Patient Resource: Understanding Therapy Options for Your CLL/SLL

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The goal of this resource is to increase your understanding of your chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL) and your treatment options. Treatment is recommended when symptoms develop, blood counts worsen, or lymph nodes/spleen enlarge. Knowledge and understanding will make you better equipped to partner in decision-making with your oncology care team.

Treatment for CLL/SLL has evolved substantially over the past decade. Whereas in the past, most patients received chemoimmunotherapy, essentially all patients should now receive targeted therapies, which are generally safer and more effective.

Note that not all patients with CLL/SLL require treatment. Your care team may recommend treatment based on factors such as the presence of disease symptoms or abnormal bloodwork results. If and when to start therapy is usually best handled as a shared medical decision. This resource was developed specifically for patients who do require treatment.

You will want as much information as possible about your cancer before you begin. If you do not have all this information yet, ask your oncology care team to help you fill out this checklist with answers about your diagnosis. Learn more about common treatments with the **CLL Medicine Cabinet**.

Common Treatments for CLL

Treatment	Mechanism	Approval
Acalabrutinib	BTK inhibitor (a targeted treatment targeting abnormal signaling in CLL cells)	Approved for the treatment of CLL/SLL
Zanubrutinib	BTK inhibitor	Approved for the treatment of CLL/SLL
Venetoclax plus acalabrutinib or obinutuzumab or rituximab	BTK inhibitor OR BCL-2 inhibitor (another targeted treatment) OR anti-CD20 antibody (an antibody treatment that targets a specific molecule on the CLL cell)	Approved for the treatment of CLL/SLL
Pirtobrutinib	BTK inhibitor (different BTK interaction mechanism than acalabrutinib, ibrutinib, or zanubrutinib)	Approved for CLL/SLL that has previously been treated with a covalent BTK inhibitor
Lisocabtagene maraleucel	CAR T-cell therapy (works by taking immune T-cells from the patient, modifying them against CLL cells, and returning them to the patient)	Approved for relapsed/refractory CLL/SLL when previously treated with at least 2 prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor

- Additional treatments used in special circumstances include ibrutinib (a BTK inhibitor), idelalisib and duvelisib (2 PI3K inhibitors rarely used due to side effects), allogeneic hematopoietic stem cell (bone marrow) transplant from a donor, or chemoimmunotherapy (such as FCR [fludarabine, cyclophosphamide, rituximab]). Clinical trials can be a strong option.

My Life Concerns: What Do I Need to Tell My Doctor?

Think carefully about your personal expectations, desires, and hopes for treatment and how treatment will affect your life. Are there events you don't want to miss or activities you don't want to give up or curtail, such as travel? Will work or family situations make it difficult to be available for treatment? How will you get to and from the clinic? Do you have a social/familial support system? Do you need help talking with loved ones? Cost issues? Fears? What other concerns do you have?

Make notes about the things you want to discuss with your doctor. Your satisfaction with treatment requires weighing all the factors for medical success and a happy life. You may need to give more weight to one or the other from time to time. Knowing what you value will help you do this.

The following table includes some of the key things to think about with different treatment options for CLL.

Factor	Impact on Treatment Decisions
How the treatment is administered (orally, intravenously)	◢ Venetoclax is taken orally but is usually combined with anti-CD20 antibodies, which are administered intravenously ◢ Acalabrutinib + venetoclax is a recently approved all-oral therapy ◢ BTK inhibitors are oral medications ◢ Many medications used with CAR T-cell therapy are administered intravenously
How long the treatment must be taken (for a limited duration of time, or continuously until the medication no longer controls the disease)	◢ Venetoclax is recommended to be taken for 1 year in the first-line setting (ie, no previous therapy for CLL/SLL), or 2 years in second-line or later settings (ie, previously treated with other therapies) ◢ BTK inhibitors are usually taken continuously until the disease progresses or the drug must be stopped because of drug resistance or side effects that are unmanageable ◢ Obinutuzumab infusions are recommended to be given for a total of six 28-day cycles
What the common side effects are	◢ Different treatment regimens have different side effect profiles; these should be discussed with your treatment team before deciding on a treatment course
Other illnesses (comorbidities) and medications	◢ Other conditions and medications can influence the safest and most effective therapy
Future therapies	◢ Most patients will need more than 1 therapy, so it is best to understand how one therapy might affect subsequent options
Your financial considerations	◢ Will the medication be covered by your insurance? What is your "out-of-pocket" expense? If not or only partially covered, are there ways to obtain the treatment through other means, such as medication assistance programs?

My Upcoming Treatment: What Do I Need My Doctor to Tell Me?

The following questions were identified by a panel of 5 experts in CLL/SLL as the key factors that help guide treatment decisions. If your answer to any question is "I don't know," consult with your specialist or a member of your healthcare team to get the answer. As you learn more about CLL/SLL, you will become more confident in decision-making for your disease. Working together, you and your doctor can make sure your health and treatment are balanced with all the other parts of your life.

Note that biomarker testing (FISH, TP53, and IgHV tests) before treatment is one of the most important things you can do for your CLL/SLL. Obtaining the appropriate biomarker tests at the right time will provide information about the specific mutations associated with your CLL/SLL and will help guide treatment decisions, along with helping predict how aggressively the disease might behave in the future. Learn more with **Test Before Treat** resources.

Newly Diagnosed Questions:

What is your treatment setting?

- ☐ Newly diagnosed (first treatment)
- ☐ Second-line therapy (you have received 1 prior treatment regimen)
- ☐ Third-line therapy (you have received 2 prior treatment regimens)
- ☐ Fourth-line therapy (you have received 3 prior treatment regimens)
- ☐ I don't know

Does your CLL have a del(17p) or *TP53* mutation?

- ☐ Yes
- ☐ No
- ☐ I don't know

Does your CLL have an *IGHV* mutation?

- ☐ Yes
- ☐ No
- ☐ I don't know

Do you have any of the following health issues that might influence which treatments are right for you?

- ☐ History of cardiac arrhythmias, presence of cardiac failure, or receiving anticoagulation therapy or doublet antiplatelet therapy
- ☐ Bulky disease, diminished creatinine clearance, or lymphocyte counts greater than 25
- ☐ Uncontrolled hypertension
- ☐ Controlled hypertension
- ☐ I don't know

Second-line Therapy Questions:

What treatment did you receive first?

- ☐ Ibrutinib
- ☐ Acalabrutinib or zanubrutinib
- ☐ Venetoclax + BTK inhibitor
- ☐ Venetoclax + anti-CD20 monoclonal antibody (rituximab or obinutuzumab)
- ☐ Chemoimmunotherapy or other
- ☐ I don't know

Why did you stop this therapy?

- ☐ (If you received continuous therapy) My disease progressed
- ☐ (If you received time-limited therapy) My disease progressed during treatment or less than 2 years after stopping treatment
- ☐ (If you received time-limited therapy) My disease progressed more than 2 years after stopping treatment
- ☐ I could not tolerate the treatment anymore
- ☐ I don't know

Third-line Therapy Questions:

What treatment did you receive second?

- ☐ I have not received a second therapy yet
- ☐ Ibrutinib
- ☐ Acalabrutinib or zanubrutinib
- ☐ Venetoclax + BTK inhibitor
- ☐ Venetoclax + anti-CD20 monoclonal antibody (rituximab or obinutuzumab)
- ☐ Chemoimmunotherapy or other
- ☐ Pirtobrutinib
- ☐ Lisocabtagene maraleucel
- ☐ I don't know

Why did you stop this therapy?

- ☐ (If you received continuous therapy) My disease progressed
- ☐ (If you received time-limited therapy) My disease progressed during treatment or less than 2 years after stopping treatment
- ☐ (If you received time-limited therapy) My disease progressed more than 2 years after stopping treatment
- ☐ I could not tolerate the treatment anymore
- ☐ I don't know

Fourth-line Therapy Questions:

What treatment did you receive third?

- ☐ I have not received a third therapy yet
- ☐ Ibrutinib
- ☐ Acalabrutinib or zanubrutinib
- ☐ Venetoclax + BTK inhibitor
- ☐ Venetoclax + anti-CD20 monoclonal antibody (rituximab or obinutuzumab)
- ☐ Chemoimmunotherapy or other
- ☐ Pirtobrutinib
- ☐ Lisocabtagene maraleucel
- ☐ I don't know

Why did you stop this therapy?

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- ☐ I could not tolerate the treatment anymore
- ☐ I don't know

This tool's recommendations are for educational purposes only and do not replace medical advice. Always talk with your oncologist about what is right for you. You may bring this survey to your next oncology appointment to review.

There are many effective treatment options available for patients with CLL/SLL, and many promising new therapies are available through clinical trials. Today, most patients with CLL/SLL can live well for many years with their disease.

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