

Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma

Overview

Lymphoma is the most common blood cancer. The two main forms of lymphoma are Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood, or other organs, and form a mass called a tumor. The body has two main types of lymphocytes that can develop into lymphomas: B lymphocytes (B cells) and T lymphocytes (T cells).

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are cancers that affect the same lymphocytes. CLL and SLL are essentially the same disease, with the only difference being the location where the cancer primarily occurs. When most of the cancer cells are located in the bloodstream and the bone marrow, the disease is referred to as CLL, although the lymph nodes and spleen are often involved. When the cancer cells are located mostly in the lymph nodes, the disease is called SLL.

Many patients with CLL/SLL do not have any obvious symptoms of the disease. Their doctors might detect the disease during routine blood tests and/or a physical examination. For others, the disease is detected when symptoms occur and the patient goes to the doctor because he or she is worried, uncomfortable, or does not feel well. CLL/SLL may cause different symptoms depending on the location of the tumor in the body. The symptoms of CLL/SLL include a tender, swollen abdomen and feeling full even after eating only a small amount. Other symptoms can include fatigue, shortness of breath, anemia, bruising easily, night sweats, weight loss, and frequent infections. However, many patients with CLL/SLL will live for years without symptoms.

Treatment Options

Treatment is based on the severity of associated symptoms as well as the rate of cancer growth. If patients show no or few symptoms, doctors may decide not to treat the disease right away, an approach referred to as “watch and wait” or “watchful waiting.” With this strategy, patients’ overall health and disease are monitored through regular checkup visits and various evaluation procedures, such as laboratory and imaging tests. Active treatment is started if the patient begins to develop lymphoma-related symptoms or there are signs that the disease is progressing based on testing during follow-up visits. Studies have shown that patients with less advanced disease managed with a watch and wait approach have outcomes similar

to those who are treated early in the course of the disease. However, patients with high-risk disease may need to start treatment right away.

There are many current first-line treatment options for CLL/SLL. The choice of treatment will depend on the stage of the disease, the patient’s symptoms, the age and overall health of the patient, and the benefits versus side effects of treatment. Treatment choice may also vary depending on whether the patient’s lymphoma cells are missing parts of certain chromosomes (called deletions). Common drugs or drug combinations used as initial treatments for CLL/SLL include:

- BR (bendamustine [Treanda] and rituximab [Rituxan])
- CG (chlorambucil [Leukeran] and obinutuzumab [Gazyva])
- FCR (fludarabine [Fludara], cyclophosphamide [Cytoxan], and rituximab)
- FR (fludarabine and rituximab)
- Ibrutinib (Imbruvica)
- Ofatumumab (Arzerra) and chlorambucil
- Rituximab and chlorambucil
- PCR (pentostatin, cyclophosphamide, and rituximab)

For patients whose disease becomes *refractory* (no longer responds to treatment) or *relapses* (returns after treatment), secondary therapies may be successful in providing another remission. Some common agents that are used either alone or in pairs for relapsed/refractory CLL and SLL include:

- Bendamustine
- Chlorambucil
- Fludarabine
- Ibrutinib
- Idelalisib (Zydelig) + rituximab
- Alemtuzumab (Campath; provided only through Campath Distribution Program; no longer commercially available)
- Obinutuzumab
- Ofatumumab
- Rituximab
- Venetoclax (Venclexta)

Other combination treatment regimens occasionally used in the relapsed/refractory setting include:

- HDMP (high-dose methylprednisolone) and rituximab
- OFAR (oxaliplatin [Eloxatin], fludarabine, cytarabine [Cytosar-U], and rituximab)
- R-CHOP (rituximab, cyclophosphamide, doxorubicin [Adriamycin], vincristine [Oncovin], and prednisone)

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Ofatumumab can also be used as maintenance therapy to prevent relapse in patients who achieve full or partial remission after at least two other therapies for CLL. It is not yet clear whether or not stem cell transplantation is helpful for patients with CLL/SLL. Stem cell transplants are usually done as part of a clinical trial in patients with high-risk or relapsed/refractory disease. Typically, stem cells from a donor are used. For more information on stem cell transplants, view the *Understanding the Stem Cell Transplantation Process* booklet on the Lymphoma Research Foundation's (LRF) website at www.lymphoma.org.

Treatments Under Investigation

Many treatments are currently being tested in clinical trials for patients with both newly diagnosed and relapsed/refractory CLL/SLL. Several chemoimmunotherapy agents are being explored as induction therapy in newly diagnosed patients. In addition, the efficacy and safety of agents such as lenalidomide (Revlimid), duvelisib, MOR00208, and MEDI-551 are being investigated alone or as part of combination therapy regimens in patients with relapsed/refractory disease. Ublituximab alone or in combination with ibrutinib, lenalidomide, pembrolizumab, or TGR-1202 is also being tested. Another area of research for treating CLL is genetically engineered T cells designed to recognize and kill CLL cells. Finally, researchers are investigating ways to improve stem cell transplantation in patients with CLL/SLL. It is critical to remember that today's scientific research is continuously evolving. Treatment options may change as new treatments are discovered and current treatments are improved. Therefore, it is important that patients check with their physician or with LRF for any treatment updates that may have recently emerged.

Clinical Trials

Clinical trials are crucial in identifying effective drugs and determining optimal doses for patients with lymphoma. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on LRF's website at www.lymphoma.org, talk to their physician, or contact the LRF Helpline for an individualized clinical trial search by calling (800) 500-9976 or emailing helpline@lymphoma.org.

Follow-up

Because CLL/SLL is generally characterized by multiple disease relapses after responses to a variety of treatments, patients in remission should have regular visits with a physician who is familiar with their medical history and the treatments they have received. Medical tests (such as blood tests and computed tomography [CT] scans) may be required at various times during remission to evaluate the need for additional treatment.

Some treatments can cause long-term effects or late effects, which can vary based on duration and frequency of treatments, age, gender, and the overall health of each patient at the time of treatment. A physician will check for these effects during follow-up care.

Patients and their caregivers are encouraged to keep copies of all medical records and test results as well as information on the types, amounts, and duration of all treatments received. This documentation will be important for keeping track of any effects resulting from treatment or potential disease recurrences.

Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and CLL, including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts for people with CLL, as well as an *Understanding Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma* patient guide and CLL e-Updates that provide the latest disease-specific news and treatment options. For more information about any of these resources, visit our websites at www.FocusOnCLL.org or www.lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.