

TREATMENT UPDATE:

Chronic Lymphocytic Leukemia (CLL)

**CANCERCARE
CONNECT®
BOOKLET SERIES**



CANCER*care*®

WWW.CANCERCARE.ORG



CANCER*care*®

The CancerCare Connect Booklet® Series offers up-to-date, easy-to-read information on the latest treatments, managing side effects and coping with cancer.

To order free copies of this e-booklet, please use the online order form on our website, www.cancercares.org.

Founded in 1944, CancerCare® is the leading national organization providing free, professional support services and information to help people manage the emotional, practical and financial challenges of cancer. Our comprehensive services include counseling and support groups over the phone, online and in person, educational workshops, publications and financial and co-payment assistance. All CancerCare services are provided by oncology social workers and world-leading cancer experts.

CancerCare relies on the generosity of supporters to provide our services completely free of charge to anyone facing a cancer diagnosis. If you have found this resource helpful and wish to donate, please do so online at www.cancercares.org/donate. You may also mail a check, payable to CancerCare, to CancerCare, Attn: Donations, 275 Seventh Avenue, New York, NY 10001.

Thank you.

CancerCare®
National Office
275 Seventh Avenue
New York, NY 10001

Toll-free 800-813-HOPE (4673)
Fax 212-712-8495
Email info@cancercares.org
Web www.cancercares.org

The content of this booklet is independent, non-promotional and free of commercial influence and bias.

Treatment Update: Chronic Lymphocytic Leukemia (CLL)

TABLE OF CONTENTS

Introduction.....	4
Treatment Options.....	4
Treatment Approaches Being Studied.....	8
Treatment Side Effects.....	10
General Side Effects.....	12
Communicating With Your Health Care Team.....	16
CancerCare’s Free Support Services and Programs.....	19
Frequently Asked Questions.....	20
Resources.....	23

EDITOR

John Pagel, MD

*Chief of Hematologic Malignancies Program,
Director, Stem Cell Transplantation, Swedish Cancer Institute,
Seattle, WA.*

© 2019 CancerCare®. All rights reserved. 4/19

All people depicted in the photographs in this booklet are models, used for illustrative purposes only.

Each year in the United States, over 20,000 people are diagnosed with chronic lymphocytic leukemia (CLL), a cancer of the blood and bone marrow.

Because of new treatment options, long-term survival and quality of life continue to improve for people diagnosed with this type of cancer.

In CLL, the body produces too many lymphocytes, a type of white blood cell that helps fight infection. The stages (progression) of CLL are determined by:

- The number of lymphocytes in the blood.
- The enlargement (if any) of the lymph nodes, liver or spleen.
- The presence of blood disorders such as anemia (too few red blood cells) or thrombocytopenia (too few platelets).

Treatment Options

Treatment options for CLL depend on several factors, including the stage of the cancer, whether or not it is causing symptoms and the person's overall health. People with early-stage CLL who are not exhibiting symptoms typically don't receive treatment; instead, their condition is monitored by their health care team, primarily through blood tests. This monitoring is often referred to as "active surveillance."

If treatment is recommended, you and your doctor will discuss the approach that is right for you, based on your individual circumstances.

Chemotherapy

Chemotherapy drugs, given intravenously (through a needle into a vein) or in pill form, can kill cancer cells. Chemotherapy has long been an effective treatment for CLL, and continues to be an important treatment option for many people.

The types of chemotherapy most often given to treat CLL are:

- **Purine analogs**, including fludarabine (Fludara), pentostatin (Nipent) and cladribine (Leustatin). Purine analogs are “antimetabolites” that interfere with DNA production and halt the growth of cancer cells.
- **Alkylating agents**, including chlorambucil (Leukeran) and cyclophosphamide (Cytoxan). These drugs are often used in combination with a purine analog.
- **Bendamustine** (Treanda), an alkylating agent that has some of the same properties as purine analogs.

Chemotherapy treatment often combines two or more drugs, as this seems to be a more effective approach than administering one drug alone (monotherapy). An often-used combination is called FCR, from the initials of the drugs it contains: fludarabine, cyclophosphamide and rituximab (rituximab is not a chemotherapy; it belongs to a group of drugs called monoclonal antibodies).

Chemotherapy-Immunotherapy

Our immune system works constantly to keep us healthy. It recognizes and fights against danger, such as infections, viruses and growing cancer cells. In general terms, immunotherapy uses our own immune system as a treatment against cancer.

Chemo-immunotherapy is a treatment option that combines chemotherapy with monoclonal antibodies, a specific type of immunotherapy. Anti-cancer monoclonal antibodies are made in the laboratory and then administered intravenously, targeting cancer cells. Monoclonal antibodies used in combination with chemotherapy in the treatment of CLL include obinutuzumab (Gazyva), ofatumumab (Arzerra), and rituximab (Rituxan).

Targeted Therapy

Targeted therapies focus on binding to specific molecules thought to be important for cancer cell survival and growth. Targeted therapy treatments are meant to spare healthy tissues and cause fewer side effects than chemotherapy.

Targeted therapies used to treat CLL include:

- **Kinase inhibitors.** Kinase proteins are molecules that serve as important signals to the cell's control center; by doing so, they can help tumor cells grow. Kinase inhibitors attack these proteins.
 - Ibrutinib (Imbruvica) and acalabrutinib (Calquence) inhibit the function of a type of kinase called Bruton's tyrosine kinase (BTK).
 - Idelalisib (Zydelig) acts as a phosphoinositide 3-kinase inhibitor and can be combined with the immunotherapy rituximab in the treatment of CLL.

- Duvelisib (Copiktra) was approved by the U.S. Food and Drug Administration (FDA) in 2018 for the treatment of people with relapsed (recurring) or refractory (not responding to treatment) CLL after at least two prior therapies. Duvelisib blocks two kinase proteins called PI3K-delta and PI3K-gamma.
- **BCL-2 inhibitors.** In 2016, the FDA approved venetoclax (Venclexta), a small molecule oral drug that targets the B-cell lymphoma 2 (BCL-2) protein, for the treatment of people with relapsed CLL who have a chromosomal abnormality called 17p deletion. The BCL-2 protein supports cancer cell growth, and is “overexpressed” (too high) in many patients with CLL. In 2018, the approval was extended to include the treatment of people with or without 17p deletion who have received at least one prior therapy.
- **Immunomodulatory agents.** Lenalidomide (Revlimid) helps the bone marrow produce healthy blood cells while killing abnormal cells. It has been shown to be an effective approach after initial treatment with chemotherapy.



Treatment Approaches Being Studied

There are a number of new approaches being studied for the treatment of CLL:

- Research is being conducted on “next-generation” versions of the targeted therapies ibrutinib and idelalisib. These drugs will work in the same way, with modifications intended to make them more effective, with fewer side effects.
- The results of a phase III clinical trial showed that ibrutinib, given with or without the immunotherapy rituximab, provided longer progression-free survival in people over the age of 65 with previously untreated CLL, when compared with the combination of rituximab and the chemotherapy bendamustine.
- In patients age 70 or younger with previously untreated CLL, a phase III trial showed that ibrutinib reduced the risk of disease progression or death by 65 percent, compared to the chemotherapy regimen FCR. (FCR consists of fludarabine, cyclophosphamide and the immunotherapy rituximab.)
- The phase II CLARITY trial showed a combination of the targeted therapies ibrutinib and venetoclax to be promising in the treatment of relapsed or refractory CLL. After 12 months of treatment with the combination, 54 percent of trial participants were in complete remission (CR) or complete remission with incomplete marrow recovery (CRi).

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new valuable treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side-effects. It's important that you report any side-effects you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so may improve your quality of life and allow you to maintain your treatment plan. It's important to remember that not all patients experience all side effects, and patients may experience side effects not listed here.

CLL itself carries a risk of infection, and treatment can increase that risk. Your doctor may recommend a medication to help prevent infection. Notify your health care team immediately if you experience a fever, as this is a sign of a possible infection.

Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include:

- Fatigue
- Nausea or vomiting
- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding (from having a low platelet count)
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

Chemotherapy can cause changes in the way food and liquids taste, including causing an unpleasant metallic taste in the mouth. Many people find that switching to plastic utensils helps. It may also help to avoid eating or drinking anything that comes in a can, and to use enamel-coated pots and pans for food preparation.

Side Effects of Immunotherapy

The immunotherapy used in combination with chemotherapy for the treatment of CLL travels through the bloodstream, helping to prompt an immune response. Because it can trigger an attack on healthy cells as well as cancer cells, certain side effects may be experienced, including fatigue, decreased appetite and digestive tract symptoms. The management of these potential side effects is discussed in the next section of this booklet.

Side Effects of Targeted Therapy

Targeted therapy doesn't have the same effect on the body as do chemotherapy drugs, but they can still cause side effects. Side effects of targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), nerve damage, high blood pressure and problems with blood clotting and wound healing.

Your specific targeted therapy treatment may have unique side effects. It's important to have a discussion with your health care team to understand what these potential side effects are, how to reduce the risk of their occurring, and how to minimize their impact should you experience them.

General Side Effects

Some side effects may occur across treatment approaches; this section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals cold or at room temperature, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.



Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes as well as liquid. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Managing Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if he or she thinks any of these conditions may be contributing to your fatigue.

Managing Pain

To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs
- When the pain occurs
- How long it lasts
- How strong it is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense
- What makes the pain feel better and what makes it feel more intense

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication, to determine if they are safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.



Communicating With Your Health Care Team

As you manage your cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurse practitioners, physician assistants, nurses, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with symptoms related to your illness or treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, you should ask your most important questions first, and be as specific and brief as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person who accompanies you can serve as a second set of ears.

He or she may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice, and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, ask if you can use it to take notes. Writing notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialists as needed.

Remember, there is no such thing as over-communication.



CancerCare's Free Support Services and Programs

It is very difficult to receive a diagnosis of cancer, and adjusting to the necessary changes in your life can be challenging.

CancerCare® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and provide information on support groups and other resources.

To learn more about how CancerCare helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network, comprised of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q: Is stem cell transplantation a treatment option for CLL?

A: A stem cell transplant is a procedure in which diseased bone marrow (the spongy tissue inside bones where blood cells are made) is replaced with healthy bone marrow. It is not a common treatment approach for CLL, as there are a number of effective drugs available that avoid the risk associated with a stem cell transplant. Stem cell transplantation may be recommended in certain circumstances; for example, in cases where the CLL has not responded to other treatment approaches.

If stem cell transplantation is chosen as a treatment for CLL, the stem cells are harvested (removed) from a donor (often a close relative, such as a brother or sister) and subsequently delivered to the patient. The stem cells are then “infused” (transplanted) into the body, where they travel to the bones and begin rebuilding bone marrow.

Q: What reasons would warrant the move from active surveillance to treatment for my CLL?

A: Many patients living with CLL can stay on active surveillance for a long period of time, even years. There are well-established criteria for beginning treatment, including the experience of certain symptoms, such as:

- Severe fatigue
- Significant unintended weight loss
- Excessive sweating

- Pain coming from the spleen
- Enlarged lymph nodes
- Certain changes in blood counts

It is essential that you visit your doctor regularly for blood tests and to alert him or her of any symptoms you might be having.

Q: My health care team says I may experience constipation as a side effect of my CLL treatment. What can I do to avoid that?

A: Constipation is a potential side effect of CLL treatments, particularly chemotherapy. If you do experience constipation, alert your health care team and be sure to follow their instructions to help alleviate your discomfort, including the possible use of medications and stool softeners.

Some general tips to avoid constipation:

- As hydration is important, make sure to drink plenty of fluids. Also, limit your intake of caffeine and alcoholic beverages, as they can cause dehydration.
- Include foods high in fiber in your daily diet, such as fruit (especially pears and prunes), vegetables and cereals. If your health care team approves, you may want to add synthetic fiber to your diet, such as Metamucil, Citrucel or FiberCon.
- Be as physically active as you can, after checking with your doctor on the level of physical activity that is right for you.
- If your doctor has prescribed a “bowel regimen,” make sure to follow it exactly.

Q: What is a treatment summary and why it is important?

A: A treatment summary, sometimes called a “shadow chart,” is a document you create and which remains in your possession. Maintaining your own records allows you and your family members instant access to the specifics of your CLL diagnosis and treatment. A treatment summary should include:

- Your name and date of birth.
- Date of diagnosis.
- Name, affiliation, and contact information of the doctor who gave the diagnosis.
- Prescribed therapy/therapies; include dates started and stopped, and dosages when appropriate.
- Dates and types of post-diagnosis testing, and the results.
- Other medication and supplements you are taking.
- Names, affiliations, and contact information of all members of your health care team.

Talk to your doctor or a member of your health care team about your intention to create a treatment summary, and ask them what else they suggest be included. Take your treatment summary with you when you visit any health care provider, not just your oncologist.

Resources

CancerCare®

800-813-HOPE (800-813-4673)
www.cancercares.org

American Cancer Society

800-227-2345
www.cancer.org

Cancer.Net

Patient information from
the American Society of
Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute

800-422-6237
www.cancer.gov

Cancer Support Community

888-793-9355
www.cancersupportcommunity.org

National Coalition for Cancer Survivorship

877-622-7937
www.canceradvocacy.org

CLINICAL TRIALS WEBSITES

EmergingMed

www.emergingmed.com

National Cancer Institute

www.cancer.gov

BLOOD CANCER ORGANIZATIONS

Be The Match®

800-627-7692
www.bethematch.org

Blood & Marrow Transplant Information Network

800-597-7674
www.bmtinfonet.org

CLL Society

www.clisociety.org

The Leukemia & Lymphoma Society

800-955-4572
www.lls.org

National Bone Marrow Transplant Link

800-546-5268
www.nbmtlink.org

This booklet was made possible by Pharmacyclics, Inc.



CANCER*care*[®]

Help and Hope

WWW.CANCERCARE.ORG
800-813-HOPE (4673)