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fighting blood cancers

The CLL Guide

Information for Patients and Caregivers

Chronic Lymphocytic Leukemia



Laura, CLL survivor

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A Message from Louis J. DeGennaro, PhD

President and CEO of The Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society (LLS) is the world's largest voluntary health organization dedicated to finding cures for blood cancer patients. Since 1954, we have invested over \$1 billion in research specifically targeting blood cancers to advance therapies and save lives. We will continue to invest in research for cures, programs and services to improve the quality of life for people with chronic lymphocytic leukemia (CLL).

We know that understanding CLL can be tough.

We are here to help and are committed to provide you with the most up-to-date information about CLL, your treatment and your support options. We know how important it is for you to understand your health information and to use it with your healthcare team toward good health, remission and recovery.

Our vision is that one day all people with CLL will be cured or be able to manage their disease with good quality of life.

Until then, we trust the information in this *Guide* will help you along your journey.

We wish you well.

A handwritten signature in black ink, appearing to read "Louis J. DeGennaro". The signature is fluid and cursive, with a long horizontal flourish extending to the right.

Louis J. DeGennaro, PhD

*President and Chief Executive Officer
The Leukemia & Lymphoma Society*

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This LLS guide about CLL is for information only. LLS does not give medical advice or provide medical services.

Introduction

Chronic lymphocytic leukemia (CLL) is a type of blood cancer. This is a hopeful time for people with CLL. There are a number of treatments for CLL. In recent years, new therapies have been approved and other possible new treatments are being studied in clinical trials. Progress toward a cure is under way.

People who have CLL need to see special blood cancer doctors, called **hematologist/oncologists** to help them.

Please use this *Guide* as a resource to help you –

- Understand CLL
- Find good doctors and other healthcare providers
- Understand complicated healthcare terms
- Find and use our Information Specialists, healthcare information, publications and resources.

This *Guide* includes

- Information on how to contact our Information Specialists: call (800) 955-4572
- Links to important free, LLS disease and treatment publications: www.LLS.org/publications
- Information about CLL treatment and care
- List of suggested questions to ask the doctor (see the healthcare guides on page 34)
- Simplified glossary of healthcare terms (See page 31).

We are here to help.

Want more information?



You can view, print or order the free LLS publications *Understanding Leukemia* and *Chronic Lymphocytic Leukemia* for more information. Go to www.LLS.org/publications or contact our Information Specialists for copies.

Resources and Information

LLS offers free information and services for patients and families touched by blood cancers. This section of the booklet lists various resources available to you. Use this information to learn more, to ask questions, and to make the most of your healthcare team.

For Help and Information

Consult with an Information Specialist. Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date disease, treatment and support information. Language services are available.

For more information, please

- Call: (800) 955-4572 (Monday through Friday, 9 a.m. to 9 p.m. ET)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org/information specialists.

Free Materials. LLS offers free education and support publications that can either be read online or downloaded and printed. Free print versions can be ordered. For more information, please visit www.LLS.org/publications.

Telephone/Web Education Programs. LLS offers free telephone/Web education programs for patients, caregivers and healthcare professionals. For more information, please visit www.LLS.org/programs.

Co-Pay Assistance Program. LLS offers insurance premium and medication co-pay assistance for certain eligible patients.

For more information, please

- Call: (877) 557-2672
- Visit: www.LLS.org/copay.

Community Resources and Networking

Online Blood Cancer Discussion Boards and Chats. Online discussion boards and moderated online chats can help cancer patients to reach out, share information and provide and receive support. For more information, please visit www.LLS.org/getinfo.

LLS Chapters. LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups and other great resources.

For more information about these programs or to contact your chapter, please

- Call: (800) 955-4572
- Visit: www.LLS.org/chapterfind.

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, locating summer camps and other needs. For more information, please visit www.LLS.org/resourcedirectory.

Clinical Trials (Research Studies). New research studies for patients with CLL are under way. Many are part of clinical trials. Patients can learn about clinical trials and how to access them.

For more information, please

- Call: (800) 955-4572 to speak with an LLS Information Specialist who can help conduct a clinical trial search
- Visit: www.LLS.org/clinicaltrials.

Advocacy. The LLS Office of Public Policy (OPP) enlists volunteers to advocate for policies and laws to speed new treatments and improve access to quality medical care.

For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy.

Additional Help for Specific Populations

Información en Español (LLS information in Spanish). For more information, please visit www.LLS.org/espanol.

Language Services. Let your doctor know if you need a language interpreter or other resources, such as a sign language interpreter. Often, these services are free.

Information for Veterans. Veterans with CLL who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs (VA). For more information call the VA at (800) 749-8387 or visit www.publichealth.va.gov/exposures/agentorange.

World Trade Center Survivors. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be eligible for help from the World Trade Center (WTC) Health Program. People offered help include

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area, lived, worked or were in school in the area
- Responders to the Pentagon and the Shanksville, PA crashes.

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html.

Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time—for example, if you feel depressed every day for a two-week period.

For more information, please

- Call: National Institute of Mental Health (NIMH) (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov, enter “depression” in the search box.

Feedback

Like this booklet? Have suggestions? We'd love to know what you think. To tell us

- Visit: www.LLS.org/publicationfeedback
 - Click on “LLS Disease & Treatment Publications—Survey for Patients, Family and Friends.”

Understanding CLL

Leukemia is the general term for some different types of blood cancer. CLL is one of four main types of leukemia.

About Blood

Blood is the red liquid that circulates in our bodies. It is created inside the bones, in a spongy place called the marrow.

Blood is made up of plasma and blood cells.

Plasma. This is the liquid part of the blood. It is mostly water. It also has some vitamins, minerals, proteins, hormones and other natural chemicals.

Blood cells. Each blood cell starts as a stem cell. Then it turns into one of three types of blood cells

- Blood platelet (helps blood to clot)
- White blood cell (fights infection)
- Red blood cell (carries oxygen).

Normal Blood Cell Count Fast Facts

The ranges of blood cell counts below are for adults. They may be a little different from lab to lab and for children and teens.

Red blood cell (RBC) count

- Men: 4.5 to 6 million red cells per microliter of blood
- Women: 4 to 5 million red cells per microliter of blood

Hematocrit (the part of the blood made up of red cells)

- Men: 42% to 50%
- Women: 36% to 45%

Hemoglobin (amount of the red cell pigment that carries oxygen)

- Men: 14 to 17 grams per 100 milliliters of blood
- Women: 12 to 15 grams per 100 milliliters of blood

Platelet count

- 150,000 to 450,000 platelets per microliter of blood

White blood cell (WBC) count

- 4,500 to 11,000 white cells per microliter of blood

Differential (also called diff)

- Shows the part of the blood made up of different types of white cells
- The types of white cells counted are neutrophils, lymphocytes, monocytes, eosinophils and basophils.
- Adults usually have about 60% neutrophils, 30% lymphocytes, 5% monocytes, 4% eosinophils and less than 1% basophils in the blood.

The Immune System

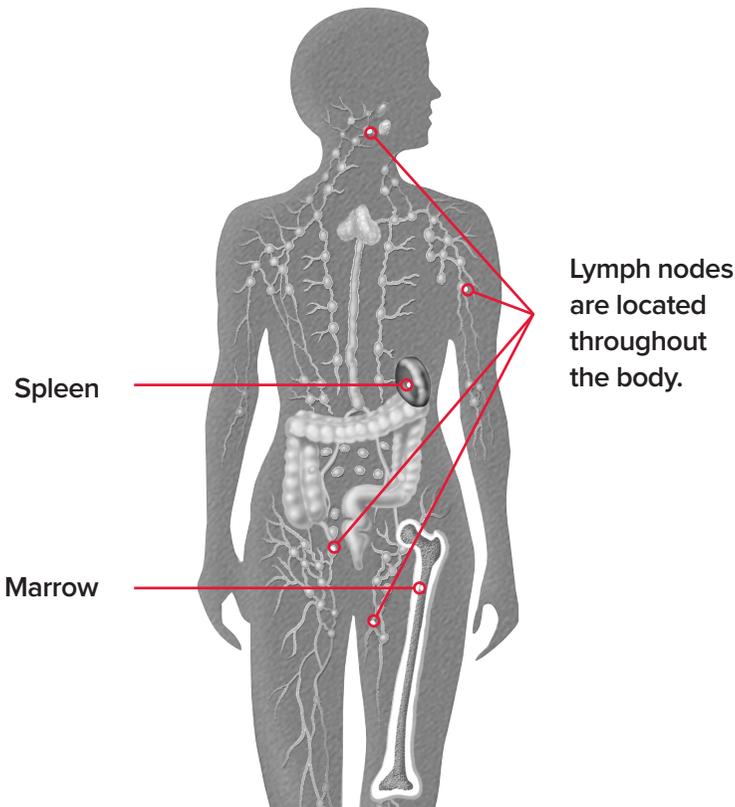
The immune system is the body's defense against infection.

The marrow and the lymphocytes are part of the immune system. Here are some other parts of the immune system:

Lymph nodes are bean-sized collections of lymphocytes found throughout the body. There are about 600 lymph nodes—in the neck, armpits, chest, abdomen, groin and some other parts of the body. Lymphatic vessels connect the lymph nodes. They contain lymph, a fluid that carries lymphocytes.

The spleen is an organ found on the left side of the body, near the stomach. It contains lymphocytes and removes worn-out cells from the blood.

Some Parts of the Immune System



What is CLL?

CLL is a type of cancer that begins in the bone marrow. It starts with a change to a lymphocyte (a type of cell that fights infection). CLL cells do not fight infection like normal lymphocytes do.

Over time, the uncontrolled growth of CLL cells in the marrow leads to an increase in the number of CLL cells in the blood. The leukemic cells that accumulate in the marrow in people with CLL do not prevent normal blood cell production as much as with acute leukemia.

Some people have CLL that grows slowly. They do not need drug therapy right away. Other people have CLL that grows more quickly. They do need drug therapy once their CLL is diagnosed. (Information about treatment begins on page 14.)

Causes of CLL. Doctors do not know what causes the cell-change that leads to CLL.

- There is no way to prevent CLL.
- You can not catch CLL from someone else.
- It's not common, but in some families more than one blood relative has CLL. Doctors are studying why some families have a higher rate of CLL.

Children do not get CLL. It's not a common disease in adults. CLL is the most common type of leukemia in adults. The number of people with CLL starts to increase after age 50. A small number of people are diagnosed with CLL in their 30s and 40s.

Signs and Symptoms

Healthy people often get a “sign” or a “symptom” when they get an illness or a disease.

- A sign is a change in the body that the doctor sees in an exam or a test result.
- A symptom is a change in the body that the patient can see or feel.

Some people with CLL have no symptoms. These people may find out they have CLL after a regular medical checkup shows certain changes in the blood. CLL symptoms often develop slowly. People with CLL may have little or no change to their health for many years.

Some Signs and Symptoms of CLL

Tiring more easily	People may have less energy due to fewer healthy red blood cells and more CLL cells.
Shortness of breath	People may have shortness of breath while doing usual day-to-day activities. This is due to fewer healthy red blood cells and more CLL cells.
Swollen lymph nodes or spleen	High numbers of CLL cells can gather in the lymph nodes or spleen as the number of CLL cells grows.
Infections	People with a very high number of CLL cells building up in the marrow may have repeated infections of the skin or other parts of the body. This is because CLL cells cannot fight off infection as well as healthy lymphocytes.
Weight loss	Some people with CLL lose weight because they eat less and/or because they are using more energy.

People with CLL sometimes have other symptoms, such as aches, fever or night sweats. Many of the signs and symptoms of CLL are more likely to be caused by other illnesses. Most people with the signs and symptoms listed here do not have CLL.

Diagnosing CLL

The doctor orders blood tests when a person has a high lymphocyte count. These tests may be done in the doctor's office or in a hospital.

Blood Tests. The testing for CLL includes blood cell counts and a blood cell examination.

- **Blood cell counts.** The doctor orders a lab test called a **complete blood count (CBC)** to check the numbers of blood cells. A person with CLL will have a high number of lymphocytes (high lymphocyte count). He or she may also have a low red blood cell count and a low platelet count.
- **Blood cell examination.** The CLL cells are usually examined with an instrument called a flow cytometer. The test is called **flow cytometry** or **immunophenotyping**. The test is done to find out if CLL is the reason for the high lymphocyte count. Flow cytometry also shows if the CLL is B-cell or T-cell. B-cell CLL is the most common.

Other lab tests for CLL include:

Immunoglobulin Test. Doctors check the immunoglobulin level in the blood. Immunoglobulins are proteins that help the body fight infection. People with CLL may have low levels of immunoglobulins. A low immunoglobulin level may be the cause of repeated infections. People who have low immunoglobulin levels and repeated infections may be given injections (shots) of immunoglobulins. Another name for immunoglobulin is gamma globulin.

Bone Marrow Tests. Bone marrow tests are not usually needed to make a CLL diagnosis. But, it's often helpful to have a bone marrow aspiration and a bone marrow biopsy before treatment begins. The results of these tests serve as a baseline that is used later on to assess the effects of treatment. These tests

- Are almost always done together
- Require a special needle.

Often patients are awake during the procedure. These patients are given medication to their hip bone to numb the biopsy and aspiration site. Once that area of the body is really numb, the bone marrow samples are taken. Some patients are sedated (asleep) for the procedure.

How Are Blood and Bone Marrow Tests Done?

Blood tests	Usually a small amount of blood is taken from the person's arm with a needle. The blood is collected and sent to a lab.
Bone marrow aspiration	A liquid sample of cells is taken from the marrow through a needle. The cells are then looked at under a microscope.
Bone marrow biopsy	A very small amount of bone filled with marrow cells is removed through a needle. The cells are then looked at under a microscope.

FISH. A test called **fluorescence in situ hybridization (FISH)** is used to see if there are changes to the chromosomes of the CLL cells. Every cell in the body has chromosomes that carry genes. Genes give the instructions that tell the cell what to do. About half of the people with CLL have CLL cells with chromosome changes. FISH may give doctors information about which people with CLL need more medical follow-up care. FISH can be done with a sample of cells from blood or marrow.

Tracking Your CLL Tests

These tips may help you save time and know more about your health.

- Ask your doctor why certain tests are being done and what to expect.
- Discuss test results with your doctor.
- Ask for and keep copies of lab reports in a file folder or three-ring binder. Organize test reports in date order.
- Find out if and when follow-up tests are needed.
- Mark appointments that are coming up on your calendar.

Want more information?



You can view, print or order the free LLS publication *Understanding Lab and Imaging Tests* to learn more about lab tests and what to expect. Go to www.LLS.org/publications or contact our Information Specialists for a copy.

Treating CLL

Finding the Right Doctor

Patients with CLL are treated by special doctors that understand cancer and the blood called **hematologist/oncologists**.

Finding the right doctor, and one that you like and feel comfortable with, is important. Refer to these resources to help you find the right cancer specialist

- Your primary care doctor
- The community cancer center
- Your health plan and its referral services
- Online doctor-finder resources, such as
 - The American Medical Association’s (AMA) “DoctorFinder.”
 - The American Society of Hematology’s (ASH) “Find a Hematologist.”
- LLS resources such as our Information Specialists who can be reached from Monday to Friday 9 a.m. to 9 p.m. ET at (800) 955-4572.

Your doctor will help you to understand CLL and create a treatment plan. When you meet with your doctor

- Ask questions
 - Use the question guides on page 34 to help
 - Read and print LLS “What To Ask” question guides at www.LLS.org/whattoask.

- Take notes or bring an audio recorder to record your visits.
- Bring a friend or family member to help you understand and take notes.
- Make sure you understand what the doctor is saying. If you don't, ask the doctor to explain things so you can understand.
- If you need more information, consider getting another opinion (a second opinion).

Want more information?



You can view, print or order the free LLS publication *Choosing a Blood Cancer Specialist or Treatment Center* at www.LLS.org/publications. For a list of questions to ask your doctor, see the question guides on page 34. You can also access and print *Healthcare Question Guides* about second opinions and other topics at www.LLS.org/whattoask. Or, contact our Information Specialists for copies.

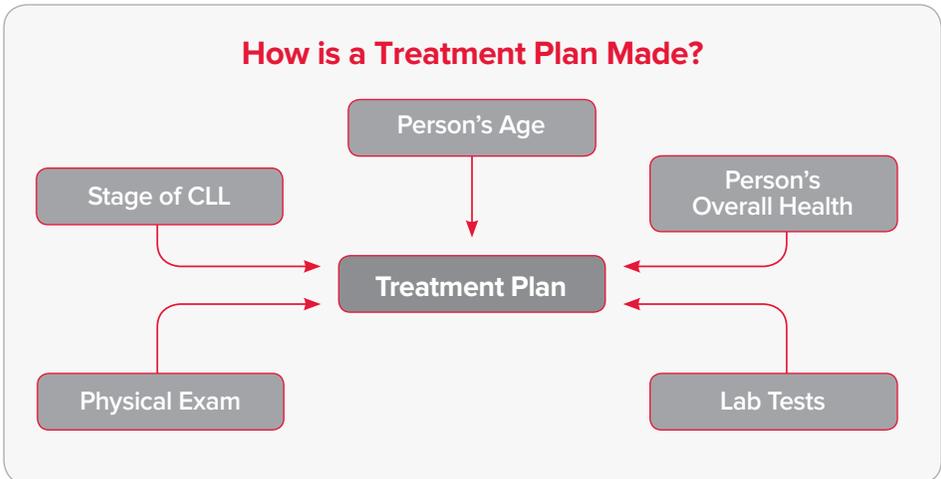
Treatment Planning

The goals of CLL treatment are to

- Slow the growth of the CLL cells
- Provide long periods of remission (when there are no signs of CLL and/or people feel well enough to carry on their day-to-day activities)
- Help people to feel better if they have infections, fatigue or other symptoms.

The treatment plan for a person with CLL depends on the

- Stage of CLL (low-risk, intermediate-risk or high-risk) (see below)
- Physical exam and lab test results
- Person's overall health
- Person's age (for some treatments).



CLL Staging. Many doctors use a system called **staging** to help plan treatment for people with CLL. Many doctors use the **Rai staging system**, which defines a person's risk as follows:

Low-Risk CLL

- High lymphocyte count in the blood and the marrow.

Intermediate-Risk CLL

- High lymphocyte count in the blood and the marrow.
- Enlarged (swollen) lymph nodes.

or

- High lymphocyte count in the blood and the marrow.
- Enlarged (swollen) liver and/or spleen.

High-Risk CLL

- High lymphocyte count in the blood and the marrow.
- Anemia (low red blood cell count).

or

- High lymphocyte count in the blood and the marrow.
- Low platelet count.

Lab test results may show signs of faster-growing disease (higher-risk CLL). This means the person needs closer follow-up with the doctor.

Blood Lymphocyte Doubling Time. A lymphocyte number that doubles in one year means that the person needs closer follow-up.

Beta₂-Microglobulin (B₂M). B₂M is a protein on CLL cells. A higher level of B₂M may mean there are more CLL cells.

Under Study. A factor called **ZAP-70** may give doctors information about a person's response to treatment. More study is needed to learn how this factor may affect treatment planning.

The doctor will use FISH and other tests to identify chromosome changes. Knowing that a patient has these chromosome changes can also help the doctor figure out the best treatment option. The following are some of the chromosome changes your doctor will be testing for.

- **Del(13q).** Part of chromosome 13 is missing and means that a person has a slightly better outcome.
- **Trisomy 12.** There are three copies of chromosome 12 and means that the person needs closer follow-up.
- **Del(11q).** Part of chromosome 11 is missing and means that the person needs closer follow-up.
- **Del(17p).** Part of chromosome 17 is missing and means that the person needs closer follow-up. CLL with this chromosome change usually does not respond well to standard therapy. Speak to your doctor about your treatment options.

Want more information?



You can view, print or order the free LLS publication *Chronic Lymphocytic Leukemia* to learn more about factors under study and other detailed information about CLL. Go to www.LLS.org/publications or contact our Information Specialists for a copy.

Treatments for CLL

Current therapies do not offer patients a cure for CLL, but there are treatments that help manage the disease. Treatments for CLL include

- Watch and Wait
- Chemotherapy
- Targeted therapies
- Monoclonal antibody therapies
- Supportive care
- Treatment in a clinical trial (see page 26).

Watch and Wait is a treatment approach that means a doctor will observe a person's condition with physical exams and lab tests. The doctor does not treat the person with drugs or other therapies during the watch and wait period.

People with CLL may think that they should have treatment right away. But for people with low-risk (slow-growing) disease and no symptoms, it is best not to start treatment. With a watch and wait approach, the person avoids the side effects of therapy until it is needed. Many studies have compared the watch and wait approach to early treatment for people with low-risk CLL. This is also an area of ongoing study in clinical trials. To date, no benefits of early treatment for people with low-risk CLL have been shown.

A person with CLL being monitored with the watch and wait approach needs follow-up visits with the doctor. At each office visit the doctor will check for any health changes.

The results of exams and lab tests over time will help the doctor advise the person about

- When to start treatment
- The type of treatment to receive.

Treatment will begin if a person develops symptoms or there are signs that the CLL is starting to grow. The doctor may advise a person to begin treatment if one or more of the following signs develop.

- The number of CLL cells is much higher than it was.
- The number of normal cells is much lower than it was.
- The lymph nodes have become larger.
- The spleen has become larger.

A person with any or all of these signs may start to feel too tired for normal daily activities.

Chemotherapy is treatment with drugs that kill or damage cancer cells. Some drugs are given by mouth. Other drugs are given through a

vein by placing a small needle in the arm (called an IV). Two or more drugs are often used together. The FDA-approved drugs fludarabine (Fludara[®]), cyclophosphamide (Cytosan[®]), bendamustine (Treanda[®]) and other standard chemotherapies are used to treat people with CLL. For a listing of drugs used to treat CLL, see page 21. Information about side effects of treatment for CLL starts on page 27.

Targeted therapies target specific substances on the cancer cell. Most targeted therapy drugs for CLL are given as pills and in general have milder side effects than chemotherapy. Ibrutinib (Imbruvica[®]) is the first targeted therapy approved for CLL. Additionally, drugs approved for other blood cancers, such as lenalidomide (Revlimid[®]), are used in CLL in some cases. Future clinical trials will determine in which order these drugs will be used in treating patients.

Monoclonal antibody therapies for CLL are treatments that use immune-system proteins (antibodies) that are made in the lab. Monoclonal antibody therapies aim for a specific target on the surface of the CLL cells. The antibody attaches to the cell and then the cell dies. This type of therapy is given through an IV. Monoclonal antibody therapies do cause some side effects. In general, the side effects are milder than the side effects of chemotherapy (see page 27).

Rituximab (Rituxan[®]), obinutuzumab (Gazyva[®]), alemtuzumab (Campath[®]) and ofatumumab (Arzerra[®]) are four FDA approved monoclonal antibody therapies used to treat people with CLL. Other new monoclonal antibodies are being studied in clinical trials to treat people with CLL.

Drugs Used to Treat CLL

Chemotherapy	Bendamustine (Treanda®) Chlorambucil (Leukeran®) Cladribine (Leustatin®) Cyclophosphamide (Cytosan®) Doxorubicin (Adriamycin®) Fludarabine (Fludara®) Prednisone
Targeted Therapy	Ibrutinib (Imbruvica®) Lenalidomide (Revlimid®) Idelalisib (Zydelig®)
Monoclonal Antibody Therapy	Alemtuzumab (Campath®) Ofatumumab (Arzerra®) Obinutuzumab (Gazyva®) Rituximab (Rituxan®)

Supportive Care. Supportive care is given to prevent or treat CLL symptoms and/or treatment side effects. Supportive care for CLL may include

- **Antibiotics to treat infections caused by bacteria or fungi.** Infections are a risk for people with CLL. The CLL treatment lowers the number of infection-fighting white blood cells in the blood. People with repeat infections may also get injections (shots) of immunoglobulin (gamma globulin).
- **Vaccinations.** Due to the high risk of infections in CLL patients, immediate vaccination for pneumococcal pneumonia with Prevnar 13® (repeated every 5 years) and a yearly flu vaccination is recommended. CLL patients should never receive live vaccines (including the shingles vaccine).

- **Blood transfusions or red blood cell growth factors to increase the red blood cell count.** Anemia (low numbers of red blood cells) is a common side effect of chemotherapy. Examples of red blood cell growth factors are darbepoetin alfa (Aranesp[®]) and epoetin alfa (Procrit[®]).
- **Growth factors to improve low white blood cell counts.** CLL-related low blood counts are often corrected by CLL therapy. Sometimes the use of white blood cell growth factors can help people with CLL who have a long period of low white blood cell counts after treatment. Examples of white blood cell growth factors are filgrastim (Neupogen[®]) or pegfilgrastim (Neulasta[®]) (also called **G-CSF**) and sargramostim (Leukine[®]) (also called **GM-CSF**).

Blood cell growth factors may help the patient tolerate the side effects of higher doses of chemotherapy. People with CLL should discuss the risks and benefits of treatment with blood cell growth factors with their doctors.

- **Radiation Therapy.** This treatment uses x-rays or other high-energy rays to kill cancer cells. Radiation therapy is sometimes used to treat a person with CLL who has an enlarged (swollen) lymph node, spleen or other organ that is blocking the function of a neighboring body part, such as the kidney or the throat. This therapy is rarely used for CLL.
- **Splenectomy.** The spleen is an organ on the left side of the body, near the stomach. CLL cells can enlarge the spleen and cause discomfort in some people with CLL. Also, an enlarged spleen may lower the person's blood cell counts to dangerous levels. An operation to remove the spleen is called a **splenectomy**. Splenectomy is helpful for some people with CLL if the spleen is very enlarged as a result of the disease. The operation may improve the person's blood cell counts.

CLL treatment is changing and treatment options are divided by age.

- Younger than 65 to 70 years without del(17p)
- Older than 65 to 70 years without del(17p)
- CLL patients with del(17p)

CLL Patient Younger Than 65 to 70 Years Without del(17p). Two or more drugs are often combined to treat people with CLL who need drug therapy. Fludara is often combined with other drugs. For example

- FC – Fludara, Cytosan
- FR – Fludara, Rituxan
- FCR – Fludara, Cytosan, Rituxan

Studies have compared treatment of Fludara or FC with FR and FCR. These have shown that FR or FCR treatment improves how often untreated patients achieve complete remission and overall survival. Fludara combined with other drugs is being studied in clinical trials.

CLL Patient Older Than 65 to 70 Years Without del(17p). Older patients represent the most common group of patients with CLL and studies have not shown much benefit to Fludara-based treatment. Some combinations for treatment which improve response rate and remission duration include

- Chlorambucil (Leukeran®) plus Rituxan
- Leukeran plus Arzerra
- Leukeran plus Gazyva (Gazyva is the only drug to have shown to prolong survival when combined with Leukeran)

Another treatment option for this patient group is bendamustine (Treanda®) plus Rituxan although evidence that this is better than Leukeran plus Gazyva is not available.

CLL Patients With del(17p). Young and older patients with del(17p) do not respond well to any type of chemotherapy or monoclonal antibody treatment. These patients are best directed toward

- Clinical trials
- Novel therapies such as Imbruvica®. Compared to other treatment approaches, Imbruvica has shown high response rates, excellent remission duration and low toxicity. Based upon these promising data, the FDA recently approved Imbruvica for del(17p) patients.
- Allogeneic stem cell transplant.

Treatment for Relapsed or Refractory CLL

Relapsed CLL is the term for CLL that responded to therapy but then stopped responding six or more months after therapy.

Refractory CLL is the term used to describe CLL that either

- Does not result in a remission (but may be stable)
- Does not result in a remission and gets worse within six months of the last treatment.

People who are treated for relapsed or refractory CLL often have good quality years of remission after more treatment. Treatment options for people with relapsed or refractory CLL are generally the same as treatment for newly diagnosed people. However, the results in clinical trials that have led to the FDA approval of Imbruvica suggest that it is better tolerated and provides the best treatment versus other current options. Patients with del(17p) respond to Imbruvica but have a higher relapse rate than other patients. These patients should speak to their doctor about a clinical trial.

Another treatment option that has been FDA approved is the oral drug idelalisib (Zydelig®) which is given with Rituxan. Zydelig is continued to be given as long as the patient continues to respond to the drug.

Patients who relapse after getting Imbruvica or Zydelig are relatively uncommon so far but likely will become more frequent as additional CLL patients are treated with these drugs. New knowledge will likely emerge over the next 1 to 2 years about how to best treat these patients.

Stem Cell Transplantation

Your doctor will talk to you about whether stem cell transplantation is a treatment option for you.

Allogeneic Stem Cell Transplantation. This is a procedure where stem cells from another person (a donor) are infused into the patient's body. The donor may be a brother or sister. Or, the donor can be an unrelated

person with stem cells that “match” the patient’s. Stem cells may also come from a cord blood unit (the blood in the umbilical cord after a baby’s birth).

The goals of an allogeneic transplant are to

- Restore the body’s ability to make healthy blood cells after high-dose chemotherapy.
- Cure the patient of CLL by killing remaining CLL cells.

This procedure may be done in the hospital. Before the transplant, the person receives CLL drug therapy to bring the disease under control. After the person responds to this treatment, the patient is given high-dose chemotherapy and/or radiation therapy. Stem cells are collected from a donor. The donor stem cells are given to the patient through an IV (intravenous) line or central line. The donor stem cells go from the patient’s blood to the marrow. They help to start a new supply of healthy red blood cells, white blood cells and platelets.

An allogeneic stem cell transplantation has a high risk of serious complications. Your doctor will explain the benefits and the risks if transplantation is suggested for you.

Doctors are working to make allogeneic stem cell transplants safer. A type of transplant called a **reduced-intensity transplant** uses lower doses of chemotherapy than a standard allogeneic stem cell transplant. This treatment is also called a **nonmyeloablative** transplant. Older and sicker people may be helped by this treatment.

Want more information?



You can view, print or order the free LLS publication *Blood and Marrow Stem Cell Transplantation* for more information. Go to www.LLS.org/publications or contact our Information Specialists for a copy.

About Clinical Trials

Doctors may recommend that a patient joins a clinical trial. Clinical trials are careful studies done by doctors to test new drugs or treatments or new uses for approved drugs or treatments. For example, changing the amount of the drug or giving the drug along with another type of treatment might be more effective. Some clinical trials combine drugs for CLL in new sequences or dosages.

There are clinical trials for

- Newly diagnosed CLL patients
- Patients who do not get a good response to treatment
- Patients who relapse after treatment.

A carefully conducted clinical trial may provide the best available therapy. Ask your doctor if treatment in a clinical trial is right for you. Drugs being studied in clinical trials now are listed in *Drugs Used to Treat CLL* on page 21. You can call our Information Specialists for information about clinical trials. Or, use our free clinical-trial service at www.LLS.org/clinicaltrials.

Want more information?



You can view, print or order the free LLS publication *Knowing All Your Treatment Options* at www.LLS.org/publications or contact our Information Specialists for a copy.

Side Effects and Treatment Response

Side Effects of CLL Treatment

The term **side effect** is used to describe the way that treatment affects healthy cells.

People react to treatments in different ways. Sometimes they have mild side effects. Other side effects may be serious and last a long time. Most side effects go away when treatment ends.

Some possible side effects of CLL treatment include

- Achy feeling
- Diarrhea
- Constipation
- Extreme tiredness
- Hair loss
- Infections
- Low blood pressure
- Low platelet count
- Low red blood cell count (anemia)
- Low white blood cell count
- Mouth sores
- Upset stomach and vomiting.

Talk to your doctor about the possible side effects and long-term effects of your treatment. You can also call our Information Specialists.

Want more information?



You can view, print or order the free LLS publication *Understanding Side Effects of Drug Therapy* for more information. Go to www.LLS.org/publications or contact our Information Specialists for a copy.

Treatment Response

People with CLL have a range of responses after treatment. Talk to your doctor about the results of your treatment. Your doctor may use the following terms to talk about response to treatment.

- **Remission.** No sign of disease; sometimes the terms complete remission (or complete response) or partial remission (or partial response) are used.
- **Complete Response (CR).** No sign of disease for at least two months after the end of treatment; normal blood counts and hemoglobin greater than 11 grams per deciliter (g/dL) without transfusions; no CLL signs or symptoms.
- **Partial Response (PR).** At least a 50 percent reduction in the number of blood lymphocytes and in lymph node and spleen enlargement; one or more of the following must also be maintained for at least two months: platelets greater than 100,000 platelets per microliter (μl) of blood; hemoglobin greater than 11 g/dL; or a 50 percent improvement over pretreatment red blood cell or platelet counts without transfusions.
- **Stable Disease.** This means the person's CLL is not growing, but the person does not have a complete or partial response.
- **Progressive Disease.** The signs of progressive disease are at least one of the following:
 - An increase of at least 50 percent in lymphocyte count or other signs of high-risk CLL. Lymphocytosis (high lymphocyte count) can be temporarily seen with Imbruvica and Zydelig and do not indicate disease progression in absence of other signs.

- An increase of at least 50 percent in liver or spleen size or a newly enlarged liver or spleen
- An increase of at least 50 percent in the combined size of at least two lymph nodes, in two exams in a row, done two weeks apart
- New appearance of enlarged lymph nodes.

Follow-up Care

After CLL treatment, people need to see their primary care doctor and oncologist for follow-up care. At these visits, the doctor will check you, and learn how you are doing. Blood tests, bone marrow tests or FISH may be needed from time to time to evaluate your treatment progress and to learn if more treatment is needed. The doctor may recommend longer periods of time between follow-up visits if a person continues to be free of CLL signs or symptoms, however, visits should be ongoing.

Minimal Residual Disease (MRD). Some people with CLL have a very low level of remaining CLL cells after treatment. The remaining CLL cells are called **minimal residual disease (MRD)**. MRD cannot be detected by the usual blood and marrow tests. The tests to detect MRD in people with CLL are **four-color flow cytometry** and **polymerase chain reaction (PCR)**. These tests may help the doctor to identify the need for more treatment.

For each follow-up visit:

- Track each visit and record what was discussed.
- Ask your doctor if and why certain tests are being done and what to expect.
- Discuss test results with your doctor.
- Ask for and keep copies of lab reports in a file folder or binder.
- Organize the reports in date order.
- Find out if and when follow-up tests are needed.
- Mark upcoming appointments on your calendar.

Ongoing Care

It is very important that you take very good care of yourself. Review the following tips to keep yourself healthy and happy.

- Keep all doctors' appointments.
- Talk about how you feel with the doctor at each visit.
- Ask any questions you may have about side effects.
- People with CLL may have more infections. Follow the doctor's advice for preventing infection.
- Eat healthy foods each day. It is okay to eat four or five smaller meals instead of three bigger ones.
- Contact the doctor about tiredness, fever or other symptoms.
- Do not smoke. Patients who smoke should get help to quit.
- Get enough rest.
- Exercise, but first talk with your doctor before starting an exercise program.
- Keep a healthcare file with copies of lab reports and treatment records.
- Have regular cancer screenings.
- See your primary care doctor to keep up with other healthcare needs.
- Talk with family and friends about how you feel. When family and friends know about CLL and its treatment, they may worry less.
- Seek medical advice if you feel sad or depressed and your mood does not improve over time. If you feel sad or depressed every day for a two-week period, seek help. Depression is an illness. It should be treated even when a person is being treated for CLL. Treatment for depression has benefits for people living with cancer.

Health Terms

Antibiotics. Drugs that are used to treat infections caused by bacteria and fungi. Penicillin is one type of antibiotic.

Antibodies. Proteins made by plasma cells. Antibodies help to fight infection in the body.

Baseline testing. Tests that are used to get information before treatment, which will be compared to information in the test results after treatment.

Beta₂-microglobulin. A cell protein that enters the blood. Measuring the amount of this cell protein can be one way to assess a person's type of CLL. A high level may mean the CLL is a faster-progressing type of CLL.

Bone marrow aspiration. A procedure to remove and examine marrow cells to see if they are normal. A liquid sample containing cells is taken from the marrow and then the cells are looked at under a microscope.

Bone marrow biopsy. A procedure to remove and examine marrow cells to see if they are normal. A very small amount of bone filled with marrow cells is taken from the body, and the cells are looked at under a microscope.

Chemotherapy or drug therapy. Treatment with chemical agents to treat CLL and other diseases.

Chromosomes. Any of the 23 pairs of certain basic structures in human cells. Chromosomes are made up of genes. Genes give the instructions that tell each cell what to do. The number or shape of chromosomes may be changed in blood cancer cells.

Clinical trials. Careful studies done by doctors to test new drugs or treatments, or new uses for approved drugs or treatments. The goal of clinical trials for blood cancers is to improve treatment and quality of life and to find cures.

Combination chemotherapy or drug therapy. The use of two or more drugs together to treat CLL and other diseases.

Diagnose. To detect a disease from a person's signs, symptoms and lab test results. The doctor diagnoses a patient.

FDA. The short name for the US Food and Drug Administration. Part of the FDA's job is to assure the safety and security of drugs, medical devices, and the US food supply.

FISH. The short name for **fluorescence in situ hybridization**, a test to measure the presence of a specific chromosome or gene in the cells. The results of this test can be used to plan treatment and to measure the results of treatment.

G-CSF. The short name for granulocyte-colony stimulating factor, a natural substance that stimulates the growth of neutrophils (a type of white cell that fights infection). Chemotherapy kills cancer cells, but also decreases the number of neutrophils in the blood and marrow. G-CSF manufactured by genetic engineering (Neupogen® and Neulasta®) may be used to treat or prevent a low neutrophil count.

GM-CSF. The short name for granulocyte macrophage-colony stimulating factor, a natural substance that stimulates the growth of macrophages and other white blood cells that fight infection. Chemotherapy kills cancer cells, but also decreases the number of macrophages and other white blood cells in the blood and marrow. GM-CSF manufactured by genetic engineering (Leukine®) is used to treat or prevent a low white blood cell count.

Hematologist. A doctor who treats blood cell diseases.

Immune response. The reaction of the body to foreign material. Examples of foreign material are an infection-causing microorganism, a vaccine, or the cells of another person used for an allogeneic stem cell transplant.

Immune system. Cells and proteins in the body that defend it against infection.

Immunoglobulins. Proteins that fight infection.

Immunotherapy. The treatments that are used to boost the body's immune system.

Lymphocyte. A type of white blood cell that is part of the immune system and fights infection.

Marrow. The spongy material in the center of bones where blood cells are made.

Monoclonal antibody therapy. Immune proteins made in the laboratory. This type of therapy targets and kills specific cancer cells. It does not cause many of the side effects of chemotherapy.

Oncologist. A doctor who treats patients who have cancer.

Pathologist. A doctor who identifies diseases by studying cells and tissues under a microscope.

PCR. The short name for **polymerase chain reaction**, a sensitive lab test that can measure the presence of cancer cell-markers in the blood or marrow. PCR is used to detect remaining cancer cells that cannot be detected by other tests.

Plasma. The liquid part of the blood.

Platelet. A type of blood cell that helps prevent bleeding. Platelets cause plugs to form in the blood vessels at the site of an injury.

Red blood cell. A type of blood cell that carries oxygen to all parts of the body. In healthy people, red blood cells make up almost half of the blood.

Refractory CLL. CLL that has not responded to initial treatment. Refractory disease may be disease that is getting worse or staying the same (stable disease).

Relapsed CLL. CLL that responded to treatment but then returns.

Remission. No sign of the disease and/or a period of time when the disease is not causing any health problems.

Richter transformation. When a patient's slow-growing CLL changes to a faster-growing form. This happens in a small number of patients. This change is not a second cancer, but a transformation of the CLL cells.

Small lymphocytic lymphoma (SLL). A disease with symptoms and treatment that are much like CLL. SLL starts in a lymphocyte in a lymph node. CLL starts in a lymphocyte in the marrow.

Stem cell. A type of cell found in marrow that makes red blood cells, white blood cells and platelets.

White blood cell. A type of blood that helps the body fight infection.



Questions to Help You Choose a Specialist

Asking questions will help you take an active role in managing your (or your child's) care. If you do not understand any part of the information your healthcare provider gives you, ask him or her to explain it in another way.

Doctor's name _____

Date of appointment or call _____

- 1.** What is your board certification and licensing? Are you a member of any professional societies?

- 2.** How much experience do you have treating patients who have my disease?

- 3.** Is your hospital, university, center or clinic accredited and experienced in treating blood cancers?

- 4.** How long would I usually have to wait for appointments or return of my phone calls?

5. Will there be nurses, social workers and case managers available to help me with support needs and quality-of-life concerns?

6. Do you know of other oncologists who specialize in treating blood cancers? Would you recommend that I speak to any of them?

7. What types of things should I call you about? What types of things should I call my family doctor about?

8. How should I contact you when I have questions?

9. How do I contact you at night? On weekends? On holidays?

To print additional copies of this question guide, or to print copies of question guides on other topics, go to www.LLS.org/whattoask. You may also request that copies be sent to you by contacting our Information Specialists at (800) 955-4572.



Asking your healthcare provider questions at any phase of your treatment will help you take an active role in managing your (or your child's) care. If you do not understand any part of the information your healthcare provider gives you, ask him or her to explain it in another way.

Doctor's name _____

Date of appointment or call _____

- 1.** What are my (my child's) treatment options? What is the goal of the treatment?

- 2.** What are the FDA-approved treatments, and are there treatments being studied in clinical trials (study treatments), for my (my child's) diagnosis?*

- 3.** What are the benefits and risks of the treatment(s) available to me (my child)? What are the expected side effects?

- 4.** Is there one treatment option (FDA-approved or study treatment) that you recommend over the others? Please explain.

5. If I (my child) enroll(s) in a clinical trial, who will be in charge of my (my child's) treatment?

6. When do you think I (my child) will need to begin treatment?

7. How long will I (my child) be treated and how many treatments will be needed?

8. Will I (my child) need to be hospitalized for all or part of the treatment?

9. What kind of testing will be done to monitor my (my child's) disease and treatment? How often will testing be needed?

10. If I am treated at an out-patient clinic or at the doctor's office, will I be able to drive/get myself home after treatments or will I need someone to assist me?

11. What are the risks if I don't (my child doesn't) get treatment?

12. How will I know if the treatment is effective? What options are available if the treatment is not effective?

13. How do I find out if my insurance will cover the costs of my (my child's) treatment or the study treatment? Who can help answer any medical questions my insurance company or health plan asks?

14. If I do not have insurance coverage, how can the healthcare team help me (my child) get treatment? Is there someone I need to speak to for assistance?

15. If I'm (my child is) getting a study treatment, will I be responsible for paying any treatment-related costs, such as tests, travel or the clinical trial drug(s)?

16. Will the healthcare team continue to check on me (my child) after the treatment is over? If so, for what period of time?

17. I (My child) would like to continue some type of lifelong follow-up care in order to be monitored for long-term and late effects of treatment. Can I (my child) follow up with you?

*For definitions of an FDA-approved treatment and a clinical trial (study treatment), visit www.LLS.org or contact an Information Specialist.

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Co-Pay Assistance

LLS's Co-Pay Assistance Program helps blood cancer patients cover the costs of private and public health insurance premiums, including Medicare and Medicaid, and co-pay obligations. Support for this program is based on the availability of funds by disease.

For more information,
call **877.557.2672** or
visit **www.LLS.org/copay**.

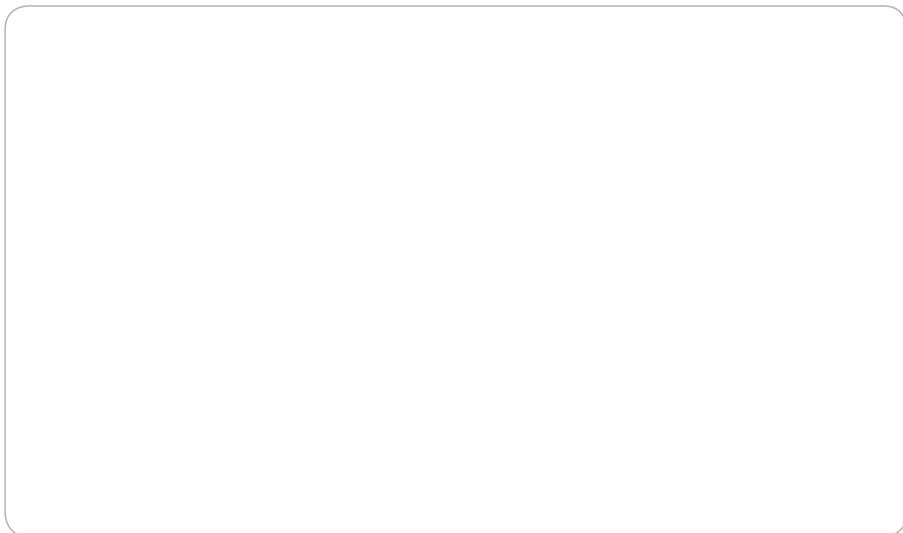


For a complete directory of our patient services programs, contact us at

800.955.4572 or www.LLS.org

(Callers may request a language interpreter.)

For more information, please contact:



or:

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1311 Mamaroneck Avenue, Suite 310, White Plains, NY 10605

Contact our Information Specialists **800.955.4572** (*Language interpreters available upon request*)

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