LEUKEMIA & LYMPHOMA SOCIETY®

Hairy Cell Leukemia

No. 16 in a series providing the latest information for patients, caregivers and healthcare professionals

Highlights

- Hairy cell leukemia (HCL) is a rare, slow-growing leukemia that starts in a B cell, a type of white blood cell.
- Most cases of HCL have a mutation in the genes of a B cell called *BRAF* V600E which can cause it to develop into a leukemia cell. The leukemic B cells are overproduced and infiltrate the bone marrow and spleen. They may also be found in the liver and lymph nodes. These excess B cells are abnormal and have projections that look like hairs under a microscope.
- Signs and symptoms of HCL include an enlarged spleen and a decrease in normal blood cell counts. Low blood cell counts can result in serious and life-threatening conditions including infections, excessive bleeding and anemia.
- While HCL cannot be cured, great progress in the treatment of HCL has resulted in prolonged survival for many patients. Most patients respond well to treatment with a type of chemotherapy called a purine analog. Cladribine (Leustatin®) and pentostatin (Nipent™) are examples of purine analogs.
- In spite of great progress in the treatment of HCL, about half of patients relapse and require additional treatment.

Introduction

Hairy cell leukemia (HCL) is a rare, slow-growing leukemia that starts in a B cell (also called a B lymphocyte). B cells are white blood cells that help the body fight infection and are an important part of the body's immune system.

Changes (mutations) in the genes of a B cell can cause it to develop into a leukemia cell. In fact, a mutation called *BRAF* V600E is found in the B cells of most HCL patients.

Normally, healthy B cells stop dividing and eventually die. In HCL, the genetic mutation tells the B cells to keep growing and dividing. Every cell that arises from the initial leukemia cell also has mutated DNA (deoxyribonucleic acid).

DNA is the genetic information inside the body's cells that gives instructions for growth and functioning.

As a result, the leukemia cells multiply uncontrollably. They usually go on to infiltrate the bone marrow and spleen, and they may also invade the liver and lymph nodes. The disease is called "hairy cell" leukemia because the leukemic cells have short, thin projections on their surfaces that look like hairs when examined under a microscope.

When the leukemic hairy cells enter the bone marrow, they affect the production of healthy blood cells. Bone marrow is the soft, sponge-like tissue in the center of most bones where blood cells are made. As the leukemia cells build up in the bone marrow, they suppress the development of other blood cells, including red blood cells, platelets and white blood cells. As a result, there are too few normal functioning blood cells because of too many leukemia cells in the bone marrow. This can cause low blood cell counts, which can lead to anemia, excessive bleeding and/or infections.

HCL is considered a "chronic" leukemia, which means it often progresses slowly, but it cannot be cured. For many patients, treatment with chemotherapy can lead to remission (fewer or no signs and symptoms of HCL) that can last for years. But in spite of great progress in controlling HCL, about half of treated patients relapse and require additional therapy.

Historically there was another type of HCL called "hairy cell leukemia variant." However, the World Health Organization (WHO) concluded that it is a separate entity from HCL and biologically distinct. It is now called "splenic lymphoma with prominent nucleoli (SLPN)." This variant is rarer than HCL and has a different clinical course and different treatments. For these reasons, this publication does not discuss it.

The WHO is an agency of the United Nations that deals with major health issues around the world. The WHO sets standards for health care and medicines and publishes scientific papers and reports.

Signs and Symptoms

The signs and symptoms of hairy cell leukemia (HCL) are not specific and may resemble those of other, less serious illnesses. It is common for someone with HCL to "not feel well" because of the underproduction of normal blood cells. This happens when the leukemia cells in the bone marrow crowd out the normal blood-making cells. Consequently, patients with HCL may not have sufficient numbers of red blood cells, white blood cells and platelets.

Signs and symptoms of HCL include:

- Enlarged spleen (swelling of the belly, feeling of fullness below the ribs)
- Extreme fatigue and weakness
- Easy bleeding or bruising
- Frequent infections
- Shortness of breath
- Unexplained weight loss

Patients may feel sick because they have:

- Anemia—a decrease in the number of red blood cells leading to fatigue, paleness and shortness of breath
- Neutropenia and monocytopenia—a decrease in the number of neutrophils and monocytes, types of white blood cells that fight infection, leading to a higher risk of infection
- Thrombocytopenia—a decrease in the number of platelets, leading to easy bruising and bleeding
- Pancytopenia—a decrease in the number of red blood cells, white blood cells and platelets

Diagnosis

Hairy cell leukemia (HCL) is rare and can be confused with other blood diseases, so it is essential to obtain an accurate diagnosis. It's best to consult a doctor with experience in diagnosing and treating HCL. Typically, a hematologist (a doctor who has special training in diagnosing and treating blood disorders) or a hematologist-oncologist (a doctor with special training in blood disorders and cancer) is seen.

For more information about choosing a doctor or a treatment center, visit www.LLS.org/booklets to see the free LLS publication *Choosing a Specialist or Treatment Center.*

It is also important for an experienced doctor to examine the laboratory samples. A doctor who examines lab samples and helps with diagnosis is called a "pathologist"; a pathologist who specializes in blood diseases is called a "hematopathologist."

A hematopathologist is a doctor who has special training in identifying blood diseases by studying cells under a microscope and performing other specialized tests on the cells.

The initial workup typically includes:

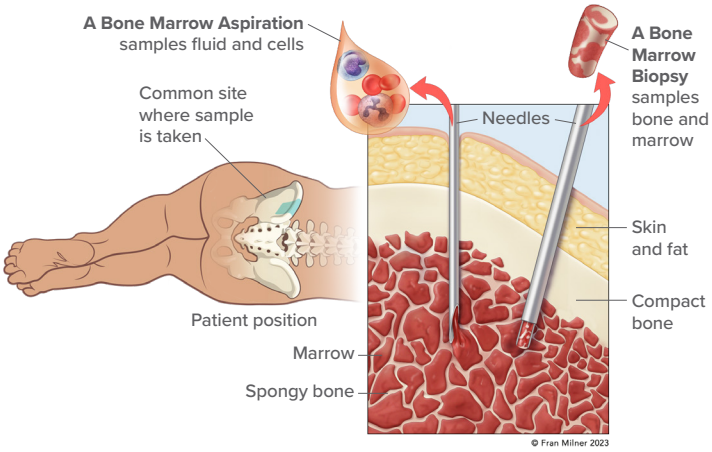
- Obtaining a medical history (information about past illnesses, injuries, treatments and medications)
- Learning about the patient's current symptoms
- Conducting a physical examination. The doctor may listen to the patient's lungs and heart and carefully examine the body for signs of infection and disease. The doctor may feel (palpate) certain areas of the patient's body—such as the armpits and the neck—to check for enlarged lymph nodes. To examine the internal organs, the doctor may also feel other parts of the patient's body. For example, the doctor may palpate the abdomen to see if the patient has an enlarged spleen or liver. Patients with HCL often have an enlarged spleen.
- A variety of laboratory and imaging tests

Laboratory and Imaging Tests

Bone marrow aspiration and biopsy. Bone marrow aspiration and biopsy are two procedures used to examine bone marrow cells for abnormalities. These two tests are generally done at the same time. The samples are usually taken from the patient's hip bone (after medicine has been given to numb the skin).

Bone marrow has both a solid and liquid part. For a bone marrow aspiration, a special hollow biopsy needle is inserted through the hip bone and into the marrow to remove (aspirate) a liquid sample of cells. For a bone marrow biopsy, a specialized wider needle is used to remove a core sample of solid bone that contains marrow. **See Figure 1.**

Figure 1. Bone Marrow Aspiration and Biopsy



Left: The place on the back of the patient's pelvic bone where a bone marrow biopsy is done. **Right:** Where the needles go inside the bone to collect the liquid sample for aspiration (the needle on the left) and the bone sample for biopsy (the needle on the right). The needles are different sizes for each of these tests.

For some patients with HCL, a successful bone marrow aspiration at diagnosis is not possible because hairy cells often produce fibrous tissue that scars the bone marrow. The scarring will cause the aspiration to be "dry," meaning a liquid sample could not be obtained.

If a bone marrow aspiration is not possible, the doctor can examine the bone marrow biopsy sample for abnormalities. Examination of bone marrow biopsy samples typically show hairy cell infiltrates with increased fibrous tissue. In some patients with HCL, the bone marrow may show hypocellularity, a lower-than-normal number of blood cells.

Complete blood count (CBC) with differential. CBC is a test that measures the number of red blood cells, platelets and white blood cells in a sample of blood. The "differential" measures the different types of white blood cells in the sample. Usually, people with HCL have low counts of white blood cells, red blood cells and platelets.

Comprehensive metabolic panel. This panel often includes testing the blood for up to 14 substances, including electrolytes, glucose and liver and kidney function markers. Abnormal levels can be caused by cancer or other health problems.

Computed tomography (CT) scan. This imaging test creates a series of detailed pictures of areas inside the body taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be swallowed or injected into a vein to help the organs or tissues show up more clearly. CT scans of the chest, abdomen and/or pelvis may be useful under certain circumstances to examine the size of the spleen, liver and lymph nodes.

Flow cytometry. Flow cytometry is a test used to classify cells (from blood or bone marrow biopsy) based on the type of proteins (markers) on the surface of the cells. Hairy cells have a characteristic surface protein pattern that differs from both healthy B cells and other abnormal (malignant) B cells. The pattern of the surface proteins is called the immunophenotype. There are certain proteins called cluster designations (CDs) that are relatively specific to HCL. In addition to the B-cell antigens CD19, CD20 and CD22, HCL cells also express CD11c, CD25, CD103 and CD123.

Antigens are substances the body does not recognize, so the body triggers an immune response. Antigens can come from outside the body (such as toxins, chemicals, bacteria, viruses); or be found inside the body on tissues and cells, including cancer cells. Antigens on the surface of cancer cells may be used as targets for treatment.

Hepatitis testing. Testing for the presence of hepatitis B or hepatitis C in the blood can be important when treating certain types of leukemia. If a patient has had hepatitis B in the past, it can become active again due to cancer or some of its treatments. The presence of hepatitis C may diminish the effectiveness of therapy.

Lactate dehydrogenase (LDH) testing. This test measures the level of LDH in the blood. LDH is a protein found in most cells. When a cell is damaged, LDH is released into the bloodstream. High levels of LDH in the blood may be caused by cancer and may also be a sign the cancer is widespread.

Molecular tests. Molecular tests are very sensitive DNA tests that check for specific genetic mutations in cells (from a sample of tissue, blood or other body fluid).

- **Polymerase chain reaction (PCR).** This test essentially increases (amplifies) small amounts of

specific pieces of either DNA (deoxyribonucleic acid) or RNA (ribonucleic acid) so the pieces are easier to detect and count. As a result, genetic abnormalities can be detected, even when these abnormalities are only present in very few cells.

- **Next-generation sequencing (NGS).** In this test two DNA samples from the patient are sequenced and compared: DNA from the cancer cells and DNA from normal, healthy cells. Comparing the cancer cell's genome to the genome of a healthy cell ensures the mutations detected are specific to the cancer cells.

In almost all cases of HCL, the leukemia cells have a mutation of the *BRAF* V600E gene. The *BRAF* V600E mutation may serve as a reliable molecular marker to distinguish HCL from other B-cell leukemias and lymphomas.

Some gene mutations may serve as a factor that will help doctors predict the likely outcome of the disease (prognosis). For example, approximately 80 to 90 percent of HCL patients have a hypermutation in immunoglobulin heavy chain variable gene called IGHV. With conventional chemotherapy, patients who have the IGHV mutation have a better prognosis (meaning a more positive outcome) than those without the mutation, who usually have a poorer prognosis (a less favorable outcome).

Peripheral blood smear. In this test, a sample of blood is viewed under a microscope to count different circulating blood cells, and also to see whether the cells look normal. In patients with HCL, the hematopathologist may observe small- to medium-sized leukemia cells with the presence of hairy-like projections.

Special tests. Certain additional tests are recommended in specific circumstances. For example, a pregnancy test if a patient is of childbearing age.

Visit www.LLS.org/booklets to view the free booklet *Understanding Lab and Imaging Tests* for more information. To view interactive 3D illustrations of various lab and imaging tests, visit www.LLS.org/3D.

Treatment Planning

The results of tests and other variables help predict the likely outcome or course of a disease and are called prognostic factors. Doctors use prognostic factors to help predict how hairy cell leukemia (HCL) will likely progress in a patient, as well as a patient's probable response to treatment. Some prognostic factors are associated with a lower risk that HCL will return after treatment (such as mutated IGHV status). These are called favorable risk factors. Other factors are associated with a higher risk that HCL will return after treatment. These are called poor risk factors.

The following signs are associated with a poor prognosis and/or possible resistance to purine analog chemotherapy (see *Treatment Options* below):

- Splenomegaly—an enlarged spleen (>3 cm)
- Leukocytosis—a high white blood cell count (>10×109/L)
- Hairy cells in the blood (>5 × 109/L)
- High beta2 microglobulin—a protein found on the surface of many cells that can indicate how much cancer is in the body (>2N)
- CD38 expression—a protein expressed on the surface of many immune cells
- Elevated lactate dehydrogenase (LDH) at diagnosis—LDH is a protein found in cells that is released into the bloodstream when cells are damaged or destroyed
- Unmutated IGHV (immunoglobulin heavy chain variable) gene—a biomarker associated with a more aggressive disease course

Each patient's medical situation is different and should be evaluated individually by a hematologist-oncologist who specializes in treating HCL. It is important for patients and their medical teams to discuss all treatment options, including treatments being studied in clinical trials.

For more information about clinical trials, see page 7.

Treatment Options

A patient has two options for treatment: standard of care or a clinical trial. It is important to talk to your medical team about the best treatment option for you.

Hairy cell leukemia (HCL) is usually slow-growing, and not all newly diagnosed patients with HCL require immediate treatment. For approximately 10 percent of patients, if they have stable blood counts and no symptoms at the time of diagnosis, the treatment may be "watch-and-wait." Watch-and-wait is an appropriate medical approach that means treatment is delayed until signs and symptoms of the disease appear or progress. Some patients with HCL live for many years without any symptoms and without

receiving any treatment. Frequent monitoring, including blood testing, is necessary so treatment can be started if the disease begins to advance.

For more information, visit www.LLS.org/booklets to view the free LLS publication *Watch and Wait.*

Patients generally begin treatment if they have low blood cell counts (low red cell, white cell or platelet counts). They may also begin treatment if they exhibit symptoms, including unexplained weight loss, recurrent infections or physical discomfort due to an enlarged spleen and/or liver.

See page 6 for specific information about the types of drugs used in HCL treatment.

Most often, initial treatment for HCL involves a type of chemotherapy called a purine analog. There are two purine analogs approved by the Food and Drug Administration (FDA) for HCL: cladribine (Leustatin®) and pentostatin (Nipent™). These drugs appear to be equally effective in achieving durable remission. The choice between the two drugs is usually determined by doctor preference or patient convenience. Various regimens have been used in clinical trials and the following options are widely accepted:

- Cladribine, administered as continuous intravenous (into a vein, or IV) infusion for 7 days
- Cladribine, administered by IV over 2 hours, once per day for 5 days
- Cladribine, injected subcutaneously (under the skin, or SC), once per day for 5 days
- Cladribine, administered by IV once weekly for 6 weeks
- Cladribine with or without rituximab (Rituxan®), a monoclonal antibody administered by IV either concurrently or following 6 months of cladribine
- Pentostatin, administered by IV, once every 2 weeks for 12 doses

More recently the oral medication vemurafenib (Zelboraf®), which is a BRAF inhibitor, has been used in certain circumstances, along with the monoclonal antibodies rituximab or obinutuzumab (Gazyva®) with good results. This is a non-chemotherapy option.

All of the above treatment options induce durable complete responses in approximately 80 to 90 percent of patients. Most patients who receive cladribine or pentostatin as first-line treatment experience a complete remission that can last for several years. A complete remission means:

- Normalization of blood counts
- Disappearance of hairy leukemia cells from the blood and bone marrow
- Reduction in size of the spleen (determined by physical examination)
- Absence of disease symptoms

Splenectomy (removal of the spleen) is rare in HCL treatment nowadays due to effective alternatives being available.

Treatment Response

Following initial treatment, patients are evaluated to determine their response to the treatment. This process may include blood tests, a physical examination and a bone marrow biopsy.

Measurable residual disease (MRD)–sometimes referred to as minimal residual disease–refers to the small number of cancer cells remaining in the body during and after cancer treatment. The number of remaining cells may be so low they do not cause any physical symptoms and often cannot even be detected through traditional methods, such as viewing cells under a microscope or getting imaging scans. However, these remaining cancer cells can start to multiply, causing a relapse of the disease. Highly sensitive laboratory methods that are able to find one cancer cell among one million normal cells are used to determine MRD.

Doctors use MRD to measure the effectiveness of treatment and to predict which patients are at risk of relapse. It can also help doctors confirm and monitor remissions, identify an early return of the cancer and guide treatment decisions, such as when to change or discontinue treatment.

Side Effects of Treatment

Neutropenia. One possible side effect of treatment is neutropenia, a condition in which there is a lower-than-normal number of neutrophils, a type of white blood cell that helps fight infections. For hairy cell leukemia (HCL) patients with neutropenia, doctors may prescribe a broad-spectrum antibiotic to prevent infections. Sometimes treatment may cause severe neutropenic fever, and if that happens, the doctor may prescribe a granulocyte colony-stimulating factor (G-CSF), a treatment that helps the body produce more white blood cells. Neulasta® and Neupogen® are examples of G-CSF drugs.

Infection. Infection is the most frequent cause of death in HCL patients. Prior to treatment, patients often already have low white blood cell counts, which puts them at risk for infection. Then, after they begin treatment, they are at greater risk for infection because many drugs are "immunosuppressive," which means they further lower white blood cell counts. This reduces the body's ability to fight infections and other diseases and places patients at higher risk of developing a life-threatening illness.

Other side effects. Some of the newer drugs, while less immunosuppressive, may cause fatigue, fever, rash, bone or joint pain.

Secondary cancers. Patients with HCL are also at an increased risk for secondary cancers, including non-Hodgkin lymphoma and skin cancer.

Thus, it's important for patients to:

- be educated about ways to prevent infections (such as frequent handwashing, etc.)
- contact their medical team right away if they have any signs or symptoms of an infection, such as fever or rash, or any other concerning conditions
- attend all medical appointments and cancer screenings (such as an annual skin check)

Treatment Options for Patients with Relapsed or Refractory HCL

Treatment with purine analogs has improved survival in hairy cell leukemia (HCL) patients. Some patients treated with purine analogs achieve remissions that last for years without additional treatments. On the other hand, some patients do not respond to treatment at all, and still others respond at first, but over time their disease relapses and they require additional treatment.

Relapsed Disease. A disease is said to relapse if it first responded to treatment but then returns. Treatment options for patients who have relapsed disease after remission depend on the quality and duration of the first remission.

Refractory Disease. Patients whose disease does not respond to primary treatment—or patients who do not achieve a complete response after initial therapy—have what is called refractory HCL.

Treatment options for patients with relapsed or refractory disease include:

- Participation in a clinical trial
- Retreatment with initial purine analog (cladribine or pentostatin) with rituximab (Rituxan®)
- A different purine analog (cladribine or pentostatin) with or without rituximab
- Rituximab (if the patient is unable to receive purine analog therapy)
- Dabrafenib (Tafinlar®) and trametinib (Mekinist®)
- Vemurafenib (Zelboraf®) with or without rituximab or obinutuzumab (Gazyva®)
- Peginterferon-alfa 2a (Pegasys®)
- Ibrutinib (Imbruvica®) or zanubrutinib (Brukinsa®)
- Bendamustine (Bendeka®) with rituximab
- Venetoclax (Venclexta®) with or without rituximab

Diagnostic testing may be repeated to reconfirm an HCL diagnosis. If HCL is confirmed, treatment with alternative therapies or participation in a clinical trial is recommended. See page 7 for information about clinical trials.

Drug Information

Various classes of drugs are used in the treatment of hairy cell leukemia (HCL).

- **Alkylating Agents.** These drugs work by either stopping or slowing the growth of cancer cells in the body. Bendamustine (Bendeka®) is an example.
- **B-Cell Lymphoma 2 (BCL2) Inhibitors.** These drugs inhibit the production of a protein that controls whether a cell lives or dies. Venetoclax (Venclexta®) is an example.
- **BRAF Inhibitors.** Almost all patients with HCL have a mutation of the *BRAF* V600E gene. This gene makes a protein which causes some cancer cells to grow and divide. BRAF inhibitors stop cells from producing this protein. Examples include vemurafenib (Zelboraf®), dabrafenib (Tafinlar®) and trametinib (Mekinist®).
- **Bruton Tyrosine Kinase (BTK) Inhibitors.** These inhibitors help stop growth signals that allow cancer cells to multiply. Examples include ibrutinib (Imbruvica®) and zanubrutinib (Brukinsa®).
- **Interferons.** Interferons are substances produced by cells in the body to help fight infections and diseases

like cancer. Interferon alpha is a synthetic (lab-made) version. Peginterferon alfa-2a (Pegasys®) is an example.

- **Monoclonal Antibodies.** Monoclonal antibodies are laboratory-produced proteins that target specific antigens on the cancer cell's surface to interfere with the cell's function and destroy it. Monoclonal antibodies cause less harm to normal cells than chemotherapy. For example, the monoclonal antibody rituximab (Rituxan®) is often used alone or in combination with other drugs for the treatment of HCL. Hairy cells, like most B cells, express CD20. Rituximab works by targeting the CD20 antigen on normal and malignant B cells. Then the body's natural immune defenses are recruited to attack and kill the marked B cells.
- **Purine Analogs.** Purine analogs kill cells by blocking important enzymes needed to make DNA (the genetic instructions for cells to develop and grow) and RNA (which carries the instructions) and by damaging DNA. Examples include cladribine (Leustatin®) and pentostatin (Nipent™).

Off-label drugs. The US Food and Drug Administration (FDA) approves drugs to treat certain health conditions. Drugs that are not FDA-approved to treat HCL can be used as an "off-label" treatment. "Off-label" prescribing is when a doctor gives a drug that is FDA-approved to treat one condition for another condition, if the doctor feels it will benefit the patient. This is a common practice.

Clinical Trials

Every new drug goes through a series of carefully controlled research studies before it can become part of standard care. These research studies are called "clinical trials," and they are used to find better ways to care for and treat people who have cancer.

In the United States, the Food and Drug Administration (FDA) requires all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat diseases.

Researchers use clinical trials to study new ways to:

- Treat disease using:
  - A new drug
  - A drug that has been approved, but to treat a different disease
  - A new combination of drugs
  - A new way of giving a drug—by mouth, intravenously (IV), etc.
- Prevent and/or manage treatment complications
- Manage signs and/or symptoms, and ease treatment side effects
- Find and diagnose disease
- Keep the disease from coming back (recurring) after treatment
- Manage long-term side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, cutting-edge therapies and provide helpful information for future patients. The treatments and information we have today are due in large part to patients being willing to join clinical trials. Anyone interested in being part of a clinical trial should talk to their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit www.LLS.org/whattoask for lists of suggested questions).
- Ask a family member or friend to go with you when you see your doctor—both for support and to take notes.

Clinical trials can be difficult to understand and to navigate, but The Leukemia & Lymphoma Society is here to help. Pediatric and adult patients and caregivers can work with Clinical Trial Nurse Navigators who will help find potential clinical trials, overcome barriers to enrollment and provide support throughout the entire clinical-trial process. Our Clinical Trial Nurse Navigators are registered nurses who are experts in adult and pediatric blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (such as past treatments, treatment responses and your cancer genetic profile), your current health and your medical history, because these might impact whether you can take part in certain clinical trials

- Help you understand how your finances, insurance coverage, support network and ability and willingness to travel might impact your choice of clinical trials
- Guide and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you enroll in a trial
- Support you throughout the clinical-trial process

Please call an LLS Information Specialist at (800) 955-4572 or visit www.LLS.org/CTSC for more information about clinical trials and the Clinical Trial Support Center at LLS.

Also, visit www.LLS.org/booklets to view the free LLS booklet *Understanding Clinical Trials for Blood Cancers.*

Long-Term Follow-Up

Hairy cell leukemia (HCL) is considered a chronic form of cancer because it never completely goes away. Periodic medical examinations and cancer screenings for patients in complete remission are important. Patients should have their blood counts checked routinely to ensure they are still in remission. If blood counts begin to decline, patients need to discuss treatment options with their doctors.

Incidence and Risk Factors

Hairy cell leukemia (HCL) is an uncommon leukemia. According to the National Cancer Institute (NCI), there are approximately 1,200-1,300 new cases of HCL in the United States each year.

NCI is the federal government's principal agency for cancer research and training.

While there is limited understanding of the genetic changes that lead to HCL, there are some factors associated with an increased risk of developing the disease. A "risk factor" is anything that increases a person's chance of being diagnosed with a disease. Having a risk factor, however, does not mean a person will definitely develop the disease. Some people with several risk factors may never get HCL, while others with no known risk factors may develop the disease. Risk factors associated with HCL include:

- **Age.** HCL occurs most often in middle-aged to older adults. It is most commonly diagnosed in people in their 50s and 60s.
- **Sex.** HCL is four to five times more common in males and people assigned male at birth than females and people assigned female at birth.
- **Environmental exposures.** For example:
  - agricultural chemicals such as pesticides
  - petroleum products such as gasoline, diesel and kerosene
  - ionizing radiation (from natural sources such as soil, water and air) or from medical imaging equipment (such as x-rays or scans)
- **Family history.** There is a higher incidence in first-degree relatives (parent or sibling) of patients with HCL.
- **Veterans exposed to Agent Orange.** HCL has been observed in patients following exposure to the herbicide Agent Orange used during the Vietnam War. There is sufficient evidence of an association between exposure to Agent Orange and later development of chronic B-cell leukemias and lymphomas, including HCL. As a result, the United States Department of Veterans Affairs considers HCL an illness presumed to be a service-related disability. See *Information for Veterans* on page 10.

Future Directions

Significant progress has been made in the understanding and treatment of hairy cell leukemia (HCL). Researchers continue to explore innovative ways to find more effective treatments (or new combinations of treatments), to minimize side effects and to improve outcomes. Patients are encouraged to participate in clinical trials to help contribute to medical advances in HCL.

Questions for Your Treatment Team

- Am I a candidate for the "watch and wait" approach for my hairy cell leukemia (HCL)?
- What are my treatment options, now or in the future, including the risks and benefits?
- What are common side effects that I may experience?
- What problems should I report to you right away?
- Are there clinical trials I could join?

Callers may request the services of a language interpreter.

ONE-ON-ONE SUPPORT

Information Specialists

Our blood cancer Information Specialists are highly trained oncology social workers and nurses who provide free, personalized assistance to patients, families and healthcare providers. Our Information Specialists offer guidance through blood cancer treatment, financial and social challenges, and give accurate, up-to-date disease, treatment and support information. Visit **www.LLS.org/InformationSpecialists** to chat online or call **800-955-4572**.

Clinical Trial Nurses

Our Clinical Trial Nurse Navigators are registered nurses with expertise in blood cancers who conduct comprehensive clinical trial searches and personally assist patients, parents and caregivers throughout the entire clinical trial process. Visit **www.LLS.org/CTSC** to learn more and complete a referral form.

Registered Dietitians

Our registered dietitians have expertise in oncology nutrition and provide patients, parents and caregivers with free nutrition consultations by phone. Visit **www.LLSnutrition.org/consult** or call **877-467-1936** to schedule.

Do you need financial assistance? Call **877-557-2672** or visit www.LLS.org/finances to learn more about financial support programs.

GET INFORMATION AND SUPPORT

We offer a wide variety of free information and services for patients and families affected by blood cancers.

- Peer-to-Peer Support
- LLS Patient Community
- Online Chats
- Podcast
- Webcasts and Videos
- Caregiver Support
- Children & Young Adults
- Information Booklets
- Local Programs
- Advocacy

Visit **www.LLS.org/PatientSupport** or call **800-955-4572** to learn more about all our offerings.

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Visit **www.LLS.org/espanol** for information in Spanish.

FREE MOBILE APPS

LLS Health Manager™

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LLS Coloring for Kids™

Allows children (and adults) to express their creativity and offers activities to help them learn about blood cancer and its treatment. Visit **www.LLS.org/ColoringApp** to download.

Both are available on the App Store and Google Play.

Visit **www.LLS.org/PatientSupport** or call **800-955-4572** to learn more about all our offerings.

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Feedback

To give suggestions about this booklet, visit www.LLS.org/PublicationFeedback.

Acknowledgment

The Leukemia & Lymphoma Society appreciates the review of this material by:

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Additional Resources

Hairy Cell Leukemia Foundation (HCLF)
www.hairycellleukemia.org
(224) 355-7201

HCLF is dedicated to improving outcomes for patients by funding research, advancing knowledge about hairy cell leukemia (HCL) among hematologists and by providing educational resources and peer-to-peer support. Their website offers a list of centers of excellence, webinars, an online patient community, a patient data registry and more.

Information for Firefighters. Firefighters are at an increased risk of developing cancer. There are steps that firefighters can take to reduce the risk. Please visit www.LLS.org/FireFighters for resources and information.

Information for Veterans. Veterans who were exposed to Agent Orange while serving in Vietnam; to airborne hazards and burn pits while serving in Iraq, Afghanistan and other areas of Southwest Asia; to contaminated water at Camp Lejeune between 1953-1987; or to ionizing radiation during service may be able to get help from the United States Department of Veterans Affairs. For more information, please

- Call: the VA (800) 749-8387
- Visit: https://www.va.gov/disability/eligibility/hazardous-materials-exposure/

Language Services. Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

Mental Health. Caring for your mental health has benefits for cancer patients. Seek medical advice if you are struggling. For more information, please:

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov

If you or your loved is experiencing a mental health crisis, call 988 to talk to a trained mental health professional. The 988 Suicide and Crisis Lifeline is free, confidential and always available. For the Crisis Text Line, text HOME to 741741.

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, patient care and other needs. For more information, please visit www.LLS.org/ResourceDirectory to view the directory.

World Trade Center Health Program. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for 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 and those who lived, worked or were in school in that 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

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