Chronic Lymphocytic Leukemia (CLL)

Learning that you have cancer can be overwhelming. The goal of this book is to help you get the best cancer treatment. It explains which cancer tests and treatments are recommended by experts of chronic lymphocytic leukemia.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 26 of the world’s leading cancer centers. Experts from NCCN® have written treatment guidelines for doctors who treat leukemias. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of chronic lymphocytic leukemia. Key points of the book are summarized in the NCCN Quick Guide™ series on chronic lymphocytic leukemia. NCCN also offers patient resources on acute lymphoblastic leukemia, chronic myelogenous leukemia, multiple myeloma, and other cancer types. Visit NCCN.org/patients for the full library of patient books, summaries, and other resources.
NCCN aims to improve the care given to patients with cancer. NCCN staff work with experts to create helpful programs and resources for many stakeholders. Stakeholders include health providers, patients, businesses, and others. One resource is the series of books for patients called the NCCN Guidelines for Patients®. Each book presents the best practice for a type of cancer. The patient books are based on clinical practice guidelines written for cancer doctors. These guidelines are called the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Clinical practice guidelines list the best health care options for groups of patients. Many doctors use them to help plan cancer treatment for their patients. Panels of experts create the NCCN Guidelines®. Most of the experts are from NCCN Member Institutions. Panelists may include surgeons, radiation oncologists, medical oncologists, and patient advocates. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors. For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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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 with chronic lymphocytic leukemia. www.LLS.org/informationspecialists

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The NCCN Foundation supports the mission of the National Comprehensive Cancer Network® (NCCN®) to improve the care of patients with cancer. One of its aims is to raise funds to create a library of books for patients. Learn more about the NCCN Foundation at NCCN.org/foundation.

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Chronic Lymphocytic Leukemia (CLL)

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How to use this book

Who should read this book?

The information in this book is about treatment of chronic lymphocytic leukemia. It is the most common type of leukemia in adults. It does not address treatment for small lymphocytic leukemia. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It may help you discuss and decide with doctors what care is best.

They can also give you more information. As you read through this book, you may find it helpful to make a list of questions to ask your doctors.

The recommendations in this book are based on science and the experience of NCCN experts. However, these recommendations may not be right for you. Your doctors may suggest other tests and treatments based on your health and other factors. If other suggestions are given, feel free to ask your treatment team questions.

Where should I start reading?

Starting with Part 1 may be helpful. It explains what chronic lymphocytic leukemia is. Knowing more about this cancer may help you better understand its treatment.

Parts 2 through 5 address issues related to treatment. Part 2 lists which health tests and other care are needed before treatment. Part 3 briefly describes all the types of treatments. Part 4 explains which treatments are options for you and describes supportive care. Tips for making treatment decisions are presented in Part 5.

Making sense of medical terms

In this book, many medical words are included. These are words that you will likely hear from your treatment team. Most of these words may be new to you, and it may be a lot to learn.

Don’t be discouraged as you read. Keep reading and review the information. Don’t be shy to ask your treatment team to explain a word or phrase that you do not understand.

Words that you may not know are defined in the text or in the Dictionary. Words in the Dictionary are underlined when first used on a page.

Acronyms are also defined when first used and in the Glossary. Acronyms are short words formed from the first letters of several words. One example is CLL for chronic lymphocytic leukemia.
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CLL basics
You’ve learned that you have or may have chronic lymphocytic leukemia. It’s common to feel shocked and confused. Part 1 reviews some basics about this leukemia that may help you learn about it and start to cope. These basics may also help you start planning for treatment.
What are lymphocytes?

There are many types of blood cells. Three main types are platelets, red blood cells, and white blood cells. Each type has a different job. Platelets help control bleeding. Red blood cells carry oxygen throughout the body. White blood cells help fight germs. They are a part of your body’s disease-fighting (immune) system.

Lymphocytes are a type of white blood cell and include NK (natural killer) cells, B-cells, and T-cells. NK 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.

Most blood cells are made in bone marrow. See Figure 1.1. Bone marrow is the soft tissue in the center of most bones. Blood cells leave bone marrow and travel in blood throughout your body.

There are many lymphocytes in bone marrow, blood, and your lymphatic system. Your lymphatic 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 your thymus, spleen, and tonsils.

Figure 1.1
Blood cells in bone marrow

Most blood cells are first formed in the marrow of bones. Red blood cells, white blood cells, and platelets are the three main types of blood cells. Lymphocytes are a type of white blood cell. They help fight illness in your body.
What is CLL?

Cancer is a disease of cells. Leukemias are cancers of white blood cells and start in bone marrow and blood. CLL (chronic lymphocytic leukemia) is one type of leukemia that starts in lymphocytes called B-cells. Lymphomas are cancers that start in lymphocytes within the lymphatic system. However, leukemias can spread to the lymphatic system, and lymphomas, to bone and bone marrow.

CLL cells are found mostly within blood, bone marrow, and lymph nodes. Related, SLL (small lymphocytic leukemia) is a cancer that also starts in B-cells but occurs mostly within the lymphatic system. CLL and SLL are thought to be the same cancer but differ in the fact that people with SLL do not have high numbers of white blood cells. Their treatment is much alike. The focus of this book is CLL. CLL occurs mostly in people who are middle aged or older.

Inside of cells are coded instructions for building new cells and controlling how cells behave. These instructions are called genes. Genes are a part of DNA (deoxyribonucleic acid), which is grouped together into bundles called chromosomes. See Figure 1.2. Changes (mutations) in genes cause normal B-cells to become cancer cells. Researchers are still trying to learn what causes genes to change and cause cancer.

Figure 1.2
Genetic material in cells

Most human cells contain the “blueprint of life”—the plan by which our bodies are made and work. The plan is found inside of chromosomes, which are long strands of DNA that are tightly wrapped around proteins. Genes are small pieces of DNA that contain instructions for building new cells and controlling how cells behave. Humans have about 24,000 genes.
Changes in genes cause cancer cells to grow more quickly and live longer than normal cells. Normal cells grow and then divide to form new cells when needed. They also die when old or damaged as shown in Figure 1.3. In contrast, cancer cells make new cells that aren’t needed and don’t die quickly when old or damaged.

CLL can be a fast- or slow-growing cancer. Often, it grows slowly. If slow, you may not know you have CLL for years because you have no symptoms. Over time, CLL cells will crowd out healthy cells in bone marrow. A normal number of red blood cells and platelets will not be made. 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.

Figure 1.3
Normal cell growth vs cancer cell growth

Normal cells increase in number when they are needed and die when old or damaged. In contrast, cancer cells quickly make new cells and live longer because of abnormal changes in genes.
Do I have CLL?

Your blood needs to be tested to confirm (diagnose) CLL. Often, CLL is diagnosed during a routine blood test that is part of your normal health care. For a blood test, your doctor will insert a needle into your vein to remove a sample of blood. The needle may bruise your skin and you may feel dizzy from the blood draw. Your blood sample will then be sent to a lab where a pathologist will test it. A pathologist is a doctor who’s an expert in testing cells to find disease.

The number of abnormal B-cells in your blood must be known for diagnosis. CLL requires the presence of 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.

For diagnosis, B-cells should also be tested for which proteins are in the cells’ surface (membrane). See Figure 1.4. This is called immunophenotyping. CLL cells typically have either kappa or lambda light chain proteins but not both. Light chain proteins are part of antibodies, which help to kill germs. CLL cells also typically have CD5, CD19, and CD23 proteins, some CD20, and no CD10 proteins.

If there are fewer than 5,000 monoclonal B-cells, no enlarged lymph nodes, and no other signs of CLL, you may have MBL (monoclonal B-lymphocytosis). BML is common, especially among older adults. It is not cancer and very few people with BML develop CLL. The recommended care for BML is observation. Observation or “watch-and wait” is a period of testing to watch for changes in status. Some people won’t need treatment for years if at all.

A common test of cells is IHC (immunohistochemistry). This method involves applying a chemical marker to cells and looking at them with a microscope. Flow cytometry is a newer method by which some cell tests can be done. Flow cytometry can be used to count B-cells, confirm clonality, and do immunophenotyping. This method involves first adding a marker—a light-sensitive dye—to cells. Then, your blood will be passed through a flow cytometry machine. The machine measures surface proteins on thousands of cells. Flow cytometry is commonly used to diagnose CLL.

When being tested for CLL, mantle cell lymphoma needs to be ruled out. This cancer has high levels of the protein called cyclin D1. There is too much cyclin...
D1 because of abnormal chromosomes in cells. To rule out mantle cell lymphoma, your blood may be tested with a cytospin machine for cyclin D1. Another test option is FISH (fluorescence in situ hybridization) to test for abnormal chromosomes.

Most often, flow cytometry on a blood sample can be used to diagnosis CLL. However, for some people, another method is needed. In these cases, a biopsy of your lymph nodes is advised. A biopsy removes tissue samples to test for cancer. You will need anesthesia to numb the site. Then, part or all of one or more lymph nodes will be removed through a cut made in your skin. B-cells from the removed nodes will be tested with an IHC panel for the immunophenotype. The panel should include testing for CD3, CD5, CD10, CD20, CD23, and cyclin D1 proteins.
Review

- White blood cells are a part of your body’s immune system. Lymphocytes are a type of white blood cell and include NK cells, B-cells, and T-cells.

- Leukemias are cancers of white blood cells and start in bone marrow and blood. CLL is one type of leukemia that starts in B-cells.

- Your blood needs to be tested to diagnose CLL. To diagnose, doctors look for very high numbers of abnormal B-cells. They also look for proteins that are common and uncommon to CLL cells.
Treatment planning
Doctors plan treatment with many sources of information. One of these sources is tests of your health and the cancer. Part 2 describes who should receive which tests before treatment. Some of these tests are repeated during and after treatment.

Besides tests, Part 2 describes other types of care that are important to receive before cancer treatment. Everyone does not need to start CLL treatment right away. Part 2 ends with explaining how doctors decide when treatment should be started.

Medical history

Your medical history includes any health events and medicines you’ve taken in your life. You will be asked about illnesses, injuries, health conditions, and more. Some health problems run in families. Thus, your doctor may also ask about the health of your blood relatives.

Some signs and symptoms of CLL are 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.

A medical history is one of the tests needed for treatment planning. See Chart 2.1 for a complete list of care that is recommended prior to treatment. Some types of care are for anyone with CLL while others may be useful for some people.
Physical exam

Doctors often give a physical exam along with taking a medical history. A physical exam is a study of your body for signs of disease. During this exam, your doctor will listen to your lungs, heart, and gut. Parts of your body will likely be felt to see if organs are of normal size, are soft or hard, or cause pain when touched.

For CLL, there are certain parts of your body that should be checked. CLL is often found in lymph nodes, so areas with lots of lymph nodes should be examined. High numbers of lymph nodes exist in the middle of your chest, neck, throat, armpit, groin, pelvis, and along your gut. The size of your spleen and liver should also be assessed.

Results of your medical history and physical exam will be used to rate your performance status. Performance status is your ability to do daily activities. It is used by doctors to assess if you can undergo certain treatments.

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<tr>
<td>• Complete blood count with differential</td>
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<td>• Echocardiogram or MUGA</td>
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<td>• Pregnancy test if you can have babies</td>
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Blood tests

Blood tests are used to diagnose CLL as discussed in Part 1. They are also used for at least three other reasons. First, blood tests can be used to know the outlook (prognosis) of CLL. Prognosis is a prediction of the pattern and outcome of a disease. Second, some blood tests are used to know the extent (stage) of cancer. How staging is related to starting treatment is discussed at the end of this chapter. Third, blood tests can help to find other diseases including those related to CLL. It’s important to treat all illnesses. Blood tests for CLL are:

Genetic tests
FISH test. It is very common for CLL cells to have abnormal chromosomes. In CLL cells, chromosomes that commonly have defects include chromosomes 11, 12, 13, and 17. FISH is a test that is used to search for abnormal chromosomes and genes. FISH is sometimes used for diagnosis as described in Part 1 but also for prognosis. It can be done using either blood or bone marrow cells. It is a helpful test but not essential for treatment planning.

Missing (deleted) parts of chromosomes 11 or 17 are signs of a poor prognosis. A good prognosis is linked to deleted parts of chromosome 13, if it is the only abnormal chromosome. Trisomy is when there are three copies of a chromosome in a cell instead of the normal two. Trisomy 12 is linked to neither a poor or good prognosis.

Karyotype. A karyotype is a picture of the chromosomes in cells. It shows if there is a defect in the size, shape, and number of chromosomes. A blood or bone marrow sample can be used. Chemicals are added to the sample to start cell growth. For CLL, a chemical called CPG should be used.

A "complex karyotype" is linked to a poorer prognosis. A complex karyotype is when there are 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. Read Part 4 for more information.

DNA sequencing. DNA sequencing is a lab test of blood or marrow that is used to look for mutations in genes. This test reveals the order of the chemicals that make up DNA. DNA sequencing is used to test for mutations in the IGHV (immunoglobulin heavy-chain variable) region and TP53 genes.

Immunoglobulins are Y-shaped proteins that help fight germs. In Part 1, they were described by their other name—antibodies. Normal antibodies are made of two heavy chain proteins and two light chain proteins. See Figure 2.1. IGHV region genes in B-cells contain instructions for making the heavy chain protein. These genes may or may not be mutated in people with CLL. Prognosis is good if IGHV is mutated.

TP53 is the gene that makes a protein that signals for either the repair or destruction of damaged cells. Thus, it helps to prevent tumors from forming. DNA sequencing can be used to learn if this gene is mutated. If mutated, prognosis is poor.

Cell protein tests
To help decide prognosis, lab tests are done to look for specific proteins in CLL cells. These proteins are CD38 and ZAP-70. They are related to the IGHV mutation. The presence of increased levels of either CD38 or ZAP-70 is a sign of a fast-growing cancer.

Flow cytometry, IHC, or methylation analysis can be used to test for ZAP-70 status. Methylation analysis is the study of chemical tags, called methyl groups, which attach to DNA. It is not a commonly used test outside of a clinical trial. Likewise, testing for ZAP-70
protein is a challenge and should only be done within a clinical trial. It is not an essential test for CLL.

**Complete blood count with differential**

A CBC (complete blood count) measures the number of blood cells in a blood sample. It includes numbers of white blood cells, red blood cells, and platelets. Your blood counts may be low or high because of cancer or another health problem. It is an essential test that gives a picture of your overall health.

There are several types of white blood cells in your body. A white cell differential counts the number of each type. It also checks if the counts are in balance with each other. Your doctor can learn from this test what the cause of an abnormal white blood count is.

It is also used to stage the cancer and check if treatment is working.

**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. The tests show if the level of chemicals are too low or high. Abnormal levels can be caused by cancer or other health problems.

**Hepatitis B testing**

CLL and some of its treatments can cause the hepatitis B virus to become active again. Thus, tell your treatment team if you’ve ever been infected with hepatitis B. For others, ask your treatment team if you should get tested.

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**Figure 2.1 Immunoglobulin (A.K.A antibody)**

Antibodies attach to germs so your immune system can find and destroy the germs. Normal antibodies are Y-shaped proteins made of two heavy chain proteins and two light chain proteins. Within CLL cells, the genes for making the heavy chain protein sometimes aren’t normal.
Quantitative immunoglobulins
There are three major types of antibodies in blood. They are IgG, IgA, and IgM. Your blood can be tested to measure the amount of each type of antibody. Testing will show if the level of any type of antibody is abnormal—too high or too low.

Some people with CLL have low levels of antibodies before cancer treatment. They may be sick often. Testing of antibodies can help your doctors know if you need treatment to prevent or cure an infection.

Haptoglobin
Haptoglobin is a protein made by the liver. It attaches to free hemoglobin in blood to mark it for removal. Free hemoglobin is a protein with iron that was released from destroyed red blood cells.

Low amounts of haptoglobin can be a result of autoimmune hemolytic anemia. Autoimmune hemolytic anemia is when your body mistakes red blood cells for invaders and destroys them. Haptoglobin level is one of the tests needed to confirm autoimmune hemolytic anemia.

Autoimmune hemolytic anemia is common among people with CLL. Advanced CLL and some of its treatments can cause it. A cancer treatment called fludarabine should not be used if you have severe autoimmune hemolytic anemia.

Reticulocyte count and direct Coombs test
Low numbers of healthy red blood cells is called anemia. There are many causes of anemia. Two of the many causes are pure red cell aplasia and hemolysis. Pure red cell aplasia is when the early (precursor) cells that form into red blood cells are almost absent in bone marrow. Hemolysis is when red blood cells are being destroyed too early.

If you have anemia, you should be tested for these causes. Reticulocytes are precursor cells of mature red blood cells. Low numbers of reticulocytes is a sign of pure red cell aplasia, and high numbers indicate hemolysis. The other test is a direct Coombs test. This test can detect if antibodies are stuck to and killing red blood cells.

Beta-2 microglobulin
Beta-2 microglobulin is a small protein made by many types of cells, including CLL cells. It is measured with a blood chemistry test. High levels of this protein may be a sign of CLL that is harder to treat.

Lactate dehydrogenase
Lactate dehydrogenase is a protein that is in most cells. It gets into your blood when a cell is damaged. Thus, a high level of lactate dehydrogenase is a sign of cell damage. High levels can be caused by cancer or other health problems. If related to cancer, high levels may be a sign that treatment may be needed now or soon.

Uric acid
Some people with CLL are at risk for tumor lysis syndrome. This syndrome can be life threatening. It 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.

Tumor lysis syndrome can occur among people with CLL who are undergoing strong cancer treatments. The cancer treatment kills many cancer cells and results in too much waste.

Your doctors may want to know your uric acid levels before starting treatment. You may be given certain medications that can help prevent tumor lysis syndrome. Also, drinking plenty of water throughout chemotherapy can help. Ask your treatment team for more information.
My notes
**Imaging tests**

*Imaging tests* make pictures (images) of the inside of your body. They can show where cancer is. Depending on the test, you may need to stop taking some medicines and stop eating and drinking for a few hours before the scan. If you are nervous, you may be given a drug, called a *sedative*, to help you relax.

Imaging machines are large. You will likely be lying down during testing. At least part of your body will be in the machine. *Figure 2.2* shows a CT machine, which is described next.

After the test, you will likely be able to resume your activities right away. If you took a sedative, you will have a waiting period. You may not learn of the results for a few days since a radiologist needs to see the pictures. A radiologist is a doctor who’s an expert in reading the images.

**CT scan**

*CT* (computed tomography) may be needed before starting and during treatment. CT takes many pictures of a body part from different angles using x-rays. A computer combines the x-rays to make detailed pictures.

A *contrast* dye is used for CT. It makes the pictures clearer. The dye will be injected into a vein in your hand or arm. You will also be given a liquid contrast to drink.

The contrast may cause you to feel flushed or get hives. Rarely, serious allergic reactions occur. Tell your doctor and the technicians if you have had bad reactions to contrast. Also, tell them if you get nervous when in small spaces. You may be given a sedative to help you relax.

CT is needed if you have symptoms suggesting your lymph nodes are large. If needed, a CT of your chest, belly area, and between your hip bones is advised. CT scans received during treatment can help your doctors know if treatment is working.

**PET/CT scan**

CT is sometimes done along with another imaging test called PET (positron emission tomography). For PET, a sugar radiotracer will be injected into...
your body. The radiotracer is detected with a special camera. Cancer cells appear brighter than normal cells because they use sugar (glucose) more quickly.

PET/CT is often not useful for CLL. If given, it is used to help 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 like diffuse large B-cell lymphoma. PET/CT is an essential test for this cancer.

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**Bone and marrow test**

A bone marrow biopsy removes a sample of bone and soft bone marrow. A bone marrow aspiration removes a small amount of liquid bone marrow. These tests aren’t needed to diagnose CLL. However, your doctor may order these tests to learn what’s causing low numbers of blood cells.

Often, these tests are done at the same time on the back of hip bone. You may receive a light sedative before the test. You will likely lie on your side as shown in Figure 2.3. Your doctor will clean your skin then give local anesthesia to numb the site. Once numb, a hollow needle will be inserted into your skin and then pushed into the bone to remove the liquid bone marrow with a syringe. Then, a wider needle will be inserted into the bone and rotated to remove bone and soft marrow. These biopsies may cause bone pain and can bruise your skin for a few days. The samples will be sent to a lab for testing.

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**Figure 2.1 Bone marrow biopsy**

Doctors use a bone marrow biopsy to remove a sample of bone and marrow for testing. A bone marrow aspiration removes a small amount of liquid bone marrow.
Heart tests

Some cancer treatments can damage your heart. Thus, your doctor may test how well your heart works to plan treatment. If it isn’t working well, you may receive other treatment.

An echocardiogram is an imaging test of your heart. It uses sound waves (ultrasound) to make pictures. During this test, you will be lying down. Small patches will be placed on your chest to track your heartbeat. Next, a probe with gel on its tip will be slid across part of your bare chest. A picture of your beating heart will be seen at once on a screen. The pictures are recorded for future viewing.

A MUGA (multi-gated acquisition) scan measures how well your heart is pumping blood. For this test, patches will be placed on your chest to track your heartbeat. Also, a radiotracer will be injected into your vein. Pictures of your heart are taken with a special camera that can detect the radiation released by the tracer.

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 father 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 and more

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

Part of treatment planning involves deciding when to start 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. The cancer stage is a rating by your doctors that suggests what the prognosis of the cancer is.

The Rai staging system is used to decide whether to start treatment. This system consists of five cancer stages. The cancer stages are defined by the results of your physical exam and blood tests. The five stages are:

- **Stage 0** is defined by normal test results except for high number of **lymphocytes** in blood. The likelihood of the cancer getting worse is low.

- **Stage I** is defined as high number of lymphocytes in blood 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. 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 stages labeled A, B, and C. The stages are based on your physical exam and blood tests. The Binet system may be helpful for prognosis but isn’t used in this book to decide starting treatment.

If you have Rai stage 0, I, and II CLL, treatment may not be needed now. You should be further assessed to learn if treatment is needed. Signs to start treatment include symptoms of active CLL, such as drenching night sweats, severe **fatigue**, fever without proof of infection, and unplanned weight loss. If these signs are present, treatment is advised. If these signs are not present, observation is advised. Treatment can be started when any the listed signs appear or the cancer advances to stage III or IV.

Most people with stage III or IV CLL need to be treated, even when newly **diagnosed**. In some cases, observation may be an option if your blood cell counts aren’t too low and don’t drop more. Treatment is advised if the cancer is stage III and IV and your blood cell counts are falling.
Review

- 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 examine your body for signs of disease. He or she will check if your lymph nodes, liver, or spleen is large. Your doctor will also rate your ability to do everyday activities.

- Blood tests can be done to assess the prognosis of CLL and for other health conditions.

- 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.

- 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.

- 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 now, get a pregnancy test since some cancer treatments can harm unborn babies.

- You may not need to start treatment for CLL right away. Your doctors will decide whether to advise starting treatment based on the signs and symptoms of CLL, test results, and the cancer stage.
Overview of cancer treatments
In Part 3, the main treatment types that are recommended by NCCN experts for CLL are briefly described. These treatments are for people who have or will be starting treatment. Knowing what a treatment is will help you understand your treatment options listed in Part 4. There is more than one treatment for CLL. Not every person with CLL will receive every treatment described in this chapter.

Clinical trials

New tests and treatments aren’t offered to the public as soon as they’re made. They first need to be studied. A clinical trial is a type of research that studies a test or treatment. Clinical trials are the preferred treatment option of NCCN experts for CLL.

Clinical trials study how safe and helpful tests and treatments are. When found to be safe and helpful, they may become tomorrow’s standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help people with CLL. Future tests and treatments that may have better results than today's treatments will depend on clinical trials.

New tests and treatments go through a series of clinical trials to make sure they're safe and work. Without clinical trials, there is no way to know if a test or treatment is safe or helpful. Clinical trials have four phases. Some examples of the four phases for treatment are:
• **Phase I trials** – aim to find the best dose of a new drug with the fewest side effects.

• **Phase II trials** – assess if a drug works to treat a specific type of cancer.

• **Phase III trials** – compare a new drug to the standard treatment.

• **Phase IV trials** – test new drugs approved by the U.S. FDA (Food and Drug Administration) in many patients with different types of cancer.

Joining a clinical trial has benefits. First, you’ll have access to the most current cancer care. Second, you will receive the best management of care. Third, the results of your treatment—both good and bad—will be carefully tracked. Fourth, you may help other people who will have cancer in the future.

Clinical trials have risks, too. Like any test or treatment, there may be side effects. Side effects are unhealthy or unpleasant physical or emotional responses to treatment. Also, new tests or treatments may not help. Another downside may be that paperwork or more trips to the hospital are needed.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. This is to know that any progress is because of the treatment and not because of differences between patients. Likewise, some clinical trials are only open to people who have not started treatment while others are.

To join, you’ll need to review and sign a paper called an informed consent form. This form describes the study in detail. The study’s risks and benefits should be described and may include others than those listed above.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you’re getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 5.
Chemotherapy

Chemotherapy, or “chemo,” includes drugs that disrupt the life cycle of cancer cells so they can’t increase in number. Some chemotherapy drugs kill cancer cells by damaging their DNA or by disrupting the making of DNA. Other drugs interfere with cell parts that are needed for making new cells. Thus, no new cells are made to replace dying cells. Chemotherapy is often used to treat CLL.

Many chemotherapy drugs work when cells are in an active growth phase. During the active growth phase, cells grow and divide to form a new cell. Chemotherapy drugs that disrupt the growth phase work well for cancer cells that are growing and dividing quickly. Other chemotherapy drugs work whether cells are in a growth or resting phase. Chemotherapy can kill both cancer and normal cells.

Most chemotherapy drugs for CLL are liquids that are slowly injected into a vein. Some are made as pills that can be swallowed. By any method, the drugs travel in your bloodstream to treat cancer throughout your body. Doctors use the term “systemic” when talking about a cancer treatment for the whole body. Chemotherapy and other drugs used to treat CLL are listed in Chart 3.1.

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 drugs are used. Often, one total cycle is 4 weeks long.

Chemotherapy may consist of one or more drugs. When only one drug is used, it is called a single agent. However, not all drugs work the same way, so often more than one drug is used. A combination regimen is the use of two or more chemotherapy drugs.

Part 4 is a guide that explain who should receive which treatments. You will learn which regimens may be part of your treatment. Chemotherapy is sometimes given in high doses and followed by a stem cell transplant. Stem cell transplant is described later in this chapter.

Side effects of chemotherapy

Side effects of chemotherapy differ between people. Some people have many side effects. Others have few. Some side effects can be very serious while others can be unpleasant but not serious. Most side effects appear shortly after treatment starts and will stop after treatment. However, other side effects are long-term or may appear years later.

Side effects of chemotherapy depend on many factors. These factors include the drug type, amount taken, length of treatment, and the person. In general, most side effects are caused by the death of fast-growing cells. These cells are found in the blood, gut, hair follicles, and mouth. Thus, common side effects of chemotherapy include low blood cell counts, not feeling hungry, nausea, vomiting, diarrhea, hair loss, and mouth sores. Long-term side effects of chemotherapy for CLL include increased risk for getting infections.

Not all side effects of chemotherapy are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.
### Chart 3.1 Drug treatment for CLL

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Brand name (sold as)</th>
<th>Type of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alemtuzumab</td>
<td>Campath®</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Bendamustine hydrochloride</td>
<td>Treanda®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>Leukeran®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Cladribine</td>
<td>Leustatin®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>—</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>Cytosar-U®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Doxorubicin hydrochloride</td>
<td>—</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Fludarabine phosphate</td>
<td>Fludara®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Ibrutinib</td>
<td>Imbruvica®</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Idelalisib</td>
<td>Zydelig®</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>Revlimid®</td>
<td>Immunotherapy</td>
</tr>
<tr>
<td>Methylprednisolone; Methylprednisolone acetate; Methylprednisolone sodium succinate</td>
<td>A-Methapred, Depo-Medrol®, Medrol®, Solu-Medrol®</td>
<td>Steroid</td>
</tr>
<tr>
<td>Obinutuzumab</td>
<td>Gazyva™</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Ofatumumab</td>
<td>Arzerra®</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>Eloxatin®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Pentostatin</td>
<td>Nipent®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Prednisone</td>
<td>—</td>
<td>Steroid</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Rituxan®</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Vincristine sulfate</td>
<td>—</td>
<td>Chemotherapy</td>
</tr>
</tbody>
</table>
Steroids

Steroids are a type of drug that is often used to relieve inflammation. Steroids can also have anti-cancer effects. Methylprednisolone is a corticosteroid used to treat CLL. Read Part 4 for more information on when it’s used.

Methylprednisolone is given in high doses along with rituximab. Rituximab is described in the Targeted therapy section in this chapter. Methylprednisolone can either be injected into your vein or swallowed in pill form. It is often taken for a few days during a 1-month cycle.

Prednisone is another steroid that is used to treat CLL. It is given along with some chemotherapy regimens. Prednisone is made in pill form and is taken once a day with food.

Most side effects of steroids fade away once the drugs are stopped. Common side effects include feeling hungry, trouble sleeping, slow wound healing, upset stomach, and swelling in the ankles, feet, and hands. Methylprednisolone with rituximab increases the likelihood of getting infections.

Immunomodulators

The immune system is your body’s natural defense against illness. Immunomodulators are drugs that modify different parts of the immune system. Lenalidomide is an immunomodulator used to treat CLL.

Lenalidomide is made in pill form. It is given in cycles of treatment days followed by days of rest. A cycle may consist of 3 weeks of treatment and 1 week of rest. It may also be given for 4 straight weeks. Cycles may repeat until the cancer grows or side effects become severe.

Lenalidomide treats cancer in more than one way. As an immunomodulator, it boosts the immune system. It also helps stop cancer cells from increasing in number. Third, it also works like a type of targeted therapy called angiogenesis inhibitors. These drugs stop the growth of new blood vessels that would provide food (nutrients) to the cancer.

Common side effects include low blood counts, diarrhea, itching, rash, and fatigue. Serious but less common side effects include blood clots, bleeding disorders, loss of vision, and skin cancer. Ask your treatment team for a full list of side effects.
Targeted therapy

Targeted therapy is a class of drugs that stops the action of molecules that help cancer cells grow. It is less likely to harm normal cells than chemotherapy. There are 6 targeted therapies that are used to treat CLL. Four of them are monoclonal antibodies and two are kinase inhibitors.

Monoclonal antibodies are man-made antibodies that attach to proteins on cancer cells. The monoclonal antibodies used to treat CLL attach to antigens. When antibodies are attached to antigens on a cell, the cell is marked to be destroyed by your immune system.

Kinases are molecules that move chemicals, called phosphates, from one molecule to another. Kinase inhibitors stop the phosphates from being moved. Kinase inhibitors often block growth signals within cancer cells. This reduces the number of new cancer cells being made.

Next, the targeted therapies for CLL are briefly described. Some side effects are listed. Ask your treatment team for a full list of common and rare side effects. In Part 4, information on who should receive these drugs is provided.

Alemtuzumab

Alemtuzumab is a monoclonal antibody that attaches to a molecule called CD52. CD52 is found on CLL cells, healthy B-cells and T-cells, as well as other cells. Alemtuzumab is used alone and sometimes with other medicines to treat CLL.

Alemtuzumab is a liquid that will be slowly injected into your vein. It may take up to two hours to get the full dose. Alemtuzumab can also be given as an injection under the skin. Alemtuzumab is often given three times a week for 12 weeks.

Common side effects include an allergic reaction when receiving the medicine. Also, you may feel nausea, vomit, get diarrhea, and have trouble sleeping. Blood counts are often low when taking this medicine. Taking alemtuzumab will increase your chances of getting a cytomegalovirus or other infection.

Ibrutinib

Ibrutinib is a kinase inhibitor. It stops a kinase called BTK (Bruton’s tyrosine kinase). This kinase is found inside of CLL cells and normal B-cells.

Ibrutinib is usually taken without other cancer medicines to treat CLL. It is made in pill form and taken once a day around the same time. Your doctor will tell you how many pills you need for your dose.

Common side effects of ibrutinib include diarrhea, tiredness, muscle and bone pain, bruising, nausea, upper respiratory tract infection, and rash. There may be a short-lived increase in lymphocytes when first taking ibrutinib. Serious but uncommon side effects include bleeding, severe infections, heart and kidney problems, and other cancers.

Idelalisib

Idelalisib is a kinase inhibitor. It stops a kinase called PI3K (phosphoinositide 3-kinase delta). This kinase is found inside of CLL cells and normal B-cells.

Idelalisib is used alone or sometimes with rituximab to treat CLL. It is made in pill form and is taken twice a day. Your doctor will tell you how many pills you need for your dose.

Common side effects of idelalisib include diarrhea, fever, fatigue, nausea, cough, lung infection, belly pain, chills, and rash. White blood counts are often low when taking this medicine. However, there may be a short-lived increase in lymphocytes when first taking idelalisib. Serious but uncommon side effects
include liver and lung problems, skin problems, severe diarrhea, and holes in your gut.

**Obinutuzumab**

Obinutuzumab attaches to a molecule on CLL cells called CD20. See Figure 3.1. It works by marking cells for destruction but it may directly kill the cells, too. It is used alone and sometimes with chemotherapy to treat CLL.

Obinutuzumab is a liquid that will be slowly injected into your vein. It takes a few hours to get the full dose. Obinutuzumab is given on some days during six 28-day treatment cycles.

You may have an allergic reaction while receiving obinutuzumab. Tumor lysis syndrome, infections, and hepatitis are more likely while taking obinutuzumab. Although not common, you may become confused, dizzy, and have difficulty walking, talking, or seeing.

**Ofatumumab**

Ofatumumab is another monoclonal antibody that attaches to CD20. However, it attaches to a different part of CD20. It is used alone and sometimes with chemotherapy to treat CLL.

Ofatumumab is a liquid that will be slowly injected into your vein. It takes about 6 hours to receive the first dose. Other doses may be given in less time. Ofatumumab is often given once a week for 8 weeks. Then it’s restarted after a 4- or 5-week break. After the break, ofatumumab is often received once a month for four months.

You may have an allergic reaction while receiving ofatumumab. Other common side effects include low blood cell counts, infections, diarrhea, nausea, fatigue, and rash. Hepatitis B can be reactivated while taking ofatumumab.

**Rituximab**

Like obinutuzumab and ofatumumab, rituximab also attaches to CD20. It works by marking cells for destruction but it may directly kill the cells, too. It is sometimes used alone, with chemotherapy, or with another targeted therapy to treat CLL.

Rituximab is a liquid that will be slowly injected into your vein. It often takes a few hours to receive the full dose. How often you will receive rituximab depends on what other cancer medicines you are receiving.

You may have an allergic reaction while receiving rituximab. Other common side effects are chills, infections, body aches, tiredness, and low blood cell counts. Rituximab also increases your chances for
Stem cell transplant

Hematopoietic stem cells are cells that develop into mature blood cells. Stem cells and mature blood cells are made in bone marrow. The goal of a stem cell transplant is to cure cancer by replacing unhealthy blood stem cells with healthy ones that will attack cancer cells. This is done by suppressing the bone marrow and cancer with chemotherapy then transplanting healthy blood stem cells. The healthy blood stem cells will grow, form new marrow and blood cells, and attack remaining cancer cells.

Using stem cells from a donor is called an allogeneic stem cell transplant. Besides a new immune system, another benefit of this transplant is the GVL (graft-versus-leukemia) effect. The GVL effect is an attack on cancer cells by the transplanted stem cells.

Allogeneic stem cell transplant is sometimes used to treat CLL. It is an option for some people after drug treatment has been received. The steps of treatment with allogeneic stem cell transplant are described next.

HLA typing

Special testing must be done to find the right donor for you. The donor and your tissue type must be a near-perfect match for this treatment to work. The test used to check tissue type is called HLA (human leukocyte antigen) typing. A blood sample is needed to perform the test.

Conditioning chemotherapy

Before the transplant, you will receive chemotherapy. The chemotherapy will suppress your immune system, allowing the donor cells to grow. The high-dose chemotherapy also destroys normal cells in the bone marrow. This greatly weakens your immune system so that your body doesn’t kill the transplanted stem cells. Not every person can tolerate the high-dose chemotherapy before the transplant. Side effects of chemotherapy are described earlier in this chapter.

Transplanting stem cells

After chemotherapy, you will receive the healthy stem cells through a transfusion. A transfusion is a slow injection of blood products through a central line into a large vein. A central line (or central venous catheter) is a thin tube. The tube will be inserted into your skin through one cut and into your vein through a second cut. Local anesthesia is used. This process can take several hours to complete.

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. You may be given an antibiotic to prevent or treat infection. You may also be given a blood transfusion to prevent bleeding and to treat anemia. While waiting for the cells to engraft, you will likely feel tired and weak.
Complementary and alternative medicine

**CAM (complementary and alternative medicine)** is a group of treatments that aren’t often given by doctors. There is much interest today in CAM for cancer. Many CAMs are being studied to see if they are truly helpful.

Complementary medicines are treatments given along with usual medical treatments. While CAMs aren’t known to kill cancer cells, they may improve your comfort and well-being. Two examples are acupuncture for pain management and yoga for relaxation.

Alternative medicine is used in place of usual medicine. Some alternative medicines are sold as cures even though they haven’t been proven to work in clinical trials. If there was good proof that CAMs or other treatments cured cancer, they would be included in this book.

It is important to tell your treatment team if you are using any CAMs. They can tell you which CAMs may be helpful and which CAMs may limit how well medical treatments work.
My notes
Review

- Clinical trials give people access to new tests and treatments that otherwise can't usually be received. These new tests and treatments may, in time, be approved by the FDA.

- Chemotherapy stops the life cycle of cancer cells so they can't increase in number.

- Some steroids have anti-cancer effects and may be used with chemotherapy.

- Lenalidomide treats CLL by modifying your immune system and by other means.

- Some targeted therapies for CLL mark the cancer cells for destruction by your immune system. Other targeted therapies stop the cancer cells from receiving signals to grow.

- A stem cell transplant destroys bone marrow then replaces it by adding healthy stem cells into your body.
Treatment guide
40  **4.1 Treatment for CLL with del(17p)**

Lists treatment options for CLL that is missing parts of chromosomes 17. Parts of chromosome 11 may or may not be missing.

42  **4.2 Treatment for CLL without del(17p) and del(11q)**

Lists treatment options for CLL that isn’t missing parts of chromosome 17 or 11.

48  **4.3 Treatment for CLL without del(17p) but with del(11q)**

Lists treatment options for CLL that isn’t missing parts of chromosome 17 but is missing parts of chromosome 11.

52  **4.4 Supportive care**

Lists treatment options for other health conditions that are common among people treated for CLL.

56  **Review**
Clinical trials are the preferred treatment option of CLL experts for people with CLL. If you are unable or don't want to join a clinical trial, Part 4 lists other treatment options for you. The first four sections in Part 4 address treatment for CLL, and the fifth section addresses supportive care.

The information in Part 4 is taken from the treatment guidelines written by NCCN experts of CLL. These treatment guidelines list options for people with CLL in general. Thus, your doctors may suggest other treatment for you based on your health and personal wishes. Fully discuss your treatment options with your doctor.

What are my options?
There are multiple treatment options for CLL. Treatment options that are best for you depend on features of the cancer and sometimes your age and health status. Thus, treatment options in Part 4 are grouped by these factors.

The cancer feature that is very important for CLL treatment is whether there are missing parts of chromosome 17. The standard of care differs based on this cancer feature. The word “del(17p)” is how doctors refer to missing parts of chromosome 17, and “del(11q)” for missing parts of chromosome 11. If unsure, ask your doctor if tests showed that there are missing chromosome parts.

Part 4.1 is for people with CLL that is missing parts of chromosome 17. TP53 is a gene within the part of chromosome 17 that is sometimes missing. A TP53 mutation assessed by DNA sequencing is another way to know if chromosome 17 is missing. Read Part 4.1 to learn what is the standard of care for CLL with del(17p).

Parts 4.2 and 4.3 are for people with CLL that isn't missing parts of chromosome 17. If CLL has no missing parts of chromosome 17 and 11, read Part 4.2. If CLL is only missing parts of chromosome 11, read Part 4.3. Treatment options in Parts 4.2 and 4.3 are further grouped by age and health status.

Before starting treatment, your doctor may want to test the cancer again. Features of cancer can change over time, so re-testing may be needed if some time has passed. Testing of chromosomes 11, 12, 13, and 17 with FISH is recommended. Also, karyotype is needed. Your doctor may advise you to get an imaging test.
4.1 Treatment for CLL with del(17p)

Chart 4.1.1 First-time treatments

<table>
<thead>
<tr>
<th>Treatment options* (best options listed first)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ibrutinib</td>
</tr>
<tr>
<td>2. High-dose methylprednisolone + rituximab</td>
</tr>
<tr>
<td>3. FCR (fludarabine, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>4. FR (fludarabine, rituximab)</td>
</tr>
<tr>
<td>5. Obinutuzumab + chlorambucil</td>
</tr>
<tr>
<td>6. Alemtuzumab + rituximab</td>
</tr>
</tbody>
</table>

*If this treatment works, consider having a stem cell transplant if complex karyotype present.

Chart 4.1.2 Treatments if prior treatment failed

<table>
<thead>
<tr>
<th>Treatment options (best options listed first)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ibrutinib</td>
</tr>
<tr>
<td>2. Idelalisib + rituximab</td>
</tr>
<tr>
<td>3. Idelalisib</td>
</tr>
<tr>
<td>4. High-dose methylprednisolone + rituximab</td>
</tr>
<tr>
<td>5. Lenalidomide ± rituximab</td>
</tr>
<tr>
<td>6. Alemtuzumab ± rituximab</td>
</tr>
<tr>
<td>7. Ofatumumab</td>
</tr>
<tr>
<td>8. OFAR (oxaliplatin, fludarabine, cytarabine, rituximab)</td>
</tr>
</tbody>
</table>
Chart 4.1.1 lists first-time treatment options for CLL that is missing parts of chromosome 17. A clinical trial is advised. If you’re unable or refuse to join a clinical trial, ibrutinib is the standard of care. Other options include high-dose methylprednisolone with rituximab, FCR, FR, obinutuzumab with chlorambucil, and alemtuzumab with or without rituximab.

If first-time treatment works, the next steps are based on the presence of a complex karyotype. If there’s no complex karyotype, you may start observation. If a complex karyotype is present, you have three options. Think about getting a stem cell transplant. Besides a stem cell transplant, you can join a clinical trial or start observation.

Chart 4.1.2 lists treatment options for if prior treatment fails. Join a clinical trial if possible. If you can’t, ibrutinib is the standard of care. A well-designed clinical trial of idelalisib with rituximab recently ended and showed this option has good results. Other options include high-dose methylprednisolone with rituximab, lenalidomide with or without rituximab, alemtuzumab with or without rituximab, ofatumumab, and OFAR.
4.2 Treatment for CLL without del(17p) and del(11q)

Frail and sick

Chart 4.2.1  Treatments excluding purine analogs

<table>
<thead>
<tr>
<th>Treatment options (best options listed first)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Obinutuzumab + chlorambucil</td>
</tr>
<tr>
<td>2. Ibrutinib</td>
</tr>
<tr>
<td>3. Ofatumumab + chlorambucil</td>
</tr>
<tr>
<td>4. Rituximab + chlorambucil</td>
</tr>
<tr>
<td>5. Obinutuzumab</td>
</tr>
<tr>
<td>6. Rituximab</td>
</tr>
<tr>
<td>7. Chlorambucil</td>
</tr>
<tr>
<td>8. Pulse corticosteroids</td>
</tr>
</tbody>
</table>
When doctors plan treatment for CLL, one of the first steps is to exclude any treatment that is likely to be life-threatening. Chemotherapy is sometimes part of the standard of care for CLL without del17(p). However, some types are more likely to cause life-threatening infections to some people. Your doctor will decide your risk based on your fitness and health. Options in Part 4.2 are grouped by fitness and health. In the first section, Frail and sick, options are listed for people who aren’t likely to be able to survive a serious infection. Purine analogs—a type of chemotherapy—are excluded as treatment options.

The second section, Older or quite sick, starts on page 44. This section is for people who are: 1) 70 years of age and older; or 2) younger than 70 years but have serious health problems in addition to cancer. Some of the treatment options for this group include a purine analog.

The third section, Younger and fairly healthy, starts on page 46. This section is for people who are younger than 70 years of age and are fairly healthy besides having cancer. The standard of care includes a purine analog.

Chart 4.2.1 lists treatment options that are the least likely to cause life-threatening infections. Purine analogs aren’t included in the list. They have been shown to suppress white blood cells and in turn, increase your chances of getting an infection. Purine analogs include fludarabine, cladribine, and pentostatin.

Purine analogs can reduce normal white blood cells to very low levels. It can take years for some white blood cells to increase to normal levels. If you take purine analogs, you may increase your chances for getting life-threatening infections.

Compared to purine analogs, there are safer treatment options if you are physically frail and overall quite sick. Some of these treatments consist of both targeted therapy and chemotherapy. They include obinutuzumab with chlorambucil, ofatumumab with chlorambucil, and rituximab with chlorambucil. The second drug listed in Chart 4.2.1 is ibrutinib. It is included based on good results in well-designed clinical trials.

Other options include taking just one cancer drug. These options are obinutuzumab, rituximab, chlorambucil, and pulse corticosteroids. Pulse corticosteroids are corticosteroids given in high doses over 3 to 5 days.
**Older or quite sick**

Chart 4.2.2  First-time treatments including purine analogs

<table>
<thead>
<tr>
<th>Treatment options (best options listed first)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Obinutuzumab + chlorambucil</td>
</tr>
<tr>
<td>2. Ibrutinib</td>
</tr>
<tr>
<td>3. Ofatumumab + chlorambucil</td>
</tr>
<tr>
<td>4. Rituximab + chlorambucil</td>
</tr>
<tr>
<td>5. Bendamustine ± rituximab</td>
</tr>
</tbody>
</table>

Chart 4.2.3  Treatments if prior treatment fails

<table>
<thead>
<tr>
<th>Treatment options* (best options listed first)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ibrutinib</td>
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<tr>
<td>2. Idelalisib + rituximab</td>
</tr>
<tr>
<td>3. Idelalisib</td>
</tr>
<tr>
<td>4. Bendamustine ± rituximab</td>
</tr>
<tr>
<td>5. Reduced-dose FCR (fludarabine, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>6. Reduced-dose PCR (pentostatin, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>7. High-dose methylprednisolone + rituximab</td>
</tr>
</tbody>
</table>

*If this treatment works, consider having a stem cell transplant next if you aren’t too sick.
**Chart 4.2.2** lists first-time treatment options for older or younger sick people who have CLL that isn't missing parts of either chromosome 17 or 11. Your doctors may think you can withstand purine analogs. However, the first few options listed aren’t as harsh on your body as purine analogs.

Obinutuzumab plus chlorambucil has been the standard of care for this group. It has had good results in well-designed clinical trials. The second drug listed in Chart 4.2.2 is ibrutinib. It is also included based on good results in well-designed clinical trials.

Chlorambucil with ofatumumab and chlorambucil with rituximab are also good options. Less preferred options are bendamustine with or without rituximab and fludarabine with or without rituximab. Obinutuzumab, chlorambucil, and rituximab may be used alone to treat CLL. Rituximab alone is the least preferred option.

**Chart 4.2.3** lists treatment options for if first-time treatment fails. Before starting treatment, your doctor may want to test the cancer again. Features of cancer can change over time, so re-testing may be needed if some time has passed. Tests of the chromosomes in the cancer cells are advised. These tests include FISH and karyotype.

If the features haven’t changed, ibrutinib alone and idelalisib with rituximab are preferred options. They are preferred due to good results measured in well-designed clinical trials. There are 11 other options in Chart 4.2.3 that are listed in order of preference of NCCN experts.
Younger and fairly healthy

Chart 4.2.4 First-time treatments including purine analogs

<table>
<thead>
<tr>
<th>Treatment options (best options listed first)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. FCR (fludarabine, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>2. FR (fludarabine, rituximab)</td>
</tr>
<tr>
<td>3. PCR (pentostatin, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>4. Bendamustine ± rituximab</td>
</tr>
</tbody>
</table>

Chart 4.2.5 Treatments if prior treatment fails

<table>
<thead>
<tr>
<th>Treatment options* (best options listed first)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ibrutinib</td>
</tr>
<tr>
<td>2. Idelalisib + rituximab</td>
</tr>
<tr>
<td>3. Idelalisib</td>
</tr>
<tr>
<td>4. FCR (fludarabine, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>5. PCR (pentostatin, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>6. Bendamustine ± rituximab</td>
</tr>
<tr>
<td>7. Fludarabine + alemtuzumab</td>
</tr>
<tr>
<td>8. RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)</td>
</tr>
<tr>
<td>9. OFAR (oxaliplatin, fludarabine, cytarabine, rituximab)</td>
</tr>
<tr>
<td>10. Ofatumumab</td>
</tr>
<tr>
<td>11. Obinutuzumab</td>
</tr>
<tr>
<td>12. Lenalidomide ± rituximab</td>
</tr>
<tr>
<td>13. Alemtuzumab ± rituximab</td>
</tr>
<tr>
<td>14. High-dose methylprednisolone + rituximab</td>
</tr>
</tbody>
</table>

*If this treatment works, consider having a stem cell transplant next if you aren’t too sick.
Chart 4.2.4 lists first-time treatment options for younger, healthy people with CLL that isn’t missing chromosome 17 or 11. Chemoimmunotherapy with FCR is the standard of care. FCR has been tested in well-designed clinical trials and has had good results. FR, PCR, and bendamustine with or without rituximab are other options.

Chart 4.2.5 lists treatment options for if first-time treatment fails. Before starting treatment, your doctor may want to test the cancer again. Features of cancer can change over time, so re-testing may be needed if some time has passed. Tests of the chromosomes in the cancer cells are advised. These tests include FISH and karyotype.

If the features haven’t changed, ibrutinib alone and idelalisib with rituximab are preferred options. They are preferred due to good results measured in well-designed clinical trials. There are 12 other options in Chart 4.2.4 that are listed in order of preference of NCCN experts.

If your treatment works, think about getting a stem cell transplant. You must be fairly healthy to have a transplant. A transplant may improve the prognosis of the cancer.
### 4.3 Treatment for CLL without del(17p) but with del(11q)

#### Older or quite sick

**Chart 4.3.1 First-time treatments including purine analogs**

<table>
<thead>
<tr>
<th>Treatment options (best options listed first)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Obinutuzumab + chlorambucil</td>
<td>6. Cyclophosphamide, prednisone ± rituximab</td>
</tr>
<tr>
<td>2. Ibrutinib</td>
<td>7. Reduced-dose FCR (fludarabine, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>3. Ofatumumab + chlorambucil</td>
<td>8. Chlorambucil</td>
</tr>
<tr>
<td>4. Rituximab + chlorambucil</td>
<td>9. Rituximab</td>
</tr>
<tr>
<td>5. Bendamustine ± rituximab</td>
<td></td>
</tr>
</tbody>
</table>

**Chart 4.3.2 Treatments if prior treatment failed**

<table>
<thead>
<tr>
<th>Treatment options* (best options listed first)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ibrutinib</td>
<td>8. Rituximab + chlorambucil</td>
</tr>
<tr>
<td>2. Idelalisib + rituximab</td>
<td>9. Ofatumumab</td>
</tr>
<tr>
<td>3. Idelalisib</td>
<td>10. Obinutuzumab</td>
</tr>
<tr>
<td>4. Bendamustine ± rituximab</td>
<td>11. Lenalidomide ± rituximab</td>
</tr>
<tr>
<td>5. Reduced-dose FCR (fludarabine, cyclophosphamide, rituximab)</td>
<td>12. Alemtuzumab ± rituximab</td>
</tr>
<tr>
<td>6. Reduced-dose PCR (pentostatin, cyclophosphamide, rituximab)</td>
<td>13. Dose-dense rituximab</td>
</tr>
<tr>
<td>7. High-dose methylprednisolone + rituximab</td>
<td></td>
</tr>
</tbody>
</table>

*If this treatment works, consider having a stem cell transplant next if you aren’t too sick.
When doctors plan treatment for CLL, one of the first steps is to exclude any treatment that is likely to be life-threatening. Chemotherapy is sometimes part of the standard of care for CLL without del17(p). However, some types are more likely to cause life-threatening infections to some people. Your doctor will decide your risk based on your fitness and health.

Treatment options in Part 4.3 are grouped by fitness and health. People who are frail and sick should avoid purine analogs. Read Chart 4.2.1 in Part 4.2 to learn which options are advised by NCCN experts for this group.

The first section in Part 4.3 is called Older or quite sick. It is for people who are: 1) 70 years of age and older; or 2) younger than 70 years but have serious health problems in addition to cancer. Some of the treatment options for this group include a purine analog.

The second section, Younger and fairly healthy, starts on page 50. This section is for people who are younger than 70 years of age and are fairly healthy besides having cancer. The standard of care includes a purine analog.

Chart 4.3.1 lists first-time treatment options for older or younger sick people with CLL that is missing parts of chromosome 11. Your doctors may think you can withstand purine analogs. However, the first few options listed aren’t as harsh on your body as purine analogs.

Obinutuzumab plus chlorambucil has been the standard of care for this group. It has had good results in well-designed clinical trials. The second drug listed in Chart 4.3.1 is ibrutinib. It is also included based on good results in well-designed clinical trials.

Other options include ofatumumab with chlorambucil, rituximab with chlorambucil, bendamustine with or without rituximab, cyclophosphamide and prednisone with or without rituximab, reduced-dose FCR, chlorambucil, and rituximab. Rituximab alone is the least preferred option.

Chart 4.3.2 lists treatment options for if first-time treatment fails. Before starting treatment, your doctor may want to test the cancer again. Features of cancer can change over time, so re-testing may be needed if some time has passed. Tests of the chromosomes in the cancer cells are advised. These tests include FISH and karyotype.

If the features haven’t changed, ibrutinib alone and idelalisib with rituximab are preferred options. They are preferred due to good results measured in well-designed clinical trials. There are 11 other options in Chart 4.3.2 that are listed in order of preference of NCCN experts.

If your treatment works, think about getting a stem cell transplant. You must be fairly healthy to have a transplant. A transplant may improve the prognosis of the cancer.
### Chart 4.3.3 First-time treatments

<table>
<thead>
<tr>
<th>Treatment options (best options listed first)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. FCR (fludarabine, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>2. Bendamustine ± rituximab</td>
</tr>
<tr>
<td>3. PCR (pentostatin, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>4. Obinutuzumab + chlorambucil</td>
</tr>
</tbody>
</table>

### Chart 4.3.4 Treatments if prior treatment fails

<table>
<thead>
<tr>
<th>Treatment options* (best options listed first)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ibrutinib</td>
</tr>
<tr>
<td>2. Idelalisib + rituximab</td>
</tr>
<tr>
<td>3. Idelalisib</td>
</tr>
<tr>
<td>4. FCR (fludarabine, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>5. PCR (pentostatin, cyclophosphamide, rituximab)</td>
</tr>
<tr>
<td>7. Fludarabine + alemtuzumab</td>
</tr>
</tbody>
</table>

*If this treatment works, consider having a stem cell transplant next if you aren’t too sick.
Chart 4.3.3 lists first-time treatment options for younger, healthy people with CLL that is missing parts of chromosome 11. Options include FCR, bendamustine with or without rituximab, PCR, and obinutuzumab with chlorambucil.

Chart 4.3.4 lists treatment options for if first-time treatment fails. Before starting treatment, your doctor may want to test the cancer again. Features of cancer can change over time, so re-testing may be needed if some time has passed. Tests of the chromosomes in the cancer cells are advised. These tests include FISH and karyotype, which are described in Part 2.

If the features haven’t changed, ibrutinib alone and idelalisib with rituximab are preferred options. They are preferred due to good results measured in well-designed clinical trials. There are 12 other options in Chart 4.3.4 that are listed in order of preference of NCCN experts.

If your treatment works, think about getting a stem cell transplant. You must be fairly healthy to have a transplant. A transplant may improve the prognosis of the cancer.
### 4.4 Supportive care

#### Chart 4.4 Supportive care by health condition

<table>
<thead>
<tr>
<th>Health condition</th>
<th>Type of supportive care</th>
</tr>
</thead>
</table>
| Severe ear, sinus, or lung infections   | • Medicine as needed  
• Test blood for antibodies  
  ◦ If IgG <500 mg/dL, infusions of gamma globulin every month |
| Flu                                     | • Influenza vaccine every year                                                                                                                                 |
| Pneumococcal infection                  | • Vaccine every 5 years; Prevnar is preferred                                                                                                                                 |
| Blood transfusion needed                | • Transfusion should be done according to hospital standards  
• All blood products should be radiated |
| Autoimmune hemolytic anemia             | • Diagnosis with reticulocyte and haptoglobin counts and direct antiglobulin test  
• If severe, stop taking fludarabine and do not take again  
• Treat with corticosteroids, IVIG, cyclosporin A, splenectomy, or rituximab |
| Immune thrombocytopenic purpura         | • Diagnosis with bone marrow test for cause of low platelets  
• Treat with corticosteroids, rituximab, IVIG, cyclosporin A, splenectomy, eltrombopag, or romiplostim |
| Pure red cell aplasia                   | • Diagnosis with bone marrow test and test for parvo B19  
• Treat with corticosteroids, cyclophosphamide, cyclosporine or anti-thymocyte globulin |
| Tumor lysis syndrome                    | • If CLL is present in large amounts and you are at risk:  
  ◦ Consider taking medicine to prevent |
| Herpes virus                            | • If receiving purine-analogs, alemtuzumab, or both:  
  ◦ Start taking medicine like acyclovir to prevent infection |
| Pneumocystis pneumonia                  | • If receiving purine-analogs, alemtuzumab, or both:  
  ◦ Start taking medicine like sulfamethoxazole and trimethoprim to prevent illness |
| Cytomegalovirus reactivation            | • If receiving alemtuzumab:  
  ◦ Start taking ganciclovir if virus is present or rising  
  ◦ Blood tests of virus are needed every 2–3 weeks |

*Continued on page 54.*
Chart 4.4 lists some of the supportive care needs of people with CLL. Supportive care doesn’t aim to treat cancer but aims to improve quality of life. It is also called palliative care.

Supportive care can address many needs. It can address emotional and physical needs, such as relieving symptoms. It can also help with treatment decisions as you may have more than one option. Supportive care also includes help with coordination of care between health providers. Talk with your treatment team to plan the best supportive care for you. Supportive care is an important part of your cancer care, especially during active cancer treatment.

You are more likely to get infections due to CLL or its treatment. Some people with CLL get severe ear, sinus, or lung (pneumonia) infections again and again. These infections may require going to the hospital or getting an injection of medicine rather than taking pills. If you get severe infections, testing your antibodies (IgG level) is advised. If your level of IgG is low (<500 mg/dL) and you have severe, recurrent infections, you could benefit by infusions of gamma globulin (IVIG) every month to raise your IgG level above 500 mg/dL.

Some vaccines to prevent illness are advised. Get a flu shot every year and a pneumococcal vaccine every five years. Some vaccines consist of live viruses or bacteria. Do not take live vaccines including the vaccine for shingles. If you are unsure about a vaccine, ask your treatment team about it.

Some people being treated for CLL will need a blood transfusion. It is very important that the transfusion is 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.

Autoimmune cytopenias are health conditions in which your immune system becomes confused and reacts against your own blood cells. The most frequent of these among people with CLL are autoimmune hemolytic anemia, immune-mediated thrombocytopenia, and pure red blood cell aplasia. Diagnosis and treatment of these conditions are listed in Chart 4.5.

Tumor lysis syndrome was described in Part 2. It can occur among people with large amounts of CLL who are undergoing strong cancer treatments. If you are at risk, think about starting medicine to prevent this illness.

Other health conditions listed in Chart 4.4 are linked to specific cancer treatments. Read through the list to see if any apply to you. Purine-analogs are a type of chemotherapy that includes fludarabine, cladribine, and pentostatin. Anti-CD20 monoclonal antibodies include obinutuzumab, ofatumumab, and rituximab.
### Chart 4.4 Supportive care by health condition *(Continued from page 52.)*

<table>
<thead>
<tr>
<th>Health condition</th>
<th>Type of supportive care</th>
</tr>
</thead>
</table>
| Hepatitis B                                                                      | • If receiving anti-CD20 monoclonal antibodies and alemtuzumab:  
  ◦ Test to assess status  
  ◦ Start taking medicine to prevent  
  • If receiving lenalidomide:  
    ◦ Consider preventing flare if large lymph nodes present  
    ◦ Prevent with prednisone 20 mg for 5–7 days then reduce amount over 5–7 days  
    ◦ If flare occurs, treat with prednisone 25–50 mg for 5–10 days  
    ◦ Antihistamines for rash and itching, such as cetirizine 10 mg 4X a day or loratadine 10 mg 1X a day                                                                 |
| An increase in the size of organs with CLL after starting treatment (ie, tumor flare reactions) | • If receiving lenalidomide:  
  ◦ Consider preventing flare if large lymph nodes present  
  ◦ Prevent with prednisone 20 mg for 5–7 days then reduce amount over 5–7 days  
  ◦ If flare occurs, treat with prednisone 25–50 mg for 5–10 days  
  ◦ Antihistamines for rash and itching, such as cetirizine 10 mg 4X a day or loratadine 10 mg 1X a day  
  • If receiving lenalidomide:  
    ◦ Start taking aspirin 81 mg a day if high number of platelets unless already on warfarin |
| Blood clot                                                                       | • If receiving lenalidomide:  
  ◦ Start taking aspirin 81 mg a day if high number of platelets unless already on warfarin  
  • If receiving ibrutinib:  
    ◦ Consider non-warfarin anti-coagulation medicine  
    ◦ If atrial fibrillation can't be controlled, switch to idelalisib                                                                 |
| Irregular, fast heart beat (ie, atrial fibrillation)                              | • If receiving ibrutinib:  
  ◦ Consider non-warfarin anti-coagulation medicine  
  ◦ If atrial fibrillation can't be controlled, switch to idelalisib  
  • If receiving ibrutinib:  
    ◦ Stop taking ibrutinib if on warfarin  
    ◦ Weigh the pros and cons of ibrutinib if on antiplatelet or anticoagulant treatment  
    ◦ Stop ibrutinib before surgery and delay re-starting afterward |
| Serious bleeding                                                                 | • If receiving ibrutinib:  
  ◦ Stop taking ibrutinib if on warfarin  
  ◦ Weigh the pros and cons of ibrutinib if on antiplatelet or anticoagulant treatment  
  ◦ Stop ibrutinib before surgery and delay re-starting afterward  
  • If receiving idelalisib:  
    ◦ Stop idelalisib until problem is solved |
| Liver damage (ie, hepatotoxicity)                                                | • If receiving idelalisib:  
  ◦ Stop idelalisib until problem is solved  
  • If receiving idelalisib:  
    ◦ Stop idelalisib if it is likely caused holes in your gut |
| Diarrhea or swollen colon (ie, colitis)                                          | • If receiving idelalisib:  
  ◦ Stop idelalisib until problem is solved  
  • If receiving idelalisib:  
    ◦ Stop idelalisib if it is likely caused holes in your gut |
| Holes in gut                                                                     | • If receiving idelalisib:  
  ◦ Stop idelalisib if it is likely caused holes in your gut  
  • If receiving idelalisib:  
    ◦ Stop idelalisib if symptoms appear |
| Inflammation of the lungs (ie, pneumonitis)                                      | • If receiving idelalisib:  
  ◦ Stop idelalisib if symptoms appear  
  • If receiving idelalisib:  
    ◦ Stop idelalisib if symptoms appear |
Review

- Treatment options for CLL are based on features of the cancer and sometimes your age and health status.

- Ibrutinib is the standard of care for CLL that is missing parts of chromosome 17.

- Treatment options for CLL that isn’t missing parts of chromosome 17 are partly based on age and health status. Obinutuzumab with chlorambucil has been the standard of care for people who are frail, older, or quite sick. However, ibrutinib has been recently added as an first-time option based on good results in clinical trials. FCR is the standard of care for people who are younger and healthy besides having cancer.

- People with CLL often need care for health conditions related to the cancer or cancer treatment. Treatment for conditions other than cancer is part of supportive care. Talk to your treatment team about creating a supportive care plan that’s best for you.
Making treatment decisions
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 4 described the cancer and the test and treatment options recommended by NCCN experts. These options are based on science and agreement among NCCN experts. Part 5 aims to help you make decisions that are in line with your beliefs, wishes, and values.
**It’s your choice**

The role patients want in choosing their 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 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 will likely 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 record your talks and get copies of your medical records. It may be helpful to have your spouse, partner, 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 include:

What’s my diagnosis and prognosis?

It’s important to know that there are different types of cancer. Cancer can greatly differ even when people have a tumor in the same organ. Based on your test results, your doctors 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 tests will I have?
2. Where did the cancer start? In what type of cell?
3. Is this cancer common?
4. What is the cancer stage? Does this stage mean the cancer has spread far?
5. Is this a fast- or slow-growing leukemia?
6. What other test results are important to know?
7. How often are these tests wrong?
8. Would you give me a copy of the pathology report and other test results?
9. Can the cancer be cured? If not, how well can treatment stop the cancer from growing?
What are my options?

There is no single treatment practice that is best for all patients. 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?
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? 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. What can be done to prevent or relieve the side effects of treatment?
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. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment?
3. How do I prepare for treatment? Do I have to stop taking any of my medicines? Are there foods I will have to avoid?
4. Should I bring someone with me when I get treated?
5. Will the treatment hurt?
6. How much will the treatment cost me? What does my insurance cover?
7. Will I miss work or school? Will I be able to drive?
8. Is home care after treatment needed? If yes, what type?
9. How soon will I be able to manage my own health?
10. When will I be able to return to my normal activities?
What is your experience?

More and more research is finding that patients treated by more experienced doctors have better results. It is important to learn if a doctor is an expert in the cancer treatment he or she is offering.

1. Are you board certified? If yes, in what area?
2. How many patients like me have you treated?
3. How many procedures like the one you’re suggesting have you done?
4. Is this treatment a major part of your practice?
5. How many of your patients have had complications?
Weighing your 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, so science isn’t helpful. Some ways to decide on treatment are discussed next.

2nd opinion

The time around a cancer diagnosis 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, 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 on which option is best can help.

Copies of the pathology report, a DVD of the imaging tests, 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 the treatment you accept to have. 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

Besides talking to health experts, it may help to talk to patients who have walked in your shoes. Support groups often consist of 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.

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
www.cancer.org/cancer/leukemia-chroniclymphocyticcll/index

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

National Cancer Institute
www.cancer.gov/types/leukemia

NCCN
www.nccn.org/patients

The Leukemia & Lymphoma Society (LLS)
www.LLS.org/informationspecialists

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 downsides may help you decide which treatment is best for you.
Glossary

Dictionary

Acronyms
<table>
<thead>
<tr>
<th>Glossary Dictionary</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>allogeneic stem cell transplant</strong></td>
<td>A cancer treatment that suppresses bone marrow then replaces it by adding healthy blood stem cells from a donor.</td>
</tr>
<tr>
<td><strong>anemia</strong></td>
<td>Abnormal low numbers of healthy red blood cells.</td>
</tr>
<tr>
<td><strong>anesthesia</strong></td>
<td>Loss of feeling with or without loss of wakefulness that is caused by drugs.</td>
</tr>
<tr>
<td><strong>antibody</strong></td>
<td>A protein made by white blood cells that helps fight off infection. Also called an immunoglobulin.</td>
</tr>
<tr>
<td><strong>antigen</strong></td>
<td>Any substance that activates the immune system.</td>
</tr>
<tr>
<td><strong>autoimmune hemolytic anemia</strong></td>
<td>The wrongful destruction of red blood cells by the immune system.</td>
</tr>
<tr>
<td><strong>B symptoms</strong></td>
<td>High fevers, heavy night sweats, and fast weight loss without dieting caused by B-cell cancers.</td>
</tr>
<tr>
<td><strong>B-cell</strong></td>
<td>One of three types of a white blood cell called a lymphocyte.</td>
</tr>
<tr>
<td><strong>beta-2 microglobulin</strong></td>
<td>A small protein made by many types of cells.</td>
</tr>
<tr>
<td><strong>biopsy</strong></td>
<td>Removal of small amounts of tissue or fluid to be tested for disease.</td>
</tr>
<tr>
<td><strong>bone marrow</strong></td>
<td>Soft, sponge-like tissue in the center of most bones where blood cells are made.</td>
</tr>
<tr>
<td><strong>bone marrow aspiration</strong></td>
<td>Removal of a small amount of bone marrow that is liquid to test for disease.</td>
</tr>
<tr>
<td><strong>bone marrow biopsy</strong></td>
<td>Removal of a small amount of solid bone and bone marrow to test for disease.</td>
</tr>
<tr>
<td><strong>cancer stage</strong></td>
<td>A rating of tumors that suggest the outlook of the disease.</td>
</tr>
<tr>
<td><strong>chemotherapy</strong></td>
<td>Drugs that stop the life cycle of cells so they don’t increase in number.</td>
</tr>
<tr>
<td><strong>chromosome</strong></td>
<td>Stands of genetic material inside of cells.</td>
</tr>
<tr>
<td><strong>clinical trial</strong></td>
<td>Research on a test or treatment to assess its safety or how well it works.</td>
</tr>
<tr>
<td><strong>complete blood count (CBC)</strong></td>
<td>A test of the number of blood cells in a sample.</td>
</tr>
<tr>
<td><strong>complex karyotype</strong></td>
<td>The presence 3 or more unrelated defects in chromosomes that occur in more than one cell.</td>
</tr>
<tr>
<td><strong>comprehensive metabolic panel</strong></td>
<td>Tests of up to 14 chemicals in your blood.</td>
</tr>
<tr>
<td><strong>computed tomography (CT)</strong></td>
<td>A test that uses x-rays to view body parts.</td>
</tr>
</tbody>
</table>
contrast
A dye put into your body to make clearer pictures during imaging tests.

deroxyribonucleic acid (DNA)
A chain of chemicals inside cells that contains coded instructions for making and controlling cells.

deroxyribonucleic acid (DNA) sequencing
A lab test used to look for abnormal changes in DNA.

diagnose
To identify a disease.

differential
Measurement of the different types of white blood cells present in a blood sample.

direct Coombs test
A lab test that detects if antibodies are stuck to and destroying red blood cells.

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.

fertility specialist
An expert who helps men and women have babies.

flow cytometry
A test that looks at certain 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.

gene
Instructions in cells for making and controlling cells.

graft-versus-leukemia (GVL) effect
An attack on cancer cells by transplanted stem cells from a donor.

haptoglobin
One of the proteins made by the liver.

hemoglobin
A protein with iron that is released from destroyed red blood cells.

hemolysis
The early death of red blood cells.

human leukocyte antigen (HLA) typing
A blood test that finds a person’s unique set of proteins on cells.

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

immune system
The body’s natural defense against disease.

immunoglobulin
A protein made by white blood cells that helps fight off infection. Also called an antibody.

immunohistochemistry (IHC)
A test of cancer cells to find specific cell traits involved in abnormal cell growth.

immunomodulator
A type of drug that modifies some parts of the body’s disease-fighting system.

lactate dehydrogenase
A protein that helps to make energy in cells.
<table>
<thead>
<tr>
<th><strong>liver</strong></th>
<th><strong>mantle cell lymphoma</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Organ that removes waste from the blood and helps to digest food.</td>
<td>A cancer that is defined by too many proteins called cyclin D1.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>local anesthesia</strong></th>
<th><strong>medical history</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A controlled loss of feeling in a small area of the body caused by drugs.</td>
<td>All health events and medications taken to date.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>lymph</strong></th>
<th><strong>methylation analysis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A clear fluid containing white blood cells.</td>
<td>A lab test that looks for chemical tags, called methyl groups, on DNA.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>lymph node</strong></th>
<th><strong>monoclonal antibody</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Small groups of special disease-fighting cells located throughout the body.</td>
<td>Man-made antibodies that attach proteins on cancer cells.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>lymph vessel</strong></th>
<th><strong>monoclonal B-lymphocytosis (MBL)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tube-shaped ducts that carry lymph throughout the body.</td>
<td>A health condition that features high numbers of B-cells but is not cancer.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>lymphatic system</strong></th>
<th><strong>multi-gated acquisition (MUGA) scan</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A network in the body that collects and transports a fluid (lymph) and fights germs.</td>
<td>A test of the heart that uses radiation to make pictures.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>lymphocyte</strong></th>
<th><strong>natural killer (NK) cell</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A type of white blood cell that helps protect the body from illness.</td>
<td>One of three types of a white blood cell called a lymphocyte.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>lymphoma</strong></th>
<th><strong>observation</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer that begins in white blood cells called lymphocytes that are within the lymphatic system.</td>
<td>A period of testing for changes in cancer status while not receiving a specific treatment.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>karyotype</strong></th>
<th><strong>pathologist</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A test that uses a microscope to examine a cell’s chromosomes.</td>
<td>A doctor who’s an expert in testing cells to find disease.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>kinase inhibitor</strong></th>
<th><strong>performance status</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A cancer treatment that stops the transfer of phosphates, which blocks growth signals to cancer cells.</td>
<td>A rating of one’s ability to do daily activities.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>physical exam</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A review of the body by a health expert for signs of disease.</td>
<td></td>
</tr>
</tbody>
</table>
**positron emission tomography (PET)**
A test that uses radioactive material to see the shape and function of body parts.

**positron emission tomography/computed tomography (PET/CT)**
A test that uses radioactive material and x-rays to view the shape and function of organs and tissues.

**prognosis**
The expected pattern and outcome of a disease based on tests.

**pure red cell aplasia**
Very low numbers of the precursor cells to red blood cells in bone marrow.

**purine analog**
A type of chemotherapy that increases the likelihood of serious infections.

**Rai staging system**
The system used to stage chronic lymphocytic leukemia.

**reticulocyte**
A precursor cell to mature red blood cells.

**sedative**
A drug that helps a person to relax or go to sleep.

**side effect**
An unplanned physical or emotional response to treatment.

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

**stem cell transplant**
A cancer treatment that destroys bone marrow then replaces it by adding healthy blood stem cells.

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

**supportive care**
Treatment for the symptoms or health conditions caused by cancer or cancer treatment.

**targeted therapy**
Drugs that stop the growth process that is specific to cancer cells.

**T-cell**
One of three types of a white blood cell called a lymphocyte.

**thymus**
A gland located in the throat, just beneath the voice box.

**tonsil**
A group of tissue within the throat that contains many white blood cells called lymphocytes and fights germs that enter the mouth and nose.

**tumor lysis syndrome (TLS)**
A condition that occurs when many cancer cells die very quickly and release their contents into the blood, which can damage the kidneys and other organs.

**ultrasound**
A test that uses sound waves to take pictures of the inside of the body.

**uric acid**
A chemical that is made and released into the blood when cells and other substances in the body break down.

**vaccine**
A biological agent inserted into the body to prevent a disease.
Acronyms

BML
monoclonal B-lymphocytosis

BTK
Bruton’s tyrosine kinase

CAM
complementary and alternative medicine

CBC
complete blood count

CLL
chronic lymphocytic leukemia

CT
computed tomography

DNA
deoxyribonucleic acid

FDA
Food and Drug Administration

FISH
fluorescence in situ hybridization

GVL
graft-versus-leukemia

HLA
human leukocyte antigen

IGHV
immunoglobulin heavy-chain variable

IHC
immunohistochemistry

MUGA
multi-gated acquisition

NK cells
natural killer cells

PET
positron emission tomography

PI3K
phosphoinositide 3-kinase delta

SLL
small lymphocytic leukemia

NCCN Abbreviations and Acronyms

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NCCN Patient Guidelines
NCCN Guidelines for Patients®

NCCN Guidelines®
NCCN Clinical Practice Guidelines in Oncology®
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- Caring for Adolescents and Young Adults (AYA)*
- Chronic Lymphocytic Leukemia
- Chronic Myelogenous Leukemia
- Colon Cancer
- Esophageal Cancer
- Hodgkin Lymphoma
- Kidney Cancer
- Lung Cancer Screening
- Malignant Pleural Mesothelioma
- Melanoma
- Multiple Myeloma
- Non-Small Cell Lung Cancer
- Ovarian Cancer
- Pancreatic Cancer
- Prostate Cancer
- Soft Tissue Sarcoma
- Stage 0 Breast Cancer
- Stages I and II Breast Cancer
- Stage III Breast Cancer
- Stage IV Breast Cancer

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206.667.5000 • fredhutch.org

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mdanderson.org

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