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Chronic Lymphocytic Leukemia

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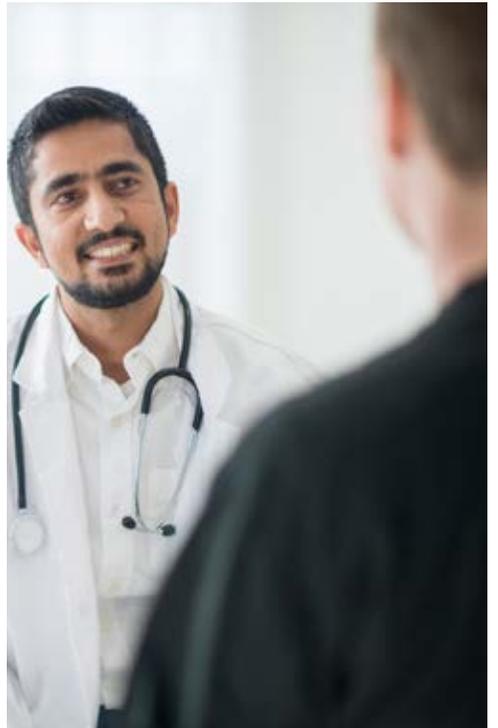
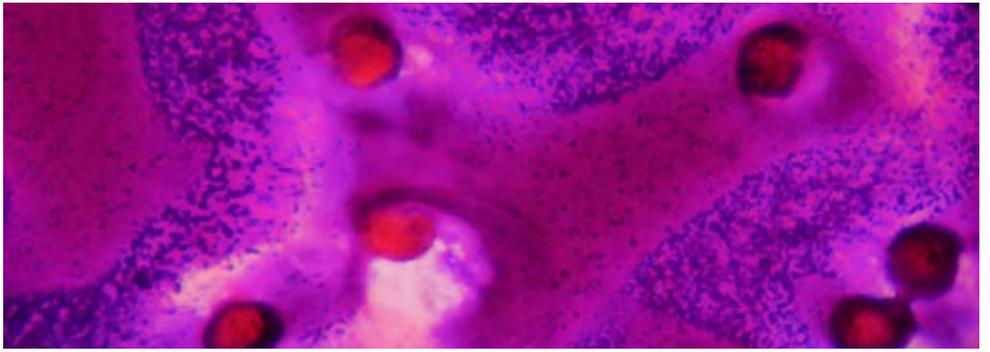
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CLL Society Inc. (CLLS)

The CLL Society is a patient–centric, physician–curated nonprofit organization focused on patient education, support and research dedicated to addressing the unmet needs of the CLL (chronic lymphocytic leukemia) community. cllsociety.org

The Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society (LLS) is dedicated to developing better outcomes for blood cancer patients through research, education and patient services and is happy to have this comprehensive resource available to patients. LLS.org/informationsspecialists



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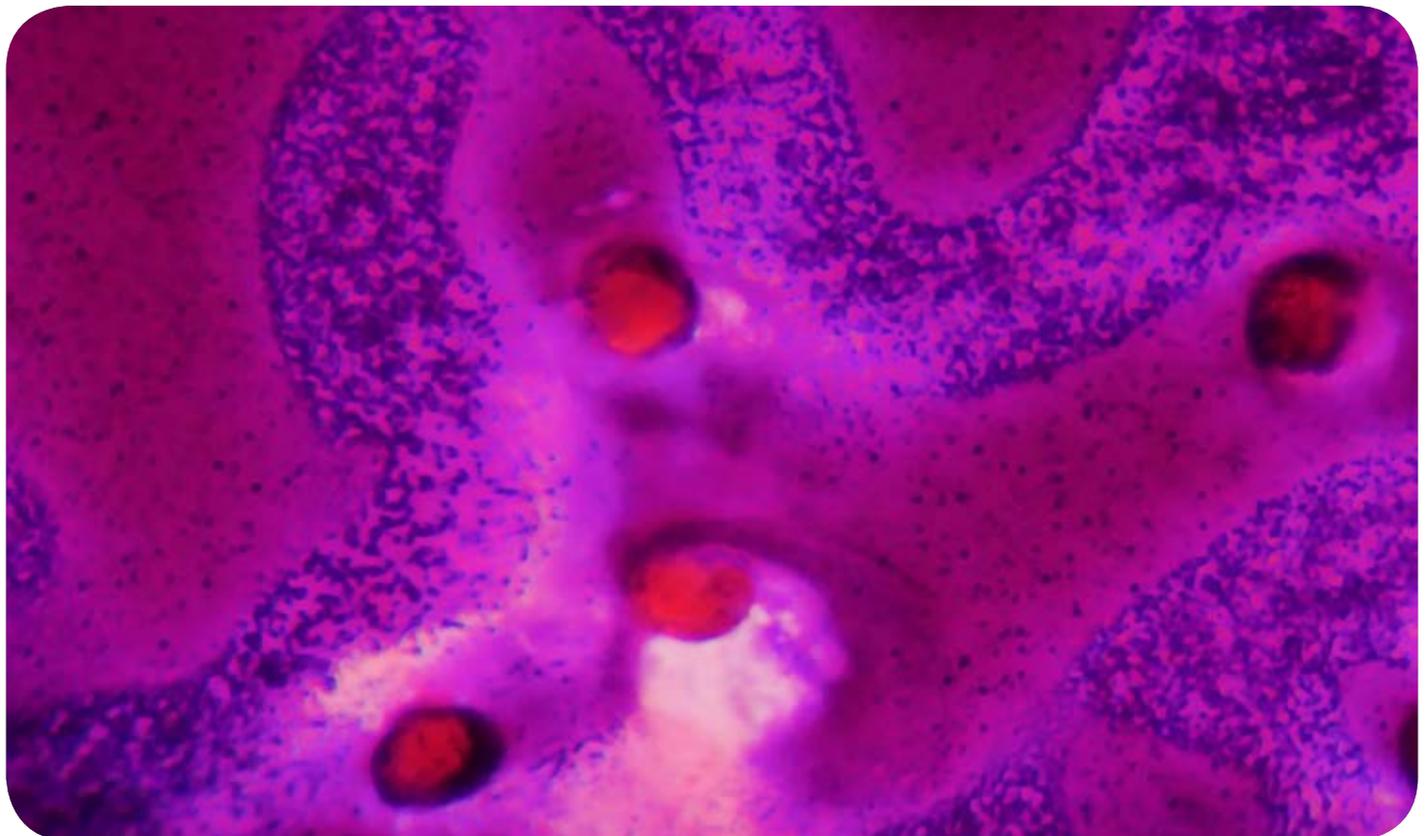
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You've learned that you have or may have leukemia. It's common to feel shocked and confused. This chapter reviews some basics that may help you learn about chronic lymphocytic leukemia.

Blood

To learn about CLL (chronic lymphocytic leukemia), you first must know about blood. Blood is one of the fluids in the body. It consists of blood cells that move within plasma. Plasma is mostly water.

Blood cells

There are three main types of blood cells. One type is red blood cells (also called erythrocytes). Another type is white blood cells (leukocytes). The third type is platelets (thrombocytes).

Blood cells have important jobs. Red blood cells carry oxygen throughout the body. White blood cells help fight germs. Platelets help control bleeding.

Most blood cells are formed in bone marrow. Bone marrow is the sponge-like tissue in the center of most bones. Within marrow are blood stem cells from which all blood cells are formed. **See Figure 1.**

Stem cells make new cells that are a step closer to being a blood cell. These cells are called

Figure 1
Blood cells

Blood stem cells are the cells from which all blood cells are formed. They make two types of progenitor cells. Lymphoid progenitor cells form into white blood cells called lymphocytes. Common myeloid progenitor cells form into red blood cells, platelets, and white blood cells called granulocytes.

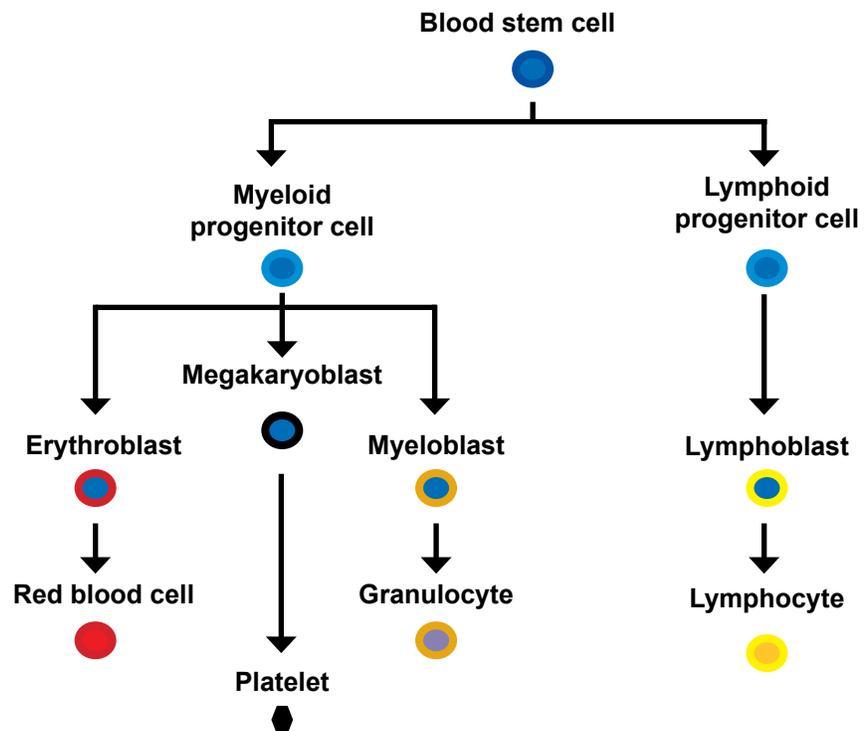


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progenitor cells. Compared to stem cells, progenitor cells are set to become a certain type of blood cell.

Lymphocytes

Lymphocytes are a type of white blood cell. They include natural killer cells, B cells, and T cells. Natural killer cells release chemicals that kill diseased cells. B cells make antibodies that mark germs for killing. T cells alert your body that germs are present, kill diseased cells, and help B cells.

Lymphocytes form in marrow and are released into the bloodstream. From the bloodstream, they are released into tissue. They return to the bloodstream through the lymphatic system. This system consists of fluid, called lymph, and a network of tissues. Lymph travels in lymph vessels and passes through lymph nodes, which filter out germs and waste. Other organs of the lymphatic system include the thymus, spleen, and tonsils.

A disease of cells

Your body is made of trillions of cells. Cancer is a disease of cells. Each type of cancer is named after the cell from which it formed.

Leukemia

Leukemia is a cancer of blood cells. A lot of people call it blood cancer. There are four common types. AML (**a**cute **m**yeloid **l**eukemia) and ALL (**a**cute **l**ymphoblastic **l**eukemia) are faster-growing blood cancers. CLL and CML (**c**hronic **m**yeloid **l**eukemia) are slower-growing blood cancers.

CLL vs. SLL

CLL and SLL (**s**mall lymphocytic lymphoma) are thought to be the same cancer. They are both cancers of B cells but differ in where they are found. With CLL, many abnormal B cells are found in the blood. With SLL, there are few, if any, abnormal

B cells in the blood. Treatment of these cancers is very similar.

Mutations

Cells have a control center called the nucleus. The nucleus contains chromosomes, which are long strands of DNA (**d**eoxyribonucleic acid) tightly wrapped around proteins. **See Figure 2.** Within DNA are coded instructions for building new cells and controlling how cells behave. These instructions are called genes.

There can be abnormal changes in genes called mutations. Some types of mutations that are linked to cancer are present in all cells. Other mutations are present only in cancer cells. Mutations cause cancer cells to not behave like normal cells and, sometimes, to look very different from normal cells.

Leukemia's threat

CLL is often a slow-growing cancer. But, sometimes it grows fast. If slow growing, you may not know you have CLL for years because you have no symptoms.

Over time, CLL results in too many abnormal B cells. The abnormal B cells will crowd out healthy cells in bone marrow. Then, there won't be enough red blood cells and platelets. As a result, you may feel tired, lose weight, and get sick easily. CLL may also spread to your lymph nodes, liver, and spleen, and cause these organs to enlarge.

Tests for CLL

Often, CLL is suspected after routine blood work. Your white blood cell counts may be high. More blood tests are needed to confirm (diagnose) CLL. Some people will need a biopsy of lymph nodes if blood tests don't work.

Blood and tissue samples will be sent to a doctor called a hematopathologist. These doctors spend all their time looking at blood, bone marrow, and lymph nodes. They become very good at diagnosing blood cancers.

Flow cytometry is a newer lab test. It can be used to count B cells and test for proteins. IHC (immunohistochemistry) is an older method that can also be used.

B-cell count

The number of abnormal B cells in your blood will be counted. Diagnosis of CLL requires at least 5,000 abnormal B cells per microliter of blood ($5 \times 10^9/L$). The B cells have to be copies of the same "parent" cell. This is called monoclonality.

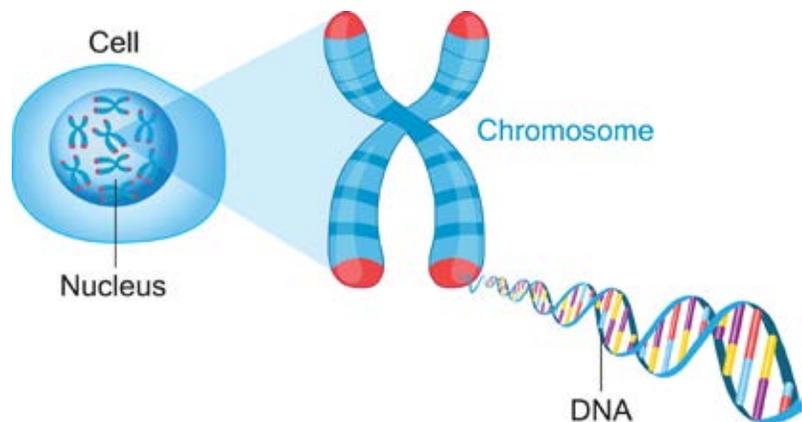


Snapshot: Monoclonal B-lymphocytosis

If you don't have CLL, you may have MBL (**m**onoclonal **B** lymphocytosis). MBL is common, especially among older adults. It is not cancer and very few people with MBL develop CLL. The first step of care is to watch and wait (also called observation). Observation is a period of testing to assess for changes in status. Some people won't need treatment for years if at all.

Figure 2 Genetic material in cells

Most human cells contain a plan called the "blueprint of life." It is a plan for how our bodies are made and work. It is found inside of chromosomes. Chromosomes are long strands of DNA that are tightly wrapped around proteins. Genes are small pieces of DNA. Humans have about 20,000 to 25,000 genes.



Protein tests

The abnormal B cells will be tested for surface proteins. This is called immunophenotyping. CLL cells have a certain pattern of proteins in their membrane. **See Figure 3.**

Rule out

Mantle cell lymphoma needs to be ruled out. This lymphoma is closely related to CLL. Its cells have high levels of proteins called cyclin D1 that are caused by abnormal chromosomes.

A cytospin machine may be used to test for cyclin D1. Protein tests of CD200 and LEF1 may also be useful. FISH (fluorescence in situ hybridization) is a lab test that may be done to test for abnormal chromosomes.

Rai stages

A cancer stage is a rating by your doctor that suggests the outcome of the cancer. It is also used

to decide if treatment is needed now. Read **Part 2** for more information on starting treatment.

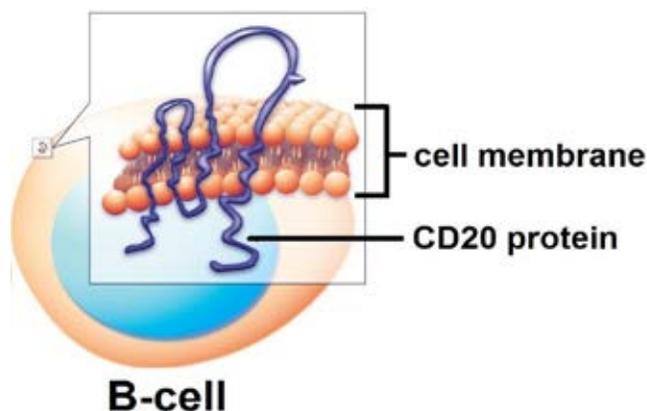
The Rai staging system is commonly used for CLL. It consists of five cancer stages:

- **Stage 0** is defined by normal test results except for a high lymphocyte count. The likelihood of the cancer getting worse is low.
- **Stage I** is defined as a high lymphocyte count and enlarged lymph nodes. The likelihood of the cancer getting worse is intermediate.
- **Stage II** is defined by an enlarged liver, spleen, or both. The likelihood of the cancer getting worse is intermediate.
- **Stage III** is defined by a low hemoglobin level. Hemoglobin is a protein in red blood cells. The likelihood of the cancer getting worse is high.
- **Stage IV** is defined by a low platelet count. The likelihood of the cancer getting worse is high.

You may hear of the Binet staging system. It is another system used to stage CLL. It has three

Figure 3 CD20 protein

CLL cells have a common pattern of proteins in their membrane. This pattern includes the presence of CD5, CD19, and CD23 proteins, some CD20, and no CD10 proteins. Immunophenotyping is the process of identifying the proteins in cells' membranes.



Derivative work of NIAID - Rituxima Binding to CD20 on a B Cell Surface, CC BY 2.0, <https://commons.wikimedia.org/w/index.php?curid=39933221>



stages labeled A, B, and C. The stages are based on your physical exam and blood tests. The Binet system may be helpful but isn't used in this book to decide starting treatment.

Treatment types

This section briefly describes treatments for CLL. Not everyone receives the same treatment. Your doctor will tailor treatment to you based on tests described in **Part 2**. Treatment options based on features of the cancer and your health are listed in **Part 3**.

Targeted therapy

Targeted therapy is a class of drugs. It impedes the growth process that is specific to cancer cells. It harms normal cells less than chemotherapy.

Kinase inhibitors

Within cells, kinases are part of many chemical pathways, some of which start cell growth. They change the action of proteins by attaching phosphates to them. Kinase inhibitors stop growth signals by blocking the transfer of phosphates. This lowers the number of new cells being made.

Kinase inhibitors are used to stop kinases within cancer cells. Ibrutinib and acalabrutinib stop a kinase called BTK (**B**ruton's **T**yrosine **K**inase). Idelalisib targets one form of PI3K (**p**hosphoinositide **3**-**k**inase) called delta. Duvelisib targets two forms of PI3K—delta and gamma.

BCL-2 inhibitors

BCL-2 is a protein inside of B cells that helps prevent cell death. In CLL, BCL-2 may build up and stop the cancer cells from dying. Venetoclax is a BCL-2 inhibitor that allows the cancer cells to self-destruct.

Antibody treatment

Antibodies are Y-shaped proteins of the immune system. They help your body detect germs and other threats. Monoclonal antibodies can be made in a lab to treat certain types of cancer.

CD20 and CD52 antibodies

CD20 antibodies attach to a surface protein on cells called CD20. Likewise, CD52 antibodies attach to CD52. Both treat CLL by marking cells for destruction by your immune system. They may directly kill cells, too. CD20 antibodies include obinutuzumab, ofatumumab, and rituximab. Alemtuzumab is a CD52 antibody.

PD-1 antibodies

PD-1 antibodies are also called immune checkpoint inhibitors. Nivolumab and pembrolizumab are PD-1 antibodies. PD-1 antibodies attach to immune cells and allow your immune system to destroy the cancer cells. More research is needed to learn how well they treat CLL that has transformed into a lymphoma. Lymphomas are cancers of white blood cells in the lymph system.



The key to managing fear is in making informed decisions. Stay positive, make a plan for yourself and go forward one step at a time.”

– Ted
Leukemia Survivor

Chemotherapy

Chemotherapy works by damaging cancer cells. As a result, cancer cells cannot make new cells. Chemotherapy can also cause cells to destroy themselves. Chemotherapy is often used with antibody treatment to treat CLL. This combined treatment is called chemoimmunotherapy.

There are many types of chemotherapy. If your health is fairly good, your treatment may include a purine analogue. Purine analogues include fludarabine, cladribine, and pentostatin. If your health is poor, you may get chemotherapy drugs called alkylating agents. Bendamustine, cyclophosphamide, and chlorambucil are alkylating agents. Other types of chemotherapy may be used if CLL transforms into lymphoma.

Immunomodulators

Immunomodulators are drugs that modify some parts of the immune system. Lenalidomide is an immunomodulator that is often used to treat a cancer called multiple myeloma. For CLL, it is sometimes used to maintain the good results of the main treatment.

Stem cell transplant

A stem cell transplant replaces unhealthy stem cells with healthy ones. An allogeneic transplant uses healthy stem cells from a donor. Testing is needed to confirm if the donor and you are a good match. An allogeneic transplant is an intense treatment so not everyone can get it.

You'll first receive treatment to kill your bone marrow and most CLL cells. Next, you'll receive the donor cells. These cells will form new, healthy marrow. They will also attack cancer cells that weren't killed by prior treatment. Visit the websites listed in **Part 4** for more information on transplants.

Clinical trial

One treatment choice may be whether to join a clinical trial. Joining a clinical trial is strongly supported. NCCN believes that you will receive the best management in a clinical trial.

A clinical trial is a type of research that studies a test or treatment in people. It gives people access to health care that otherwise couldn't usually be received. Ask your treatment team if there is an open clinical trial that you can join.

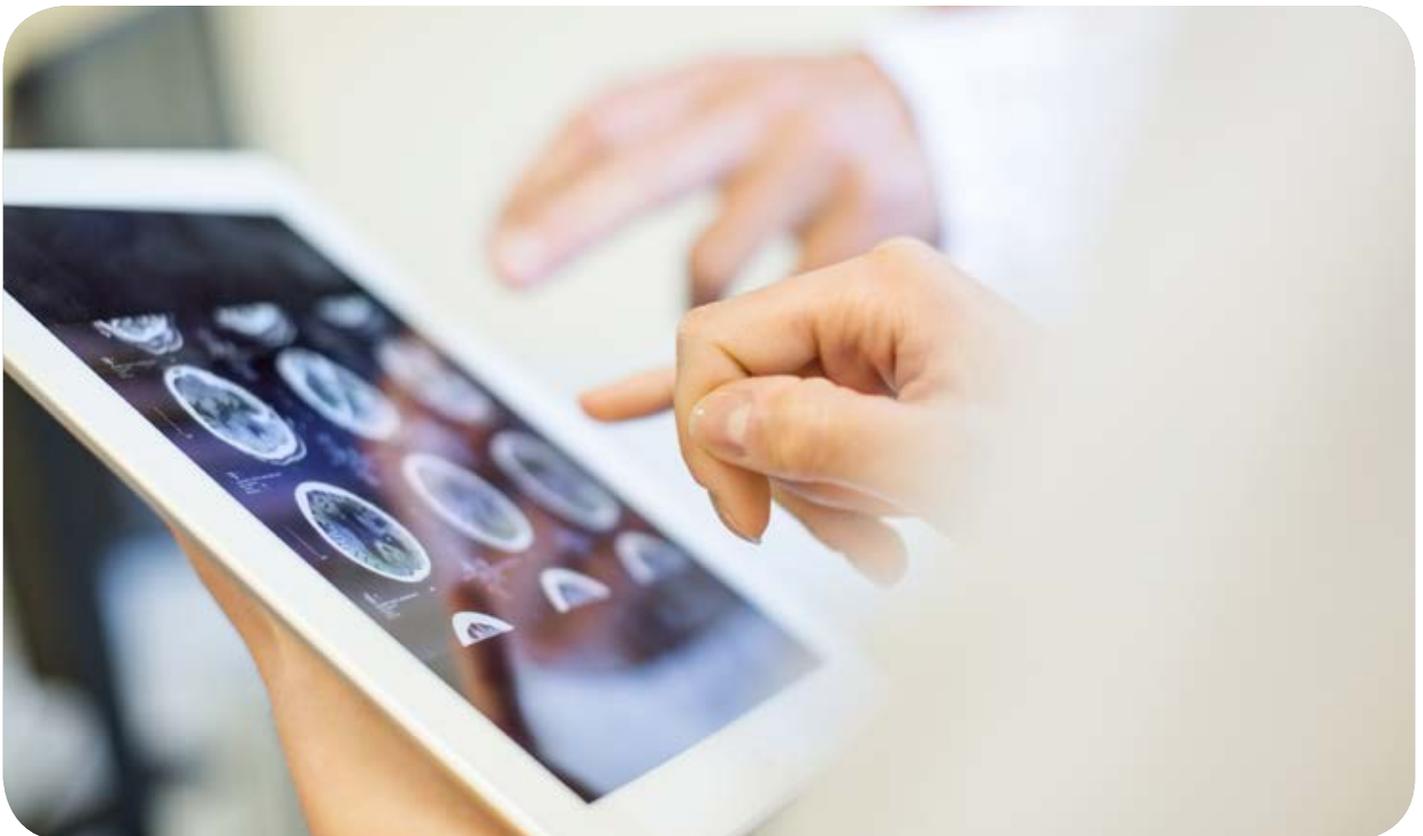
Review

- ▶ White blood cells are a part of your body's immune system. Lymphocytes are a type of white blood cell and include natural killer cells, B cells, and T cells.
- ▶ Leukemias are cancers of blood cells. CLL is one type of leukemia that causes too many abnormal B cells.
- ▶ Your blood needs to be tested to diagnose CLL. Doctors look for very high numbers of abnormal B cells. They also look for proteins that are common and uncommon to CLL cells.
- ▶ The Rai system is used to stage CLL and decide when to begin treatment.
- ▶ Common treatments for CLL are targeted therapy, antibody treatment, and chemotherapy.
- ▶ Clinical trials give people access to new tests and treatments that they otherwise couldn't have received.

2

Treatment planning

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Your doctors want to learn all about the leukemia you have. This chapter describes who should receive which tests before cancer treatment. It also describes other types of care needed before treatment.

Doctors plan treatment using many sources of information. These sources include the health care listed in [Guide 1](#). Another source is you. Tell your doctor your concerns and goals for treatment. Together, you can share in the decision-making process. Read **Part 4** to learn more about making treatment decisions.

Medical history

Your doctor will ask about any health problems and their treatment during your lifetime. Be prepared to tell what illnesses and injuries you have had. You will also be asked about health conditions and symptoms. It may help to bring a list of old and new medicines to your doctor's office.

Your doctor will ask about symptoms that may be related to CLL. Such symptoms include enlarged lymph nodes, tiredness, a feeling of fullness in your belly, and getting sick. CLL may also cause "B symptoms." It's important that your doctor knows if you have them. These symptoms include fevers, chills, night sweats, and weight loss without dieting.

Some cancers and other health conditions can run in families. Thus, your doctor will ask about the medical history of your close blood relatives. Such family includes your siblings, parents, and grandparents. Be prepared to tell who has had what diseases and at what ages.

Guide 1. Health care before cancer treatment

Must haves

- Medical history
- Physical exam with performance status
- CBC with differential
- Comprehensive metabolic panel
- FISH for chromosomes 11, 12, 13, and 17
- Karyotype
- DNA sequencing for *IGHV* and *TP53* mutations

Sometimes useful

- Beta-2 microglobulin
- Haptoglobin, reticulocytes, DAT
- LDH
- Quantitative immunoglobulins
- Uric acid
- Bone marrow biopsy and aspiration
- Diagnostic CT with contrast
- PET/CT
- Hepatitis B tests
- Echocardiogram or MUGA
- Fertility support
- Pregnancy test if you can have babies

Physical exam

A physical exam is a study of your body. It is done to look for signs of disease. It is also used to help assess what treatments may be options.

To start, your basic body functions will be measured. These functions include your temperature, blood pressure, and pulse and breathing rate. Your weight will also be checked.

Your doctor will listen to your lungs, heart, and gut. He or she will also assess your eyes, skin, nose, ears, and mouth. Parts of your body will be felt. Your doctor will note the size of organs, such as your liver and spleen. He or she will see if organs feel soft or hard. Tell your doctor if you feel pain when touched.

Your doctor will also rate your performance status. Performance status is your ability to do daily activities. It is used by doctors to assess if you can have certain treatments.

Blood tests

Doctors test blood to look for signs of disease. Blood tests require a sample of your blood. Blood samples can be removed with a blood draw.

Blood draw

Some blood draws require no eating and drinking for hours. Your doctor will say if you can eat or drink. Blood samples will be removed from a vein with a needle.

CBC with differential

A CBC (**complete blood count**) measures parts of the blood. Test results include counts of white blood cells, red blood cells, and platelets. Cancer and other health problems can cause low or high counts.

There are several types of white blood cells. A differential counts the number of each type of cell. It also checks if the counts are in balance with each other.

Comprehensive metabolic panel

Chemicals in your blood come from your liver, bone, and other organs. A comprehensive metabolic panel often includes tests for up to 14 chemicals. Low or high levels can be caused by cancer or other health problems.

Beta-2 microglobulin

Beta-2 microglobulin is a small protein found on most cells. It is released by cells into the blood, especially by B cells. High levels may be a sign of CLL that is harder to treat.

Haptoglobin, reticulocytes, DAT

Hemoglobin is a protein in red blood cells. It carries oxygen from your lungs to the rest of your body. When red blood cells die, hemoglobin is released into the blood. Low amounts of hemoglobin is called anemia. There are many types of anemia based on what is causing it.

Autoimmune hemolytic anemia

Autoimmune hemolytic anemia is when your body destroys red blood cells. It can be caused by advanced CLL and some of its treatments. Fludarabine should not be used if you have severe autoimmune hemolytic anemia.

Three tests are needed to confirm autoimmune hemolytic anemia. One test is the haptoglobin level. Haptoglobin attaches to hemoglobin in blood to mark it for removal. Another is the reticulocyte count. Reticulocytes are young red blood cells. The third test is DAT (**direct antiglobulin test**; also called direct Coombs' test). This test can detect if antibodies are stuck to and killing red blood cells.

LDH

LDH (lactate dehydrogenase) is a protein that is in most cells. Dying cells release LDH into blood. Fast-growing cells also release LDH. High levels may be a sign that treatment may be needed now or soon.

Quantitative immunoglobulins

Immunoglobulins (also called antibodies) are Y-shaped proteins made by immune cells. They help your body detect germs and other threats. Quantitative immunoglobulins measure the amount of 3 types—IgG, IgA, and IgM—in blood.

Some people with CLL have low levels of antibodies before cancer treatment. They may be sick often. Levels can also drop during cancer treatment. Lab results are used to decide if you need treatment to prevent or cure infections.

Uric acid

Uric acid is released by cells when they break down and die. Too much uric acid in the body is called hyperuricemia. You may have a high level of uric acid before starting treatment. Levels can be high due to kidney disease or other health problems.

Pathology report

All lab results are included in a pathology report. This report will be sent to your doctor. Ask him or her for a copy. Your doctor will review the results with you. Take notes and ask questions.

Genetic tests

Genetic tests assess for abnormal changes in genes and chromosomes in CLL cells. Such changes are not present at birth. Genetic tests are performed by pathologists. It often takes several days before the lab results are known. Results are used to assess the outcome (prognosis) of CLL and plan treatment.

FISH

It is very common for CLL cells to have abnormal chromosomes. Chromosomes that commonly have defects are chromosomes 11, 12, 13, and 17. FISH is a test that detects abnormal chromosomes and genes. It can be done using either blood or bone marrow cells.

Missing (deleted) parts of chromosomes 11 or 17 used to be signs of a poor outcome, but now treatment is better. A good outcome is linked to deleted parts of chromosome 13, if it is the only abnormal chromosome. Three copies of a chromosome instead of the normal two is called trisomy. Trisomy 12 is linked to neither a poor nor a good outcome.

Karyotype

A karyotype is a picture of chromosomes. It shows if there is a defect in the size, shape, and number of chromosomes. **See Figure 4.** A blood or bone marrow sample can be used. This lab test adds chemicals to the sample to start cell growth. For CLL, a chemical called CPG should be used.

A “complex karyotype” is linked to a poorer outcome. A complex karyotype is 3 or more unrelated defects in chromosomes that occur in more than one cell. The presence of a complex karyotype may affect your treatment options.

DNA sequencing

DNA sequencing is a lab test of mutations in genes. It reveals the order of the chemicals that make up DNA. A blood or marrow sample can be used.

IGHV mutation

Normal antibodies are made of two heavy chain proteins and two light chain proteins. *IGHV region* genes contain instructions for making the heavy chain protein. These genes may or may not be mutated in people with CLL. The outlook is good if *IGHV* is mutated.

Surface proteins CD38, CD49d, and ZAP-70 are markers for the *IGHV* mutation. If *IGHV* testing can't be done, testing for these markers is an option. But, *IGHV* testing is preferred as protein levels are not as reliable.

TP53 mutation

TP53 is the gene for a protein that signals whether damaged cells should be repaired or destroyed. It helps to prevent tumors from forming. If *TP53*

is mutated, there are treatment options that may prevent poor outcomes.

Bone and marrow tests

Two procedures are used to remove bone marrow. A bone marrow aspiration removes a small amount of liquid bone marrow. A bone marrow biopsy removes a core of bone. These procedures may be done at the same time. They may be done to learn what's causing low numbers of blood cells.

Hepatitis B tests

Hepatitis B can become active again due to certain cancer treatments. Tell your treatment team if you've been infected with hepatitis B. If you're unsure, testing is advised. A sample of your blood is needed for testing.

Figure 4 Karyotype

A karyotype is a picture of chromosomes. It shows if there is a defect in the size, shape, and number of chromosomes.



Imaging

Imaging makes pictures of the insides of your body. It can show which body parts have cancer. A radiologist is a doctor who is an expert in reading images. He or she will convey the test results to your doctor.

Diagnostic CT scan

CT takes many pictures of a body part from different angles using x-rays. **See Figure 5.** A computer combines the x-rays to make detailed pictures. A contrast dye should be used. It makes the pictures clearer.

CT is needed if your organs are enlarged. Leukemia cells can build up in lymph nodes, the spleen, and the liver. If needed, a CT of your chest, belly area, and between your hip bones is advised.

PET/CT scan

Sometimes CT is combined with PET (positron emission tomography). PET shows how your cells are using a simple form of sugar (glucose). PET/CT is often not useful for CLL. If given, it is used to direct a needle into a lymph node for a biopsy. Your lymph nodes may be tested if your doctor thinks that CLL is turning into a fast-growing cancer.

Heart tests

Some cancer treatments can damage your heart. To plan treatment, your doctor may test how well your heart pumps blood. You may get an echocardiogram or MUGA (multigated acquisition) scan. An echocardiogram uses sound waves to make pictures of your heart. A MUGA scan makes pictures using a radiotracer and special camera.

Figure 5 CT machine

Pictures of the insides of your body can be made with imaging. During the scan, you will lie on a table that will move into the tunnel of the imaging machine. The pictures will be viewed by a doctor who will look for signs of cancer.



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Fertility and pregnancy

Some cancer treatments can limit your ability to have a baby. If you want the choice of having babies after treatment or are unsure, tell your doctors. It may also help to talk with a fertility specialist before you begin cancer treatment.

A fertility specialist is an expert in helping people have babies. The fertility specialist can discuss with you how to have a baby after treatment. Some methods of fertility preservation are discussed next. If you are a woman of childbearing age, important information on pregnancy is also addressed.

Sperm banking

Men who want to have children after cancer treatment can use sperm banking. Sperm banking stores semen for later use. This is done by freezing semen with sperm in liquid nitrogen. Talk to your treatment team about the costs of and how well sperm banking works.

Egg freezing

Like sperm banking, a woman's eggs can be removed, frozen, and stored for later use. Your frozen eggs can be fertilized with sperm beforehand. Also, a part of your ovary that contains eggs can be frozen and stored.

Pregnancy test

Some cancer treatments can harm an unborn baby. Get a pregnancy test before treatment if you may be pregnant now. Your treatment options will depend on the results. During treatment, take steps to avoid getting pregnant. Your doctors can tell you which birth control methods are best to use while on treatment.

Starting treatment

Not all people with CLL need to start treatment right away. Starting treatment is based on symptoms of CLL, test results, and the cancer stage. If the cancer is Rai stage 0, I, II, and III, your doctor will assess if treatment is needed now.

There are several reasons to start treatment for stages 0–II CLL. You may be able to take part in a clinical trial. Results of blood tests may be getting worse. Some organs may be getting larger. Some organs may stop working well soon. Major symptoms of CLL may appear, such as:

- Drenching night sweats,
- Severe fatigue,
- Fever without proof of infection, and
- Unplanned weight loss.

If these reasons are not present, watching and waiting (observation) are advised. Tests during observation include physical exams and blood tests. Treatment can be started when needed.

Most people with stage III CLL need to be treated. In some cases, observation may be an option if blood cell counts aren't too low and don't drop more. Treatment is advised when blood cell counts start falling.

Review

- Your doctor will ask you about any health problems and treatment in your lifetime. Tell your doctor if you have recently had fevers, night sweats, and weight loss without dieting. These can be symptoms of CLL.
- Your doctor will study your body to assess your health. He or she will check the size of your liver and spleen. Your doctor will also rate your ability to do everyday activities.
- Blood tests can be done to assess the outlook of CLL and for other health conditions.
- Genetic tests assess for abnormal changes in chromosomes and genes. Results can help your doctor plan treatment.
- A bone marrow biopsy removes a piece of bone and marrow to test for cancer cells. An aspiration removes liquid marrow. These tests may be helpful before starting treatment.
- Testing for hepatitis B may be done since it can become active again.
- Imaging tests allow your doctors to see inside your body without cutting into it. CT and PET/CT scans may be useful in certain cases.
- You may undergo heart tests to see if you are healthy enough to have certain cancer treatments.
- Talk to a fertility specialist to learn about ways to have babies after cancer treatment. If you may be pregnant, get a pregnancy test now. Some cancer treatments can harm unborn babies.
- You may not need to start treatment for CLL right away. Treatment is started based on the signs and symptoms of CLL, test results, and the cancer stage.



It is essential to have a doctor that you trust implicitly, and who knows that you are the ultimate decision-maker in your treatment regimen. If you can't advocate for yourself, ask a family member or friend for help.”

– Dixie

Leukemia survivor

3

Treatment guide

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- 23 First-line treatment
- 24 Relapsed or refractory CLL
- 26 Transformed CLL
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- 28 Review



This chapter presents the treatment options for CLL. It also reviews some key parts of supportive care. Discuss with your doctor which options are right for you.

Overview

Treatment of CLL includes treatment of the cancer and support for you. At this time, CLL is rarely cured. Instead, the aim of treatment is to reduce symptoms, control the cancer, and extend life.

Del(17p)/TP53 mutation

Treatment options depend on many factors. One main factor is whether there are missing parts of chromosome 17 called “del(17p).” Del(17p) is linked with loss of the *TP53* gene. In this chapter, treatment options are listed by whether del(17p) or the *TP53* mutation is present.

Treatment results

During and at the end of treatment, you will receive tests to assess the results. These tests include physical exams and blood tests. There are four types of treatment response:

- **Complete remission** is the best outcome. Enlarged organs and lymph nodes are back to normal size. Blood counts are within normal range. You have no cancer symptoms like fever.
- **Partial remission** is a good response. The size of enlarged organs and nodes has been greatly reduced. Blood counts are returning to normal.
- **Stable disease** is less than a partial remission. The cancer is not getting worse.
- **Progressive disease** is a worsening of the cancer.

If remission is achieved, your doctor may give you maintenance treatment. At this time, it is not used often for CLL. The goal is to maintain the good results of prior treatment.

Relapsed or refractory CLL

A relapse is the return of cancer after it's been in remission for more than 6 months. You may not need treatment right away. When treatment is needed, your doctor may give the same or a different type of treatment than was given before. The goal of treatment is to achieve remission again.

Refractory disease is cancer that is not in remission at the end of treatment. It also includes progressive disease within 6 months after treatment has ended. In these cases, a different treatment may be tried. Good results are often achieved with a different treatment.

Supportive care

Supportive care aims to improve your quality of life. It includes care for health issues caused by cancer or cancer treatment. It is a key part of treatment for everyone, not just people at the end of life. Talk with your treatment team to get the best supportive care for you.

First-line treatment

Before starting first-line treatment, your doctor may want to test the cancer again. Important markers are del(17p), *TP53* mutation, karyotype, and *IGHV* mutation. Imaging may also be done. If CLL is now a different type of cancer, read the section, *Transformed CLL*, in this chapter.

Options for first-line treatment are listed in [Guide 2](#). They are grouped by whether del(17p) or a *TP53* mutation is present. A clinical trial may be an option for you. NCCN experts recommend a clinical trial when CLL cells have del(17p) or a *TP53* mutation.

Ibrutinib

Ibrutinib is the preferred first-line treatment, especially if you are older. In well-designed studies, it had better results than the treatment to which it was compared.

Other treatments

Other options in Guide 2 are listed in alphabetical order. For CLL with del(17p) or *TP53* mutation, chemotherapy does not work well. Antibody treatment has better results. If the cancer growth is controlled, keep taking the antibody treatment until your doctor tells you to stop.

For CLL without del(17p) and *TP53* mutation, chemoimmunotherapy is a common treatment. An alkylating agent—bendamustine or chlorambucil—with a CD20 antibody may be an option. If you are younger and healthy enough, fludarabine-based chemoimmunotherapy may be received. Fludarabine is a purine analog, which can cause serious infections. If you can't take chemoimmunotherapy, there are other options but more research is needed.

For CLL without del(17p) and *TP53* mutation, there are first-line options not widely supported by NCCN experts. Research showed that PCR (pentostatin,

Guide 2. First-line treatment del(17p) or *TP53* mutation is present

What are the options?

- Clinical trial
- Ibrutinib (preferred)
- Alemtuzumab ± rituximab
- High-dose methylprednisolone + rituximab
- Obinutuzumab

del(17p) and *TP53* mutation are absent

Older or sick

What are the options?

- Ibrutinib (preferred)
- Bendamustine + CD20 antibody treatment
- Chlorambucil + CD20 antibody treatment
- High-dose methylprednisolone + rituximab
- Ibrutinib + obinutuzumab
- Obinutuzumab

Younger and fairly healthy

What are the options?

- Ibrutinib (preferred)
- Bendamustine + CD20 antibody treatment
- FCR (fludarabine, cyclophosphamide, rituximab)
- FR (fludarabine, rituximab)
- High-dose methylprednisolone + rituximab
- Ibrutinib + rituximab

cyclophosphamide, rituximab) did not work any better than fludarabine-based chemoimmunotherapy. When used alone, rituximab or chlorambucil does not work as well as other treatments among older or really ill people. But, the side effects of these treatments are not severe.

Maintenance

After immunochemotherapy, your doctor may give you lenalidomide for maintenance treatment. It is sometimes given if the cancer is likely to relapse. Relapse is more likely if very small amounts of cancer cells remain in your blood after treatment. This small amount is called MRD (**minimal residual disease**).

Relapsed or refractory CLL

Before starting treatment, your doctor may want to test the cancer again. Important markers are del(17p), *TP53* mutation, and karyotype. Imaging may also be done. If CLL is now a different type of cancer, read the section, *Transformed CLL*, in this chapter.

Options for relapsed or refractory CLL are listed in [Guide 3](#). Ibrutinib, venetoclax with rituximab, duvelisib, and idelalisib with rituximab are preferred for all types of CLL no matter your age or health. Venetoclax is also a preferred treatment for CLL with del(17p) or a *TP53* mutation. The other options listed have had some good results.

A clinical trial and allogeneic stem cell transplant may be options. Ask your doctor if there is an open clinical trial. For a transplant, you must not have major health problems other than the cancer.



What to expect: Ibrutinib

- ✓ Is taken once a day around the same time.
- ✓ Is made as tablets and capsules.
- ✓ May cause an increase in lymphocytes even when treatment is working.
- ✓ Can cause side effects, such as tiredness, fever, rash, nausea, diarrhea, pain, bleeding, and heart problems.
- ✓ Should not be stopped unless your doctor tells you to stop.

Maintenance

If remission is achieved, your doctor may start you on maintenance treatment. Lenalidomide is sometimes given if very small amounts of cancer cells (MRD) remain in your blood after treatment. Another option for maintenance treatment is ofatumumab, but more research on it is needed.

Guide 3. Next-in-line treatment del(17p) or *TP53* mutation is present

What are the preferred options?

- Ibrutinib
- Venetoclax + rituximab
- Duvelisib
- Idelalisib + rituximab
- Venetoclax

What are the other options?

- Acalabrutinib
- Alemtuzumab ± rituximab
- High-dose methylprednisolone + rituximab
- Idelalisib
- Lenalidomide ± rituximab
- Ofatumumab



Approach your ‘recovery’ in whatever way you deem best for your situation. Allow yourself to heal. Be positive and stay proactive.”

– Ted

Leukemia survivor

del(17p) and *TP53* mutation are absent

What are the preferred options?

- Ibrutinib
- Venetoclax + rituximab
- Duvelisib
- Idelalisib + rituximab

What are the other options?

- Acalabrutinib
- Alemtuzumab ± rituximab
- Bendamustine + rituximab (younger and healthy)
- Chlorambucil + rituximab (older or sick)
- Dose-dense rituximab (older or sick)
- FC + ofatumumab (younger and fairly healthy)
- FCR (reduced dose if older or sick)
- PCR (reduced dose if older or sick)
- High-dose methylprednisolone + rituximab
- Idelalisib
- Lenalidomide ± rituximab
- Obinutuzumab
- Ofatumumab
- Venetoclax
- Bendamustine, rituximab ± ibrutinib
- Bendamustine, rituximab ± idelalisib

FCR = fludarabine, cyclophosphamide, rituximab;
FR = fludarabine, rituximab;
PCR = pentostatin, cyclophosphamide, rituximab

Transformed CLL

For a few people, CLL changes into a faster-growing cancer. This is called Richter's transformation.

CLL may change into DLBCL (diffuse large B-cell lymphoma) or Hodgkin lymphoma. Lymphoma is a cancer of white blood cells within the lymph system.

Transformed CLL needs to be confirmed with testing. A biopsy is needed. The tissue samples will be assessed for surface proteins. Blood tests and imaging will be done, too.

DLBCL

Treatment options depend on if the transformed cells are like CLL cells. If the cells are not alike, read [NCCN Guidelines for Patients®: Diffuse Large B-Cell Lymphoma](#) for options.

For DLBCL that has CLL features, a clinical trial is preferred. Another option is chemoimmunotherapy with RCHOP, R-DA-EPOCH, R-hyper-CVAD, or OFAR. If chemotherapy works, an allogeneic stem cell transplant may be an option if you are healthy enough.

If chemotherapy doesn't work, there are two options. You may receive treatments listed in [NCCN Guidelines for Patients®: Diffuse Large B-Cell Lymphoma](#). The other option is a PD-1 inhibitor with or without ibrutinib, but this treatment needs more research.

Hodgkin lymphoma

A clinical trial is preferred. For other options, read [NCCN Guidelines for Patients®: Hodgkin Lymphoma](#).

Supportive care

Supportive care is an important part of your cancer care. It can address many needs. It can prevent or relieve emotional or physical symptoms. It can also help with making treatment decisions. Supportive care also includes help with coordination of care between health providers.

[Guide 5](#) lists some of the supportive needs of people with CLL. Some apply to all people with CLL. Other needs are linked to specific cancer treatments. Talk with your treatment team to get the best supportive care plan for you.

All cancer treatments can cause unwanted health issues. Such health issues are called side effects. Ask your treatment team for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worse symptoms you get. There may be ways to help you feel better. Sometimes, a treatment may be stopped until you are better.

Infections

You are more likely to get infections due to CLL or its treatment. Get a flu shot every year and a pneumococcal vaccine every five years. But, don't get a live virus vaccine. If you get frequent infections in your ear, sinuses, or lungs, you may get infusions of immunoglobulin to help prevent new infections.

Cancer

It is important to get screened for other cancers if needed. You may get screened for prostate cancer (men), breast and cervical cancer (women), and colon cancer. People with CLL are also at risk for skin cancer, the non-melanoma type. See a dermatologist once a year.

Autoimmune cytopenia

Autoimmune cytopenia is a condition in which your immune system attacks your blood cells. The

most frequent of these among people with CLL are autoimmune hemolytic anemia, immune-mediated thrombocytopenia, and pure red blood cell aplasia. Treatment may consist of corticosteroids, rituximab, IVIG, cyclosporin A, splenectomy, eltrombopag, or romiplostim.

Tumor lysis syndrome

Tumor lysis syndrome occurs when the waste released by dead cells is not quickly cleared out of your body. This results in kidney damage and severe blood electrolyte disturbances. It can be life threatening. Strong cancer treatments can cause

tumor lysis syndrome. Drink lots of water to help prevent it. There are also medicines you can take.

Blood transfusion

Some people being treated for CLL will need a blood transfusion. The transfusion should be done according to hospital standards. All blood should be treated with radiation before the transfusion. This will prevent the new blood from attacking your body.

Guide 5. Supportive care

Health condition	Type of supportive care
Flu	<ul style="list-style-type: none"> Influenza vaccine every year; avoid live vaccine
Pneumococcal infection	<ul style="list-style-type: none"> Pneumococcal vaccine every 5 years
Frequent, severe infections of ears, sinuses, or lungs	<ul style="list-style-type: none"> Antimicrobials (eg, antibiotics) If IgG <500 mg/dL, infusions of immunoglobulin every month
Cancer	<ul style="list-style-type: none"> Cancer screening as needed
Autoimmune cytopenia	<ul style="list-style-type: none"> Treat with corticosteroids, rituximab, IVIG, cyclosporin A, splenectomy, eltrombopag, or romiplostim
Tumor lysis syndrome	<ul style="list-style-type: none"> Prevent with hydration, managing hyperuricemia, and taking allopurinol, febuxostat, or rasburicase
Herpes	<ul style="list-style-type: none"> Prevent with a drug like acyclovir
Pneumocystis pneumonia	<ul style="list-style-type: none"> Prevent with drugs like sulfamethoxazole and trimethoprim
Cytomegalovirus reactivation	<ul style="list-style-type: none"> Take ganciclovir if virus is present or rising
Hepatitis B reactivation	<ul style="list-style-type: none"> Prevent or treat with entecavir
Tumor flare reaction	<ul style="list-style-type: none"> Prevent with steroids if lymph nodes are enlarged Treat with steroids and antihistamines
Blood clot	<ul style="list-style-type: none"> Treat with aspirin if not on an anticoagulant
Blood transfusion needed	<ul style="list-style-type: none"> Transfusion should be done according to hospital standards All blood products should be radiated

Review

- The goal of treatment is to achieve a remission and stop CLL from growing.
- The preferred first-line treatment is ibrutinib. Other options may be chemoimmunotherapy or CD20 antibody treatment.
- If first-line therapy doesn't work or the cancer relapses, you may receive the same or a different type of treatment. Options are similar to first-line treatment.
- CLL can transform into a faster-growing cancer. Clinical trials, chemotherapy, and PD-1 antibodies may be options if this happens.
- Supportive care is an important part of your cancer care. It can help prevent life-threatening infections.

4

Making treatment decisions

- 30 It's your choice
- 30 Questions to ask your doctors
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Having cancer is very stressful. While absorbing the fact that you have cancer, you have to learn about tests and treatments. In addition, the time you have to accept a treatment plan feels short. Parts 1 through 3 described the cancer and treatment options. Part 4 aims to help you make decisions that are in line with your beliefs, wishes, and values.

It's your choice

The role each person wants in choosing his or her treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. But, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which option to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still have to agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. Most patients do. In shared decision-making, you and your doctors

share information, weigh the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you are likely to get a higher quality of care and be more satisfied. You'll likely get the treatment you want, at the place you want, and by the doctors you want.

Questions to ask your doctors

You may meet with experts from different fields of medicine. Strive to have helpful talks with each person. Prepare questions before your visit and ask questions if the person isn't clear. You can also take notes and get copies of your medical records.

It may be helpful to have your spouse, partner, family member, or a friend with you at these visits. A patient advocate or navigator might also be able to come. They can help to ask questions and remember what was said. Suggested questions to ask are listed on the following pages.

What's my diagnosis and prognosis?

It's important to know that there are different types of cancer. Cancers with the same name can even greatly differ. Based on your test results, your doctor can tell you which type of cancer you have. He or she can also give a prognosis. A prognosis is a prediction of the pattern and outcome of a disease. Knowing the prognosis may affect what you decide about treatment.

1. What type of cancer do I have? From what type of cell did it form? Is this cancer common?
2. What is the Rai stage? Does this stage mean the leukemia is advanced?
3. Is this a fast- or slow-growing leukemia?
4. What tests do you recommend for me?
5. Where will the tests take place? How long will the tests take and will any test hurt?
6. What if I am pregnant?
7. How do I prepare for testing?
8. Should I bring a list of my medications?
9. Should I bring someone with me?
10. How often are these tests wrong?
11. Would you give me a copy of the pathology report and other test results?
12. Who will talk with me about the next steps? When?

What are my options?

There is no single treatment practice that is best for all people. There is often more than one treatment option along with clinical trial options. Your doctor will review your test results and recommend treatment options.

1. What will happen if I do nothing?
2. Can I just carefully monitor the cancer?
3. Do you consult NCCN recommendations when considering options?
4. Are you suggesting options other than what NCCN recommends? If yes, why?
5. Do your suggested options include clinical trials? Please explain why.
6. How do my age, health, and other factors affect my options? What if I am pregnant?
7. Which option is proven to work best?
8. Which options lack scientific proof?
9. What are the benefits of each option? Does any option offer a cure or long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?
10. What are the risks of each option? What are possible complications? What are the rare and common side effects? Short-lived and long-lasting side effects? Serious or mild side effects? Other risks?
11. How do you know if treatment is working?
12. What are my options if treatment doesn't working?
13. What can be done to prevent or relieve the side effects of treatment?
14. What are my chances that the cancer will relapse?

What does each option require of me?

Many patients consider how each option will practically affect their lives. This information may be important because you have family, jobs, and other duties to take care of. You also may be concerned about getting the help you need. If you have more than one option, choosing the option that is the least taxing may be important to you:

1. Will I have to go to the hospital or elsewhere? How often? How long is each visit?
2. What do I need to think about if I will travel for treatment?
3. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment?
4. How do I prepare for treatment? Do I have to stop taking any of my medicines? Are there foods I will have to avoid?
5. Should I bring someone with me when I get treated?
6. Will the treatment hurt?
7. How much will the treatment cost me? What does my insurance cover?
8. Will I miss work or school? Will I be able to drive?
9. Is home care after treatment needed? If yes, what type?
10. How soon will I be able to manage my own health?
11. When will I be able to return to my normal activities?

Deciding between options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another. Some ways to decide on treatment are discussed next.

2nd opinion

The time around deciding a treatment is very stressful. People with cancer often want to get treated as soon as possible. They want to make their cancer go away before it spreads farther. While cancer can't be ignored, usually there is time to think about and choose which option is best for you.

You may wish to have another doctor review your test results and suggest a treatment plan. This is called getting a 2nd opinion. You may completely trust your doctor, but a 2nd opinion about which option is best can help.

Copies of the pathology report, imaging, and other test results need to be sent to the doctor giving the 2nd opinion. Some people feel uneasy asking for copies from their doctors. However, a 2nd opinion is a normal part of cancer care.

When doctors have cancer, most will talk with more than one doctor before choosing their treatment. What's more, some health plans require a 2nd opinion. If your health plan doesn't cover the cost of a 2nd opinion, you have the choice of paying for it yourself.

If the two opinions are the same, you may feel more at peace about treatment. If the two opinions differ, think about getting a 3rd opinion. A 3rd opinion may help you decide between your options. Choosing

your cancer treatment is a very important decision. It can affect your length and quality of life.

Support groups

Support groups often include people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other people with CLL. If your hospital or community doesn't have support groups for people with CLL, check out the websites on the next page.

Compare benefits and downsides

Every option has benefits and downsides. Consider these when deciding which option is best for you. Talking to others can help identify benefits and downsides you haven't thought of. Scoring each factor from 0 to 10 can also help since some factors may be more important to you than others.

Websites

American Cancer Society

cancer.org/cancer/leukemia-chroniclymphocyticcll/index

Be The Match

bethematch.org

CLL Society Inc. (CLLS)

cllsociety.org

The Leukemia & Lymphoma Society (LLS)

[LLS.org/InformationSpecialists](https://lls.org/InformationSpecialists)

National Cancer Institute

cancer.gov/types/leukemia

National Coalition for Cancer Survivorship

canceradvocacy.org/toolbox

NCCN for Patients®

nccn.org/patients

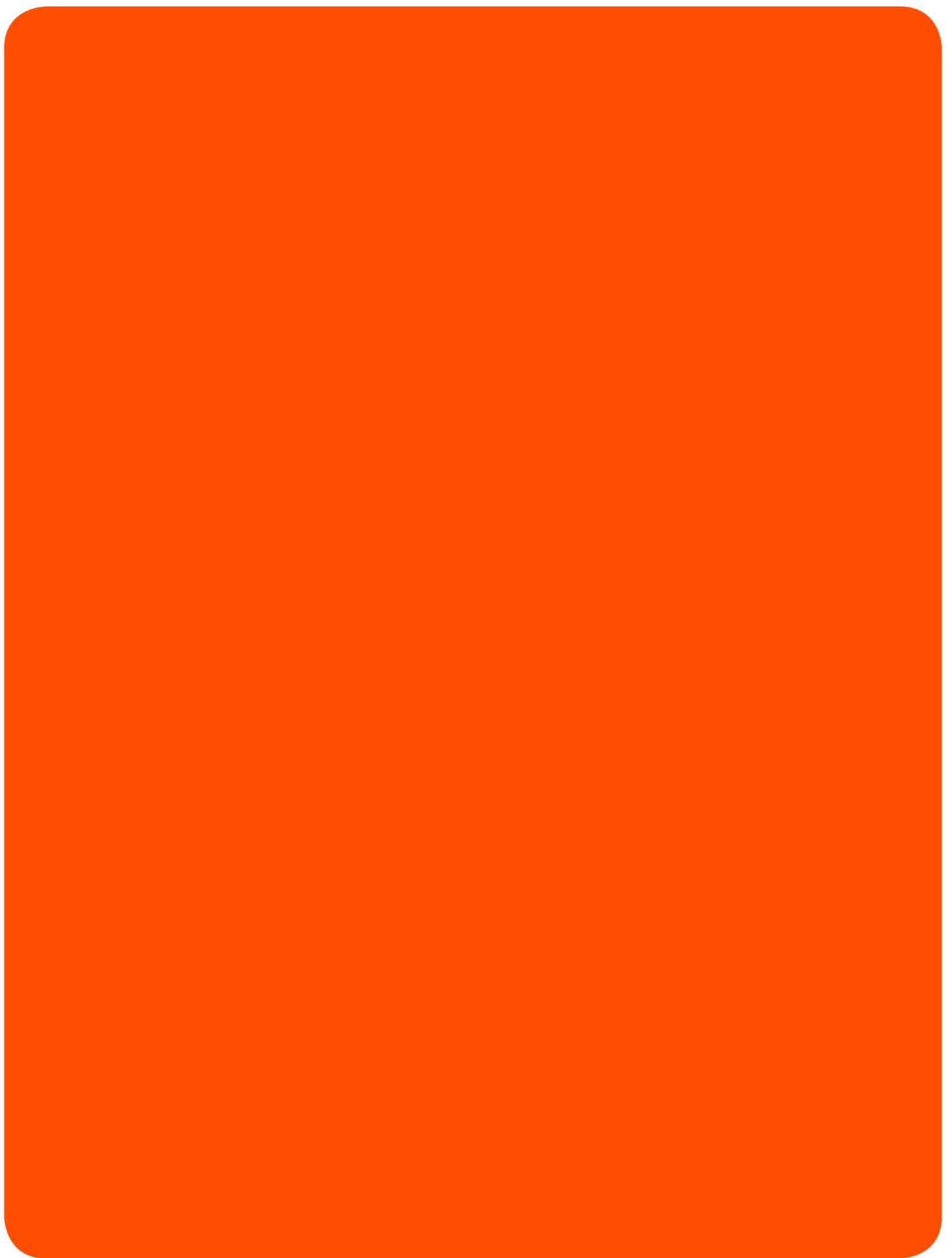
Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make informed decisions.
- Getting a 2nd opinion, attending support groups, and comparing benefits and risks may help you decide which treatment is best for you.



Meeting with and learning from other CLL patients is one of the best sources of emotional and educational support that I have seen. In a CLL support group we can share our feelings, experiences, and encouragement with the only ones who are able to see CLL from the inside out - the patients!”

– Barbara
Leukemia survivor



Words to know

alkylating agent

A drug that damages a cell's DNA by adding a chemical to it.

ALL

acute lymphoblastic leukemia.

allogeneic stem cell transplant

A cancer treatment that replaces abnormal blood stem cells with healthy donor cells. Also called allogeneic hematopoietic cell transplant.

AML

acute myeloid leukemia

anemia

A health condition in which hemoglobin is low.

antibody

A protein in blood that helps fight off infection. Also called an immunoglobulin.

autoimmune hemolytic anemia

An attack on red blood cells by the disease-fighting (immune) system.

B cell

A type of a white blood cell called a lymphocyte. Also called B-lymphocyte.

beta-2 microglobulin

A small protein made by many types of cells.

biopsy

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

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.

B symptoms

A set of symptoms caused by some B-cell cancers.

BTK

Bruton's tyrosine kinase

cancer stage

A rating of the outlook of a cancer based on its growth and spread.

CBC

complete blood count

chemotherapy

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

chromosome

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

clinical trial

A type of research that assesses how well health tests or treatments work in people.

CLL

chronic lymphocytic leukemia

CML

chronic myeloid leukemia

complete blood count (CBC)

A lab test that measures the number of red blood cells, white blood cells, and platelets.

comprehensive metabolic panel

Lab tests of up to 14 chemicals in your blood. Also called comprehensive chemistry panel.

computed tomography (CT)

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

contrast

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

CT

computed tomography

DAT

direct antiglobulin test

deoxyribonucleic acid (DNA)

A chain of chemicals in cells that contains coded instructions for making and controlling cells. Also called the "blueprint of life."

deoxyribonucleic acid (DNA) sequencing

A lab test used to detect abnormal changes in DNA.

diagnosis

An identification of an illness based on tests.

differential

A lab test of the number of white blood cells for each type.

DLBCL

diffuse large B-cell lymphoma

DNA

deoxyribonucleic acid

echocardiogram

A test that uses sound waves to make pictures of the heart.

fatigue

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

FDA

U.S. Food and Drug Administration

fertility specialist

An expert who helps people to have babies.

FISH

fluorescence in situ hybridization

flow cytometry

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

fluorescence in situ hybridization (FISH)

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

gene

Coded instructions in cells for making new cells and controlling how cells behave.

haptoglobin

One of the proteins made by the liver.

hemoglobin

A protein with iron in red blood cells.

hemolysis

The early death of red blood cells.

IGHV

immunoglobulin heavy-chain variable

IHC

immunohistochemistry

imaging

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

immune system

The body's natural defense against infection and disease.

immunoglobulin

A protein that is made by B cells to help fight off infection. Also called antibody.

immunohistochemistry (IHC)

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

immunomodulator

A cancer drug that modifies some parts of the body's disease-fighting system.

karyotyping

A lab test that makes a map of chromosomes to find defects.

kinase inhibitor

A drug that blocks the transfer of phosphate.

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.

lymph vessel

A small tube-shaped structure through which a fluid called lymph travels.

lymphatic system

A network of organs and vessels that collects and transports a fluid called lymph.

lymphocyte

One of three main types of white blood cells that help protect the body from illness.

lymphoma

A cancer of white blood cells called lymphocytes that are within the lymph system.

mantle cell lymphoma

A cancer of B cells that have too many proteins called cyclin D1.

MBL

monoclonal B lymphocytosis

medical history

A report of all your health events and medications.

monoclonal antibody

A type of cancer drug that stops growth signals.

monoclonal B lymphocytosis (MBL)

A health condition that causes a high number of B cells.

MRD

minimal residual disease

MUGA

multi-gated acquisition

multigated acquisition (MUGA) scan

A test that uses radiation to make pictures of the heart.

observation

A period of testing for changes in cancer status while not receiving treatment.

pathologist

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

performance status

A rating of one's ability to do daily activities.

PET

positron emission tomography

physical exam

A study of the body by a health expert for signs of disease.

PI3K

phosphoinositide 3-kinase delta

positron emission tomography (PET)

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

prognosis

The likely course and outcome of a disease based on tests.

pure red cell aplasia

A health condition in which the number of young red blood cells is very low.

purine analogs

A drug that prevents the DNA "building blocks" labeled A and G from being used.

Rai staging system

A rating scale of the outlook of chronic lymphocytic leukemia.

reticulocyte

A young red blood cell that is formed in bone marrow and present briefly in blood.

Richter's transformation

A change from a slow-growing leukemia into a fast-growing lymphoma. Also called Richter's syndrome.

side effect

An unhealthy or unpleasant physical or emotional response to treatment.

SLL

small lymphocytic leukemia

spleen

An organ to the left of the stomach that helps protect the body from disease.

steroid

A drug used to reduce redness, swelling, and pain, but also to kill cancer cells.

supportive care

Health care that includes symptom relief but not cancer treatment. Also called palliative care.

targeted therapy

A drug treatment that impedes the growth process specific to cancer cells.

tumor lysis syndrome (TLS)

A health condition caused by the rapid death of many cancer cells by treatment.

ultrasound

A test that uses sound waves to take pictures of the inside of the body. Also called ultrasonography.

uric acid

A chemical that is made when cells and certain eaten food break down.

vaccine

A dead or weak germ that is inserted into the body to prevent a disease.

NCCN Contributors

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

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Center and Cleveland Clinic Taussig
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uhhospitals.org/seidman
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case.edu/cancer

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cityofhope.org

Dana-Farber/Brigham and
Women's Cancer Center
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
877.332.4294
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massgeneral.org/cancer

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Fox Chase Cancer Center
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Mayo Clinic Cancer Center
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507.538.3270 • Minnesota
www.mayoclinic.org/cancercenter

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800.525.2225
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moffitt.org

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University of Alabama at Birmingham
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UC San Diego Moores Cancer Center
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cancer.ucsd.edu

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