

## Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

### 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 lymphocytes, a type of white blood cell, grow abnormally. The body has two main types of lymphocytes that can develop into lymphomas: B-lymphocytes (B-cells) and T-lymphocytes (T-cells). Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood or other organs, and can accumulate to form tumors.

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are B-cell NHLs. CLL and SLL are essentially the same disease with slightly different manifestations. The only difference is where the cancer primarily occurs. When the cancer cells are located mostly in the lymph nodes, the disease is called SLL. 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.

CLL tends to be an indolent (slow-growing) cancer. However, over time, it can progress to a more aggressive type of lymphoma. Approximately 15,000 new cases of CLL are diagnosed annually. Common signs of disease include a swelling of the liver and spleen and enlargement of the lymph nodes in the neck, underarm, stomach or groin. Other symptoms of CLL can include, fatigue, shortness of breath, anemia, bruising, night sweats, weight loss and frequent infections. Oftentimes, people with CLL have no obvious symptoms of the disease at diagnosis.

Approximately one-third of all CLL patients will live for years—and even decades—without symptoms. Another one-third will require therapy immediately or will be symptomatic within three to five years, requiring treatment. Another one-third will experience intermediate disease progression in which the cancer is dormant and then becomes active, but will respond to treatment.

### Treatment Options

Treatment is based on the severity of associated symptoms as well as the rate of cancer growth. Since CLL grows slowly, doctors may decide not to treat it right away, an approach referred to as “watch and wait” or “watchful waiting.” Studies have shown that patients treated early in their disease course, compared to those followed with a “watch and wait” approach, exhibit similar overall survival. The treatment options available for CLL patients include:

**Chemotherapy** is treatment with medication that circulates throughout the body. Two types of chemotherapy most often used in CLL treatment:

- Purine nucleoside analogues: cladribine (Leustatin), fludarabine (Fludara) and pentostatin (Nipent)
- Alkylating agents: chlorambucil (Leukeran), cyclophosphamide (Cytoxan) and bendamustine (Treanda). Prednisone (a steroid) is often given together with chlorambucil or cyclophosphamide.

**Monoclonal antibodies** can recognize specific proteins on the surface of lymphoma cells and destroy them. Three commonly used monoclonal antibodies include:

- Alemtuzumab (Campath) has been approved for use in patients with advanced CLL who are no longer responding to other treatments.
- Ofatumumab (Arzerra) received approval for the treatment of patients with CLL whose disease is refractory to fludarabine (Fludara) and alemtuzumab (Campath).
- Rituximab (Rituxan) was approved in combination with fludarabine and cyclophosphamide for patients with untreated or previously treated CD20-positive CLL.

**Stem cell transplantation** is a treatment option typically reserved for patients whose CLL does not respond to standard therapies. Patients, whose disease has transformed into a more aggressive

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The Lymphoma Research Foundation offers the following patient education and support programs:

- *Lymphoma Helpline*
- Clinical Trials Information Service
- Lymphoma Support Network
- Publications
- Teleconferences
- Webcasts & podcasts
- In-person conferences

## Medical reviewer:

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## Developed in collaboration with:



cllifogroup.org

## Supported through grants from:



Genentech

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Last Updated June 2010

form, could potentially benefit from a stem cell transplant. In CLL, the patient's own stem cells (autologous transplant) are rarely used. Typically, stem cells from a donor are used (allogeneic transplant), most commonly in a reduced intensity allogeneic transplant (sometimes referred to as a "mini-allogeneic transplant").

Common combination drug regimens used to treat CLL include:

- R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)
- FR (fludarabine, rituximab)
- FCR (fludarabine, cyclophosphamide, rituximab)
- BR (bendamustine, rituximab)
- BCR (bendamustine, cyclophosphamide, rituximab)
- PCR (pentostatin, cyclophosphamide, rituximab)

For some patients, CLL does not return after initial treatment. However, for many patients the disease does return. For patients who become refractory (disease does not respond to treatment) or relapse (disease returns after treatment), secondary therapies may be successful in providing another remission. Some common single-agent therapies used in the relapsed setting include:

- Alemtuzumab (Campath)
- Chlorambucil (Leukeran)
- Fludarabine (Fludara)
- Rituximab (Rituxan)
- Ofatumumab (Arzerra)
- Bendamustine (Treanda)

Some common combination treatment regimens used in the relapsed or refractory setting include:

- R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)
- FR (fludarabine, rituximab)
- FCR (fludarabine, cyclophosphamide, rituximab)
- BR (bendamustine, rituximab)
- R-CVP (cyclophosphamide, vincristine, prednisone)

## Treatments Under Investigation

Many treatments are currently being tested in clinical trials for both newly diagnosed and relapsed/refractory CLL patients. For a listing of treatments under investigation, visit the Lymphoma Research Foundation's website (lymphoma.org) or order the publication entitled *Understanding CLL/SLL: A Guide for Patients, Survivors and Loved One*. 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 the Lymphoma Research Foundation or their physician for any treatment updates that may have recently emerged.

## Participating in Clinical Trials

Clinical trials are crucial in identifying effective drugs and determining optimal doses for lymphoma patients. Patients interested in participating in a clinical trial should talk to their physician. Contact the Lymphoma Research Foundation's *Helpline* for an individualized clinical trial search by calling (800) 500-9976 or emailing [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

## Resources

The Lymphoma Research Foundation offers a wide range of resources that address treatment options, the latest research advances and coping with all aspects of lymphoma. The Foundation also provides many educational activities, from in-person meetings to teleconferences and webcasts. For more information about any of these resources, visit the website at [lymphoma.org](http://lymphoma.org), e-mail the *Helpline* at [helpline@lymphoma.org](mailto:helpline@lymphoma.org) or call at (800) 500-9976.