformation is very low. However, transformed FL is very serious.

Certain gene rearrangements can be found in DLBCL. In gene rearrangements, part of a gene has broken off and attached to another gene.

- *MYC*, *BCL2*, and *BCL6* gene rearrangements are commonly found in DLBCL.
- Fluorescence in situ hybridization (FISH) will be done to look for gene rearrangements.

After little or no therapy

If FL changed into DLBCL after little or no treatment, then it will be treated with a chemoimmunotherapy such as RCHOP or Pola-R-CHP. Radiation therapy might be given. Involved-site radiation therapy (ISRT) treats cancer found in a small region or one area of your body. The goal of treatment is remission.

- RCHOP consists of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.
- Pola-R-CHP consists of polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, and prednisone.

Other possible chemoimmunotherapy options include:

- DA-EPOCH is dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab.
- RCDOP is rituximab, cyclophosphamide, liposomal doxorubicin (Doxil), vincristine, and prednisone.
- RCEOP is rituximab, cyclophosphamide, etoposide, vincristine, and prednisone.
- RGCVP is rituximab, gemcitabine (Gemzar or Infugem), cyclophosphamide, vincristine, and prednisone.
- RCEPP is rituximab, cyclophosphamide, etoposide, prednisone, and procarbazine (Matulane).

Treatment response

After treatment, you will have imaging (PET/CT) and lab tests to see if any cancer remains.

- In a complete response (CR) or complete remission, no cancer remains. Observation or a clinical trial are options. If disease relapses, you will have a biopsy before treatment.
- If a partial response (PR), then you will be given a different chemoimmunotherapy.
- If your disease did not respond to treatment or has progressed, then you will be given a different chemoimmunotherapy.

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



After multiple lines of therapy

If FL changed into DLBCL after multiple lines of therapy, then the treatment recommendations include:

- Clinical trial
- Systemic therapy. Options are based on what you were treated with before, your unique situation, and other factors. A type of radiation therapy called involved-site radiation therapy (ISRT) might be added to treat cancer located in a small region or one area of your body.
- ISRT alone
- Best supportive care

The goal of treatment is remission. If a hematopoietic cell transplant (HCT) is being considered, it is usually decided early in

treatment planning because having an HCT will affect future treatment options. Certain treatments are not recommended before or after an HCT. For example, HCT is not recommended after CAR T-cell therapy. However, bispecific monoclonal antibody therapy can be given after HCT or CAR T-cell therapy.

Systemic therapy options are based on if an HCT is planned.

- If an HCT is planned, **see Guide 5.**
- If an HCT is not planned, **see Guide 6.**

If cancer returns or does not respond to treatment, another systemic therapy will be given. After multiple lines of systemic therapy, CAR T-cell therapy or bispecific antibody therapy might be given.

Guide 5

Systemic therapy options: HCT planned

Preferred options

Cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab (RCHOP) if you did not have it before

If previously treated with anthracycline-based regimen such as doxorubicin

- Dexamethasone and cytarabine (DHA) with carboplatin, cisplatin, or oxaliplatin (platinum-based chemotherapy). Rituximab might be added.
- Gemcitabine, dexamethasone, and cisplatin (GDP) or (gemcitabine, dexamethasone, and carboplatin). Rituximab might be added.
- Ifosfamide, carboplatin, and etoposide (ICE). Rituximab might be added.

Note: An FDA-approved biosimilar might be used in place of rituximab.

CAR T-cell therapy options include the following:

- Lisocabtagene maraleucel (Breyanzi)
- Axicabtagene ciloleucel (Yescarta)
- Tisagenlecleucel (Kymriah).

Bispecific monoclonal antibody therapy options include:

- Epcoritamab-bysp (Epkinly)
- Glofitamab-gxbm (Columvi)

Treatment response

After treatment, you will have imaging (PET/CT scan) and lab tests to see if any cancer remains.

Complete response

In a complete response or remission (CR) no cancer remains. You might enter observation. An autologous (self) hematopoietic cell transplant (HCT) or an allogeneic (donor) hemopoietic cell transplant (HCT) are options in some cases. ISRT might be added if you did not have it before and cancer is in a small region or one area of your body. After treatment, you will enter surveillance and be monitored for relapse.

Guide 6

Systemic therapy options: HCT not planned

	Cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab (RCHOP) if you did not have it before
Preferred options	<p>If previously treated with anthracycline-based regimen such as doxorubicin</p> <ul style="list-style-type: none"> • Polatuzumab vedotin-piiq. Bendamustine and/or rituximab might be added. • Tafasitamab-cxix and lenalidomide
Other recommended	<ul style="list-style-type: none"> • Cyclophosphamide, etoposide, vincristine, prednisone (CEOP). Rituximab might be added. • Gemcitabine, dexamethasone, and cisplatin (GDP) or (gemcitabine, dexamethasone, and carboplatin). Rituximab might be added. • Gemcitabine and oxaliplatin (GemOx). Rituximab might be added. • Loncastuximab tesirine-lpyl

Note: An FDA-approved biosimilar might be used in place of rituximab.

Partial response

In a partial response (PR), treatment options are based on the types of treatment you had before. Options listed below depend on your individual situation:

- CAR T-cell therapy (preferred, if not given before)
- Allogeneic HCT in some cases. ISRT might be added if not given before and an HCT is not planned.
- ISRT (if not given before and disease is in a small region or one area of your body)
- Observation with follow-up tests

Relapse

If disease relapses, you will have a biopsy before treatment. Treatment might include a clinical trial, a systemic therapy not used before, ISRT (if not given before and disease is in a small region or one area of your body), CAR T-cell therapy, bispecific antibody therapy, or best supportive care. In best supportive care, the focus is improving quality of life and relieving discomfort.

No response or disease progresses

When disease progresses during treatment or does not respond to treatment, treatment might include a clinical trial, a systemic therapy not used before, ISRT (if not given before and disease is in a small region or one area of your body), CAR T-cell therapy, bispecific antibody therapy, or best supportive care.



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](https://www.nccn.org/patients/response)

Key points

- Follicular lymphoma (FL) can transform into diffuse large B-cell lymphoma (DLBCL). This means your slow-dividing FL has turned into a large-celled, fast-dividing, aggressive lymphoma.
- The goal of treatment is remission.
- If FL changed into DLBCL after little or no treatment, then it will be treated with a chemoimmunotherapy such as RCHOP or Pola-R-CHP. Radiation therapy might be given.
- If FL changed into DLBCL after multiple lines of therapy, then the treatment recommendations include a clinical trial, systemic therapy, radiation therapy, or best supportive care.
- A hematopoietic cell transplant (HCT) might be an option in some cases after multiple lines of systemic therapy. If an HCT is being considered, it is usually decided early in treatment planning.
- The order of treatment matters.
- Bispecific antibody therapy is an option after HCT or CAR T-cell therapy.

Need help paying for medicine or treatment?

Ask your care team what options are available.

7

Making treatment decisions

60 It's your choice

60 Questions to ask

70 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
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

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

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

Second opinion

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

Things you can do to prepare:

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

Support groups

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

Questions to ask

Possible questions to ask your care team are listed on the following pages. Feel free to use these questions or come up with your own.

Questions about testing and diagnosis

1. What grade and stage of follicular lymphoma do I have?
2. What does the cancer grade and stage mean in terms of length of survival and quality of life?
3. Is there a cancer center or hospital nearby that specializes in follicular lymphoma?
4. What tests will I have? How often will they be repeated?
5. Will my insurance pay for this test?
6. How soon will I know the results and who will explain them to me?
7. What will you do to make me comfortable during testing?
8. How will my biopsy be performed? What else might be done at this time?
9. How often will I have blood tests?
10. How long will it take to get these test results?

Questions about your care team's experience

1. What is your experience treating follicular lymphoma? What else do you treat?
2. What is the experience of those on your team?
3. I would like a second opinion. Is there someone you can recommend?
4. I would like another pathologist or hematopathologist to review my blood samples. Is there someone you recommend?
5. How many people like me (of the same age, gender, race) have you treated?
6. Will you be consulting with experts to discuss my care? Whom will you consult?
7. How many procedures like the one you're suggesting have you done?
8. Is this treatment a major part of your practice?
9. How often is a complication expected? What are the complications?
10. Who will manage my day-to-day care?

Questions about options

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

Questions about treatment

1. Which treatment(s) do you recommend and why?
2. Does the order of treatment matter?
3. When will I start treatment?
4. How long will treatment likely take?
5. What should I expect from treatment?
6. What will you do to make me comfortable during treatment?
7. How much will my insurance pay for treatment?
8. Are there programs to help me pay for treatment?
9. What are the chances my cancer will return after treatment?
10. What are my chances of developing a different cancer later in life?

Questions 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 about side effects

1. What are the side effects of treatment?
2. How are these side effects treated?
3. How long will these side effects last?
4. What side effects should I watch for that could be life-threatening?
5. When should I call my care team?
6. What should I do on weekends and other non-office hours?
7. What emergency department or ER should I go to?
8. Will my treatment team be able to communicate with the ER team?
9. What medicines can I take to prevent or relieve side effects?
10. What can I do to help with pain and other side effects?

Questions about clinical trials

1. What clinical trials are available for my grade and stage 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 cancer?
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?

Questions 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 are the risks to me and/or the donor?
4. How will the transplant affect my prognosis?
5. How will a transplant affect the quality and length of my life?
6. What should I expect from a transplant?
7. How long should I expect to be in the hospital?
8. How will I feel before, during, and after the transplant?
9. Will a transplant cure my lymphoma?
10. What is the chance my lymphoma will return?

Questions about resources and support

1. Who can I talk to about help with housing, food, and other basic needs?
2. What help is available for transportation, childcare, and home care?
3. How much will I have to pay for treatment?
4. What help is available to pay for medicines and other treatment?
5. What other services are available to me and my caregivers?
6. How can I connect with others and build a support system?
7. How can I find in-person or online support?
8. Who can help me with my concerns about missing work or school?
9. Who can I talk to if I don't feel safe at home, at work, or in my neighborhood?
10. How can I get help to stop smoking or vaping?

Resources

AnCan Foundation

Ancan.org

The Leukemia & Lymphoma Society

LLS.org/PatientSupport

Be the Match

bethematch.org/one-on-one

Triage Cancer

triagecancer.org

Blood & Marrow Transplant Information Network

bmtinfonet.org

CancerCare

cancercares.org

Cancer Hope Network

cancerhopenetwork.org

Imerman Angels

Imermanangels.org

Lymphoma Research Foundation

lymphoma.org

MedlinePlus

medlineplus.gov

National Bone Marrow Transplant Link (nbmtLINK)

nbmtlink.org

National Cancer Institute (NCI)

cancer.gov/types/lymphoma/patient/adult-nhl-treatment-pdq

National Coalition for Cancer Survivorship

canceradvocacy.org



Words to know

allogeneic hematopoietic cell transplant (allogeneic HCT)

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

autologous hematopoietic cell transplant (autologous HCT)

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

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.

chromosome

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

clinical trial

A type of research that assesses health tests or treatments.

complete response (CR)

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

computed tomography (CT)

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

consolidation

One of the post-induction phases of treatment given to kill any remaining cancer cells.

contrast

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

deoxyribonucleic acid (DNA)

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

flow cytometry (FCM)

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

fluorescence in situ hybridization (FISH)

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

gene

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

hematopathologist

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

hematopoietic cell transplant (HCT)

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

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.

involved-site radiation therapy (ISRT)

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

karyotype

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

lactate dehydrogenase (LDH)

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

lymph

A clear fluid containing white blood cells.

lymph node

A small, bean-shaped disease-fighting structure.

lymphadenopathy

Lymph nodes that are abnormal in size or consistency.

lymphatic system

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

lymphedema

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

lymphocyte

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

magnetic resonance imaging (MRI)

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

maintenance

The last phase of treatment used over a long period to prevent cancer from returning.

monitoring

A period of testing for changes in cancer status.

mutation

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

partial response (PR)

Lymphoma is still present but has reduced in size.

pathologist

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

peripheral blood (PB)

Blood that circulates throughout the body.

platelet (PLT)

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

polymerase chain reaction (PCR)

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

positron emission tomography (PET)

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

prognosis

The likely course a disease will take.

radiation therapy (RT)

A treatment that uses high-energy rays.

recovery

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

recurrence

The return of cancer after a cancer-free period.

red blood cell (RBC)

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

refractory cancer

A cancer that does not improve with treatment.

relapse

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

remission

Minor or no signs of disease.

side effect

An unhealthy or unpleasant physical or emotional response to treatment.

spleen

An organ that is part of the lymphatic system. The spleen makes lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach.

supportive care

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

translocation

A switching of parts between two chromosomes.

tumor lysis syndrome (TLS)

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

white blood cell (WBC)

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

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas Version 2.2024. It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

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

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

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

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

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

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

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

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

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

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

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

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

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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



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