Your Guide to Non-Chemotherapy Treatment Options for CLL/SLL

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Learning about your lymphoma can be like learning a new language. It takes time and practice. Please keep this document handy so you can refer back to it as often as you need to. It will become easier to understand the more you read it.

Many people believe that if you are diagnosed with a cancer like **Chronic Lymphocytic Leukaemia (CLL)** or **Small Lymphocytic Lymphoma (SLL)**, then you're going to need chemotherapy (chemo). But did you know that many treatments for CLL and SLL have been developed that don't include any chemotherapy at all?

Today, many people with CLL/SLL can be treated with targeted therapies that are tablets, capsules or infusions, often with fewer side effects than traditional chemotherapy.

Some people don't even need treatment and instead are actively monitored by their haematologist instead. We call this Watch & Wait, and during this time, your CLL or SLL is "asleep" and not actively growing or causing any harm. But as with any sleeping thing, CLL/SLL can "wake up" and need treatment. This is why your haematologist actively monitors you with regular appointments – usually every 3-6 months, to make sure they catch it if it wakes up. To learn more about Watch & Wait visit our website or download our factsheet here.

Non-chemotherapy options for CLL/SLL

In this newsletter, you'll learn about non-chemotherapy options, how they're given, when they might be used, and what side effects to look out for. This guide is written for you - to help you feel more confident when talking with your doctor about your choices.

Before we get started, there are some things you should know about how your doctor works out the best treatment for you.

Genetic Mutations and Why Do They Matter?

Genetic mutations are small changes in your cancer cells' DNA. These changes can affect how fast your CLL or SLL grows, and they help your doctor work out which treatments will work best.

Some common mutations include:
- 17p deletion
- TP53 mutation
- IGHV status (mutated or unmutated).

These mutations don't come from your parents. They happen only in the cancer cells, not the rest of your body.

Knowing if you have any of these mutations helps your doctor choose the most effective treatment for you. Some medicines work better for certain mutations, and some might not work at all if you have one.

For example, researchers have found that if you have **17p deletion, TP53 mutation or an UNmutated IGHV status**, then chemotherapy probably won't work at all for you. But, some of the treatments we discuss in this newsletter may work very well.

What Genetic Tests Should Be Done for CLL/SLL?

Doctors use special tests to look at your CLL/SLL cells and check for changes in their genes. These are called genetic tests. The results help your doctor choose the best treatment for you.

Testing is usually done with a blood test or bone marrow sample.

Here are the most common tests:

FISH Test (Fluorescence In Situ Hybridisation)

Looks for:
- 17p deletion
- 13q deletion
- 11q deletion
- Trisomy 12.

Why it matters:
If you have a **17p or 11q deletion**, chemotherapy may not work well. Targeted therapies are often better.

When you should have this test:
- This test should be done before you start your first treatment, and every time you're about to start a new treatment.
- If treatment stops working, and the CLL/SLL progresses (meaning it gets worse).
- If your CLL/SLL relapses (comes back after a time of remission).

TP53 Mutation Test

Looks for:
Changes in the TP53 gene.

Why it matters:
If this gene is mutated, your cancer may grow faster and not respond well to some treatments like chemo. Your doctor may suggest a targeted medicine instead.

When you should have this test:
- This test should be done before you start your first treatment, and every time you about to start a new treatment.
- If treatment stops working, or the CLL/SLL progresses.

IGHV Mutation Status Test

Looks for:
Whether your IGHV gene is mutated or unmutated.

Why it matters:
If it's unmutated, your cancer may behave more aggressively. This helps guide your doctor toward the right treatment choice.

When you should have this test:
The results of this test do not change over time, so you should have this test only before you start your first treatment.

Next-Generation Sequencing (NGS) Panel (sometimes used)

Looks for:
A group of gene mutations all at once (including NOTCH1, SF3B1, and more).

Why it matters:
It gives a bigger picture of your cancer's behaviour, especially if you're starting second-line treatment or considering clinical trials.

When you should have it:
You may not need this, but your doctor may recommend it if they want to learn more about your CLL/SLL.

Questions to ask your doctor

Ask your doctor:

- Have I had genetic testing?
- What were my results?
- What do they mean for my treatment?
- What are all my treatment options?
- What are the benefits and risks of this treatment?
- Who do I contact if I have a concern, am unwell, or having side-effects?

Getting the right tests at the right time helps you get the **best possible care** for your CLL/SLL.

What Are Targeted Therapies?

Targeted therapies are medicines that **block specific proteins or signals** that help CLL/SLL grow. They work differently to chemotherapy. Instead of killing all fast-growing cells, they focus on a target (a protein or enzyme marker) in, or on the cancer cells. Some treatments are tablets or capsules, and others are infusions given through a drip.

Before we start though, there are some terms you need to understand.

- **First-line treatment** is the **first treatment** you have to treat your CLL/SLL. It's chosen because it usually works well for most people with the same diagnosis and genetic mutations, and has the best balance of results and side effects.

- **Second-line treatment** is the **next treatment** you get if the first one doesn't work, stops working, or causes problems you can't manage. You may also have second-line treatment if the first-line treatment worked and you went into remission, but the CLL/SLL comes back later (relapses). Sometimes people need more than two treatments. These are called third-line or fourth-line treatments etc.

- **TLS** – stands for **Tumour Lysis Syndrome.** It is a side effect that can happen when lots of cancer cells die quickly during treatment. When this happens, the dead cells release their contents into the blood, which can upset the balance of salts and waste in your body.
    - *If you are at risk of TLS, you may need to start treatment in hospital. You'll be given extra fluids through a drip and medicine to help your kidneys flush out the waste safely. This helps protect your body while the treatment starts working.*

Difference between capsules, tablets, and infusions

Capsule	Tablet	Infusion
A capsule is a **small pill with a soft or hard shell** that holds the medicine inside. The shell breaks open in your stomach to release the medicine. Capsules should not be opened or crushed unless your doctor says it's safe.	A tablet is a **solid, flat pill** that you swallow with water. It's made by pressing the medicine into a firm shape. Some tablets can be broken in half (but only if your doctor says it's okay).	An infusion is **liquid medicine that goes into your body through a drip (IV)** in a vein. It's given slowly at the hospital or clinic, usually over a few hours. You'll be watched closely during and after the infusion to check for any reactions.

Non-chemotherapy Treatment Options

Acalabrutinib

When it's used: First-line treatment if you have a **17p deletion, TP53 mutation, or unmutated IGHV,** or as second-line treatment.

How it's taken: Capsule.

Common side effects: Headache, tiredness, diarrhoea.

Serious side effects: Bleeding, infection, irregular heartbeat.

When to see your doctor: If you feel faint, have signs of bleeding or fever.

Acalabrutinib + Obinutuzumab

When it's used: First-line treatment.

How it's taken: Acalabrutinib is a capsule, obinutuzumab is an infusion.

Common side effects: Chills, fever during infusion, low white blood cells.

Serious side effects: Infections, in fusion reactions.

When to see your doctor: Fevers, chills, shortness of breath after infusion.

Ibrutinib

When it's used: First, or second-line, including people with **17p deletion**.

How it's taken: Tablet.

Common side effects: Diarrhoea, muscle pain, bruising.

Serious side effects: High blood pressure, irregular heartbeat.

When to see your doctor: Chest pain, dizziness, or new bruising.

Ibrutinib + Venetoclax

When it's used: First-line treatment.

How it's taken: Both are tablets.

Common side effects: Diarrhoea, infections, tiredness.

Serious side effects: Tumour lysis syndrome (TLS), low blood counts.
When to see your doctor: Feeling very weak, trouble breathing, or fever.

Idelalisib + Rituximab

When it's used: Second-line when chemo isn't suitable.

How it's taken: Idelalisib is a tablet, rituximab is an infusion.

Common side effects: Diarrhoea, nausea, infections.

Serious side effects: Liver problems, lung inflammation.

When to see your doctor: Yellow skin/eyes, cough, or shortness of breath.

Venetoclax + Obinutuzumab

When it's used: First-line if fludarabine-based chemo isn't recommended.

How it's taken: Venetoclax is a tablet, obinutuzumab is an infusion.
Common side effects: Low white blood cells, diarrhoea.

Serious side effects: TLS, severe infection.

When to see your doctor: Fever, vomiting, or severe fatigue.

Venetoclax + Rituximab

When it's used: Second-line treatment.

How it's taken: Venetoclax is a tablet, rituximab is an infusion.

Common side effects: Nausea, low blood counts.

Serious side effects: TLS, serious infections.

When to see your doctor: High fever, feeling very unwell, or confusion.

Zanubrutinib

When it's used: First-line or second/third-line if not previously used, including if you have 17p deletion and/or TP53 mutation.

How it's taken: Capsule.

Common side effects: Tiredness, bruising, low white cells.

Serious side effects: Bleeding, irregular heartbeat.

When to see your doctor: Bleeding, dizziness, shortness of breath.

Medicine Table: What they are and what they target

Medicine	Type of Medicine	What it targets
Acalabrutinib Ibrutinib Zanubrutinib	BTK inhibitors	Blocks signals that cause CLL/SLL cells to grow, by targeting the protein on CLL/SLL cells called BTK.
Venetoclax	BCL-2 inhibitor	Turns on a signal that helps cancerous CLL/SLL cells to self-destruct.
Obinutuzumab Rituximab	Monoclonal antibody (infusion)	Targets CD20 on B-cells to help immune system fight CLL/SLL.
Idelalisib	PI3K delta inhibitor	Blocks signals that cause CLL/SLL cells to grow, by targeting enzymes on CLL/SLL cells called PI3K.

In Summary

You have more choices than ever before when it comes to treating CLL or SLL - many of them without chemotherapy. Some treatments are oral tablets or capsules, while others may include infusions. Knowing how these medicines work and what to expect can help you feel more confident.

Always talk to your doctor about what treatments are best for you and the benefits and side-effects of each. They will look at your test results, overall health, and type of CLL/SLL to decide what suits you best.

Resources and support

Lymphoma Australia offers a wide range of resources and support for people living with lymphoma or CLL, and their carers. How to access our resources:

- **Visit** our website www.lymphoma.org.au for more information.
- **Phone** our Lymphoma Care Nurse Hotline on 1800 953 081.
- **Email** our Lymphoma Care Nurses nurse@lymphoma.org.au
- **Downloadable information:** Visit our website, or give us a call if you would like some more information on a variety topics related to lymphoma
- **Join** our Facebook page Lymphoma Down Under (make sure you complete all the membership questions when you join).

Disclaimer:
This information has been written with care, but it does not include every possible side effect. Talk to your doctor or nurse to learn the full list of side effects for any treatment and what signs mean you should seek help.