FACT SHEET

Chronic Lymphocytic Leukaemia (CLL) & Small Lymphocytic Lymphoma (SLL)

OVERVIEW

Lymphoma is the 6th most common cancer in Australia in adult men and women. It can affect people of all ages and is the most common blood cancer. Lymphoma is a cancer of the immune system and affects lymphocytes - a type of white blood cell. When lymphocytes gain certain genetic changes, they divide and grow uncontrollably resulting in lymphoma.

There are two main types of lymphocytes called B lymphocytes (B-cells) and T lymphocytes (T-cells). Lymphomas caused by B-cells are more common and account for around 85% of lymphoma cases and lymphomas caused by T-cells account for around 15% of lymphoma cases. The first lymphoma to be discovered was called "Hodgkin lymphoma" (around 15% of all B-cell lymphomas), after Thomas Hodgkin, who described it. All subsequent lymphomas discovered were called "non-Hodgkin lymphoma" (around 90% of all lymphomas, both B-cell and T-cell lymphomas).

There are over 80 different subtypes of lymphoma, that are classified according to its clinical behaviour. "Aggressive" (high-grade or fast growing) lymphomas are those that grow quickly, usually weeks to months and need treatment immediately. "Indolent" (low-grade or slow growing) lymphomas usually develop over years and often are not treated straight away but are monitored. It is important to know your subtype of lymphoma. Lymphoma cells can travel to any part of the body and be found in lymph nodes, the bone marrow, the spleen, blood, bone, skin and almost any organ or tissue.

Chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL) are subtypes of indolent (slow growing) lymphoma that arise from B lymphocytes that account for around 20% of lymphomas. CLL or SLL (CLL/SLL) are essentially the same disease with the only difference, is where the lymphoma cells are more located. When the lymphoma cells are mostly located in the blood stream and bone marrow, the lymphoma is called CLL. When the lymphoma cells are located mostly in the lymph nodes, the lymphoma is called SLL. Most patients with CLL/SLL do not appear to have any obvious symptoms initially and are commonly diagnosed on an incidental finding with a blood test and/or a physical examination. Some patients have symptoms that may include fatigue, shortness of breath, anaemia, bruising easily, recurrent infections, night sweats and unintentional weight loss, that may depend on where the lymphoma is present in the body.

DIAGNOSIS AND STAGING

A biopsy is always required for a diagnosis of CLL/SLL and is checked for any genetic abnormalities. A biopsy is a surgical procedure to remove part or all of an affected lymph node or other abnormal tissue such as bone marrow or blood to look at it under the microscope. The biopsy can be done under local or general anaesthetic depending on what part of the body is being performed on.

Once a diagnosis of CLL/SLL is made there are further tests that need to be performed to see where else in the body the lymphoma may be and is referred to as staging. Because CLL/SLL are both blood cancers the lymphoma can travel all over the body, so it is important that a check of the entire body is done looking for the lymphoma. Staging tests may include:

- Positron emission tomography (PET) /CT scan
- Computed tomography (CT) scan
- Bone marrow biopsy (not always for SLL)
- Blood tests
- Cytogenetic testing

It is recommended that all patients with CLL/SLL have cytogenetic testing prior to starting treatment. Cytogenetics are tests performed in the laboratory on bone marrow, blood and other tissue from a biopsy to look at any abnormalities in the patient's chromosomes. Normally we have 23 pairs of chromosomes but in patients with CLL/SLL we can see certain changes to these chromosomes.

One change that can be seen is called a deletion, where a part of the chromosome is missing. In CLL/SLL we can see patients with deletions in chromosomes 13 and 17 referred to as 13p deletion and 17p deletion and other changes include an extra copy of chromosome 12 referred to as trisomy 12 and translocation of chromosome 11 and 14 where a piece of one chromosome swaps places with a piece on another chromosome referred to as t(11:14).

Certain chromosome abnormalities have been studied to help guide treatment for patients. These tests include:

IgHV mutation status	Test before first treatment (remains stable over time)
IgHV mutated	For standard treatment options
IgHV unmutated	Not suitable for chemotherapy treatment options
Test FISH	Before every treatment (may change over time)
17p deletion	Can be more fast-growing in behaviour. Not suitable for chemotherapy treatment options
13p deletion	Generally slow growing in behaviour for standard treatment options
Test TP53 mutation	Before every treatment (may change over time)
Mutation present	Not suitable for chemotherapy treatment options

Patients will also undergo a number of baseline tests prior to any treatment commencing to check their organ function and these baseline tests may include a heart scan, kidney scan, and blood tests.

TREATMENTS OPTIONS

CLL/SLL are generally indolent lymphomas and patients can have the lymphoma for years without having any signs or symptoms. Once the lymphoma is diagnosed the need for treatment may not be required straight away and some patients will be actively monitored by their doctor or otherwise known as 'watch and wait'. Research has shown that patients with less advanced disease and managed with active monitoring approach have outcomes similar to those who are treated earlier in the course of the lymphoma. Your doctor will take into account your symptoms versus the side effects of treatment before making a decision.

Once treatment is required genetic testing is recommended to determine the right course of treatment for you. Treatment decisions are based on the presence of genetic abnormalities, rate of growth of the lymphoma, severity of symptoms, patient's age and overall health. Fortunately, there are many treatments available for CLL/SLL and many more are being researched in clinical trials.

Standard first line treatments (most people):

- Fludarabine, cyclophosphamide & rituximab (FC-R)
- Chlorambucil & Obinutuzumab
- Chlorambucil
- Bendamustine & rituximab (BR – rituximab is PBS listed & bendamustine TGA approved but not PBS listed)
- Participation in a clinical trial

First line treatments for patients not suitable for chemotherapy-based regimens:

- Ibrutinib
- Acalabrutinib (TGA approved but not PBS listed)
- Venetoclax & Obinutuzumab
- Idelalisib & rituximab
- Participation in a clinical trial

CLL/SLL usually respond well to treatment, but it is common due to the chronic nature of these lymphomas for them to come back (relapse) and further treatment is required. Recommended standard treatments for relapsed/refractory CLL/SLL include:

- Venetoclax & rituximab
- Ibrutinib
- Acalabrutinib
- Bendamustine (not PBS listed)
- Idelalisib & rituximab
- Allogeneic stem cell transplant (donor cells – only suitable for some patients)
- Participation in a clinical trial

TREATMENTS UNDER INVESTIGATION

Many new individual and combination medicines are currently being tested in clinical trials around the world for both newly diagnosed and relapsed/refractory CLL/SLL. They include new combinations of therapies listed above and/or new medications that include:

- Zanubrutinib
- Umbralisib
- Ublituximab
- Pembrolizumab
- Chimeric Antigen Receptor (CAR) T-cell therapy

CLINICAL TRIALS

Clinical trials are essential in identifying effective medicines and determining optimal doses of these medicines for

people diagnosed with lymphoma. People who are interested in participating in a clinical trial can find one using the following methods:

1. Speak to their specialist to see what options are available
2. See 'Understanding Clinical Trials' fact sheet for websites to find a clinical trial; https://bit.ly/3c4Hi5o

FOLLOW UP

Once treatment is completed, people with lymphoma need to be followed up by their specialist with regular appointments to monitor:

- Evaluate the effectiveness of the treatment
- Ongoing treatment side effects
- Recovery from treatment
- Signs of lymphoma relapsing
- Potential late effects caused by treatment that can occur months or years later, that can be based on the duration and frequency of treatment, age, gender and overall health of each person

RESOURCES AND SUPPORT

Organisation	How can they help?

Lymphoma Australia	• Lymphoma Australia offers a wide variety of resources and support for people with lymphoma or CLL and their caregivers. Please visit our website lymphoma.org.au for further information:
	• Lymphoma Australia Fact sheets & booklets including:
	  • What you need to know about lymphoma booklet
	  • Living with CLL/SLL booklet
	  • Lymphoma subtypes
	  • Understanding Clinical Trials
	  • Emotional impact of a lymphoma diagnosis & treatment
	  • https://bit.ly/3kShk9e
	• Lymphoma Australia YouTube Channel: Presentations and interviews on a variety of topics about lymphoma subtypes, management and supportive care.
	• youtube.com/user/LymphomaAustralia
	• Lymphoma Nurse Support Line: 1800 953 081 or email: nurse@lymphoma.org.au

	• Online private Facebook group: **Lymphoma Down Under** http://bit.ly/2mrPA1k • Online private Facebook group: **CLL Down Under** https://bit.ly/3kUm7qU

SOME QUESTIONS TO ASK YOUR DOCTOR

- What stage of CLL/SLL do I have?
- Do I have any genetic abnormalities detected in my blood or biopsy tissue?
- What type of treatment will I have, and do I need to have treatment straight away?
- What are the side effects of the treatment?
- How long do you think this type of treatment should keep my CLL/SLL under control?
- Are there any clinical trials available for my CLL/SLL?

This resource was last reviewed and updated March 2021