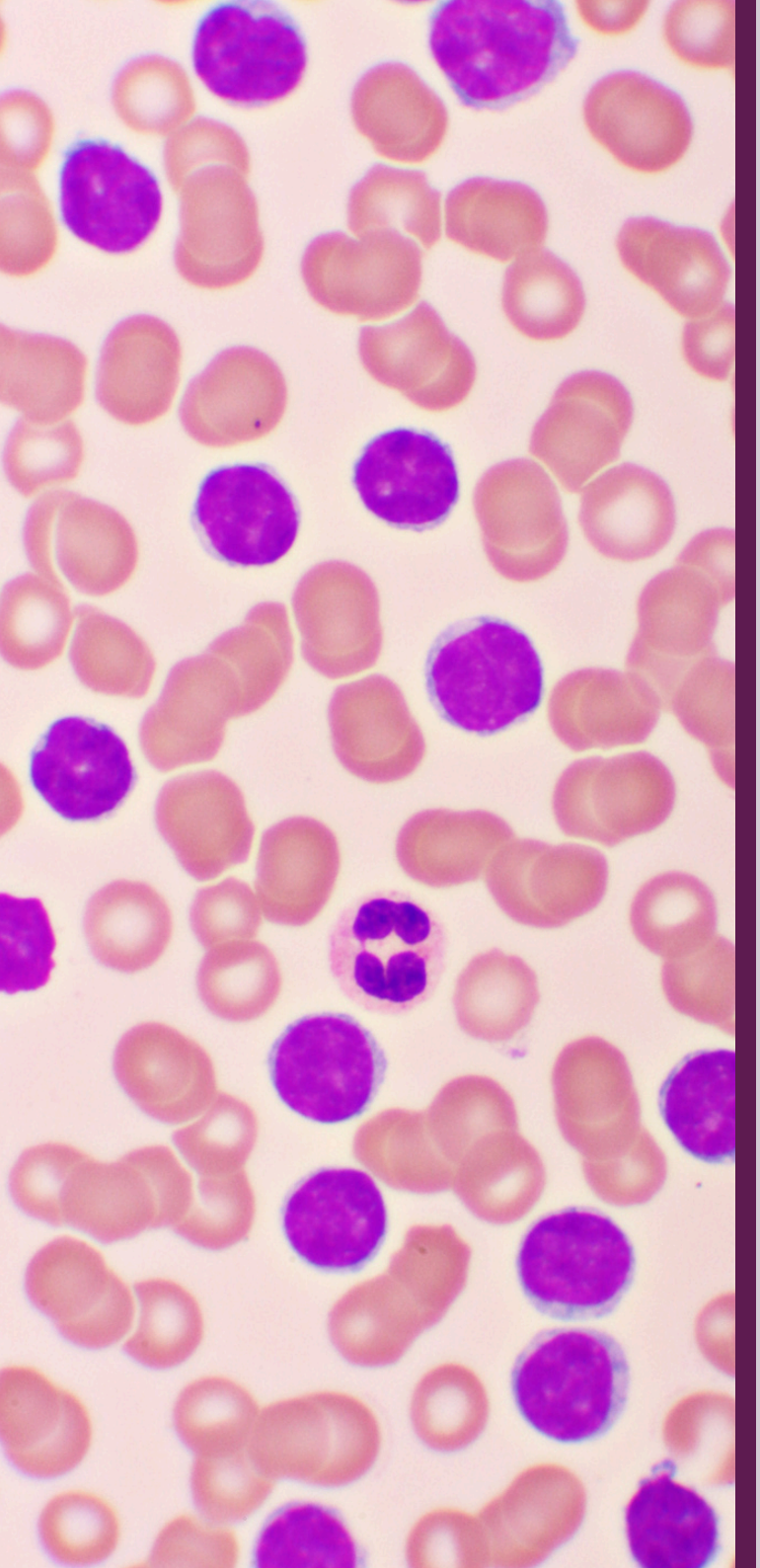


Chronic Lymphocytic Leukemia (CLL)

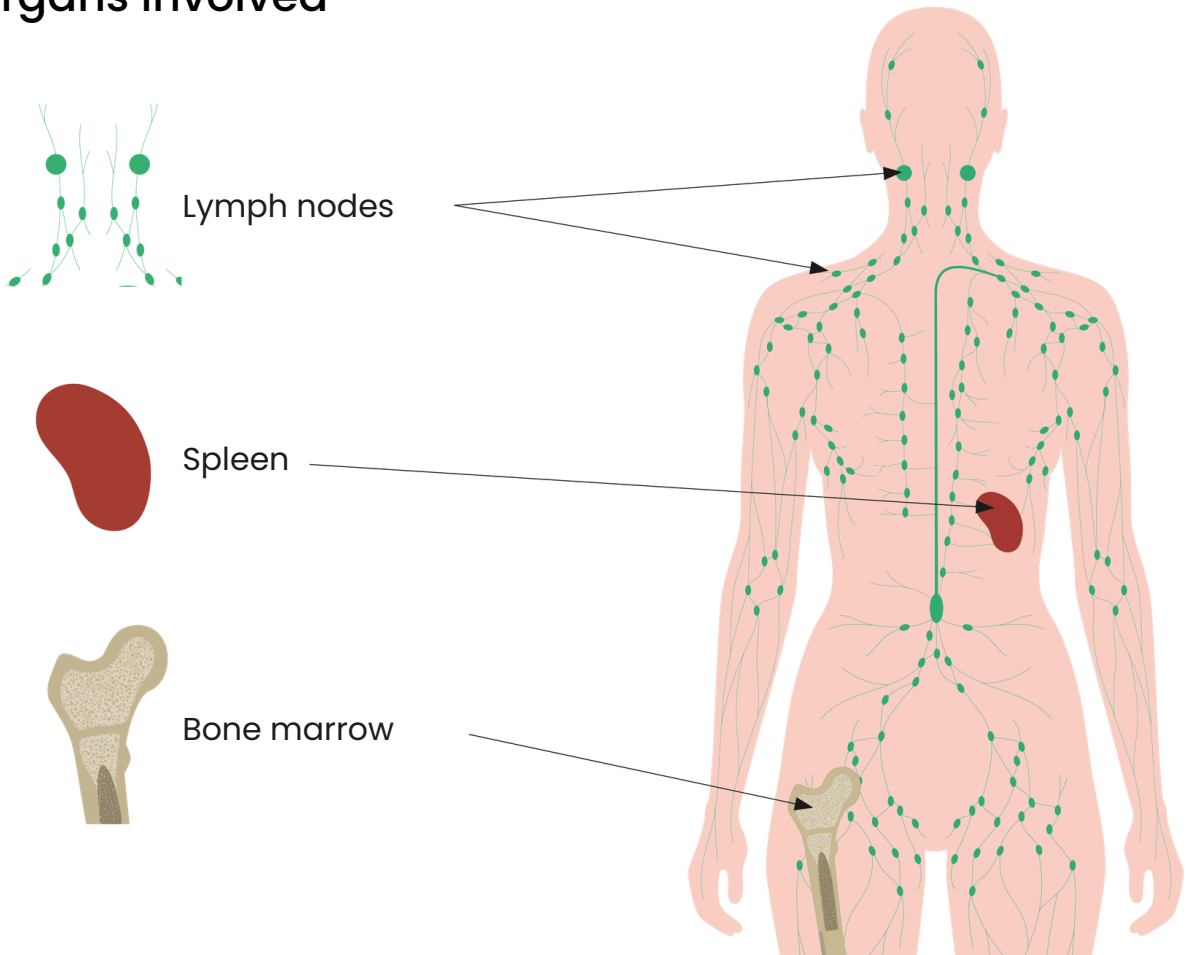
Material for healthcare professional - conversation with the patient

BeOne

What is Chronic Lymphocytic Leukemia (CLL)?

CLL is an indolent, and the most common form of blood cancer in adults.

Organs involved



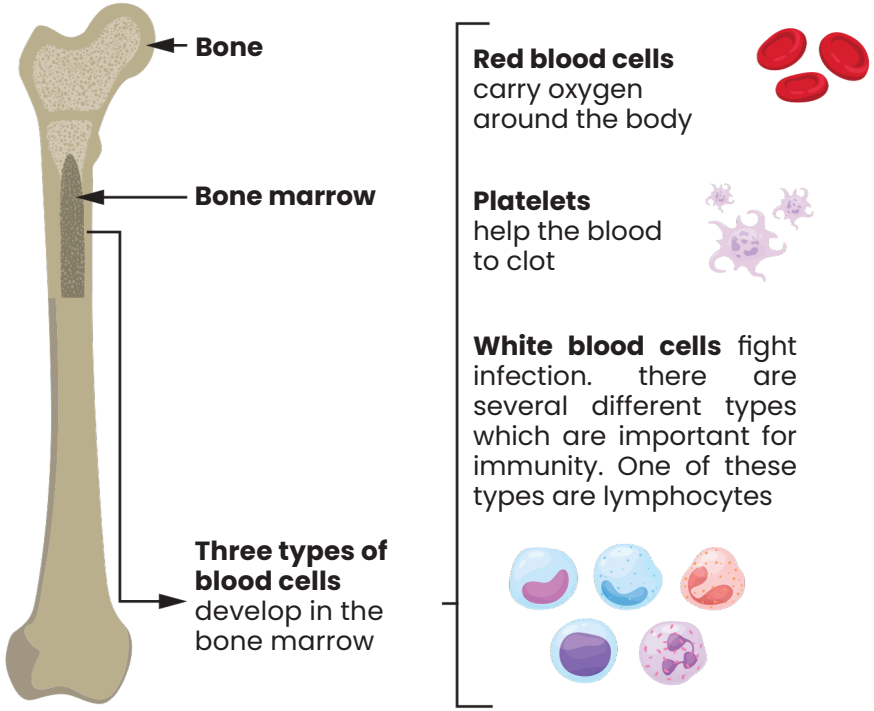
Rare disease:
- Much more common among men
- Median age is 72
- People ≤ 40 can also get sick, but it is rare
- Often an accidental finding

Risk factors:
- Family history
- Age
- Sex
- Exposure to chemicals
- Monoclonal B-cell lymphocytosis

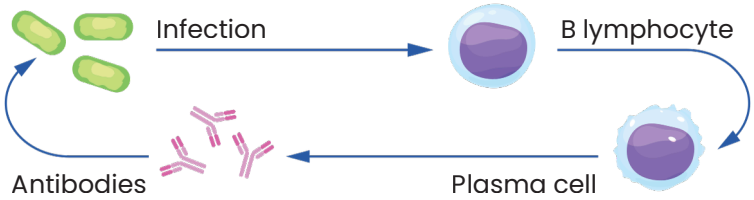
What is Chronic Lymphocytic Leukemia (CLL)?

All blood cells are made in the bone marrow which is a spongy material found inside our bones. CLL is usually caused by **mutations** in the genes of a blood cell. These changes are typically caused by ageing. The blood cells involved in CLL are called **lymphocytes** (type of white blood cell). There are 3 types of lymphocytes: natural killer cells, T cells and B cells.

Normal blood cell production



What do B lymphocytes do?



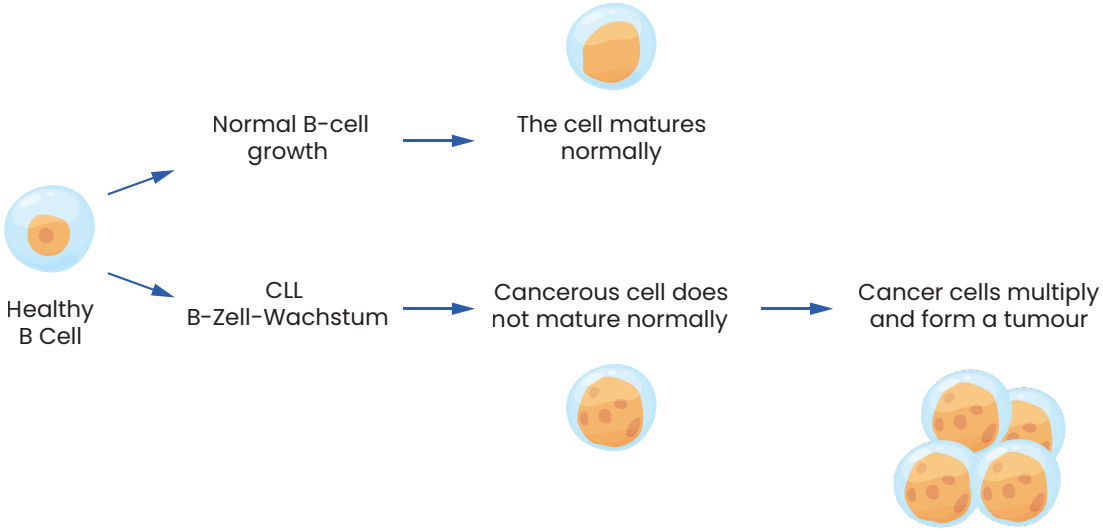
Once B lymphocytes are activated, they turn into a plasma cell and start to produce antibodies. An antibody is a protein that helps the body defend itself against something harmful such as a bacteria or virus.

What is Chronic Lymphocytic Leukemia (CLL)?

In CLL, large numbers of abnormal B lymphocytes are produced.

In CLL, the B cells do not develop properly and may not produce sufficient amount of antibodies. This means that patients with CLL are more likely to develop infections and have difficulty fighting them.

Abnormal B cells also accumulate in the immune system, preventing normal cell production and the normal functioning of red and white blood cells and platelets. This causes, among other things, anemia, blood clotting problems and swollen glands.



Symptoms

Most patients

No symptoms

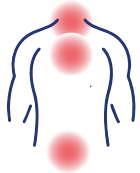
Anaemia

Weakness, Fatigue

Hepatomegaly

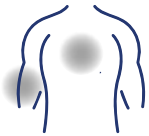
Splenomegaly

Lymphadenopathy (Swelling of lymph nodes)



Higher risk of infections

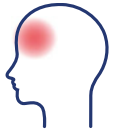
Excessive bruising



Frequent or severe nose bleeds

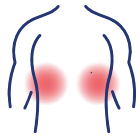
Bleeding gums

Fever



Night sweats

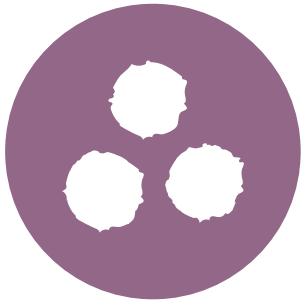
Pain or sense of fullness under your ribs



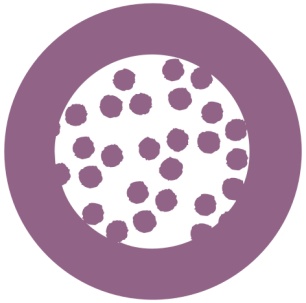
Weight loss

Diagnosis

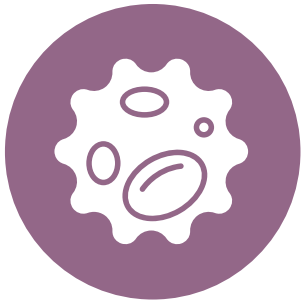
Laboratory tests



Complete blood count (CBC)



Peripheral blood smear



Immunophenotyping (flow cytometry)

Genetic testing

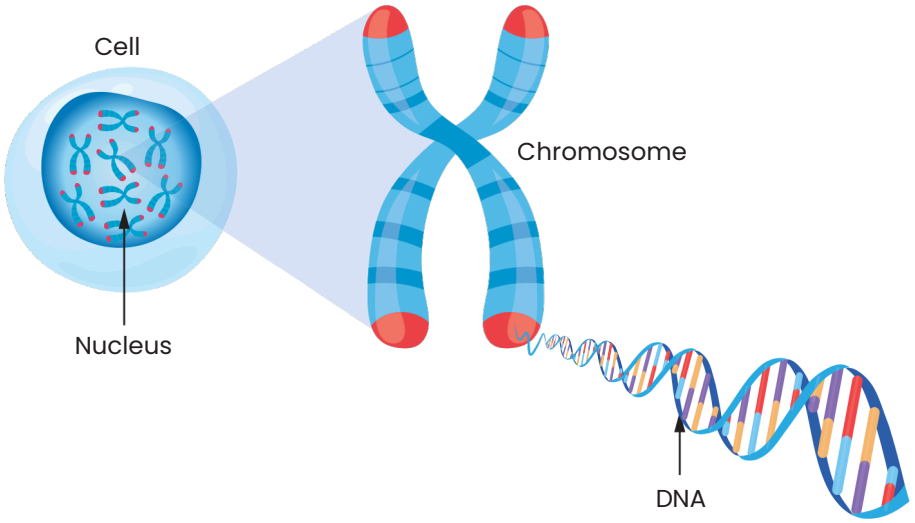
Quantitative immunoglobulin test

CT scan, sonography or MRI or PET (optionally, in some specific cases)

Cariological assessment depending on the planned therapy

Diagnosis

Genetic testing



A number of blood tests may be performed to diagnose CLL and during treatment. These may include:

- **cytogenetic tests**, which check all chromosomes in the leukemia cells,
- DNA sequencing,
- PCR (polymerase chain reaction).

FISH: Fluorescence in situ hybridisation testing is an important cytogenetic test that looks for specific changes in genes or chromosomes in CLL cells. The results inform doctors about the efficacy of certain drugs and help plan treatment.

Gene mutation tests check for the presence of important changes. For example, they can check if a gene called TP53 is missing or if the gene does not work.

Genetic markers

Genetic markers can provide specific information about CLL:

- determine whether CLL is low or high risk predict,
- how the disease may change over time,
- inform about treatment options.

WHAT THE GENETIC MARKERS MAY MEAN?	
Should be performed at the beginning of the diagnosis.	
IGHV	The IGHV gene contains instructions for making antibodies which help the body fight off infections. In CLL, these genes are either mutated or unmutated. **Mutated IGHV** is often associated with a favorable outlook, whereas **unmutated IGHV** genes can mean that your CLL is higher risk and may not respond as well to certain treatments. **More than 1 in 2 people (56%) with CLL have the unmutated IGHV gene.**
Should be performed at the time of the decision to start treatment, as this will influence the choice of treatment.	
TP53	The TP53 gene signals whether damaged cells should be repaired or destroyed. If this gene is **mutated** it may mean that **CLL is higher risk**. More than **80% of people with del 17p also have the TP53 mutation.**
del17p	When part of a chromosome is missing, it's called a deletion. One type of deletion that occurs in chromosome 17 is called del 17p, which is common in CLL. This deletion may **affect how cancer grows**. It is considered a risk factor that may suggest that the disease will progress more quickly. **Some people with del 17p may not respond to certain treatment.**

CLL Staging

The Rai and Binet staging systems are used to predict CLL's progression and develop an appropriate treatment plan.

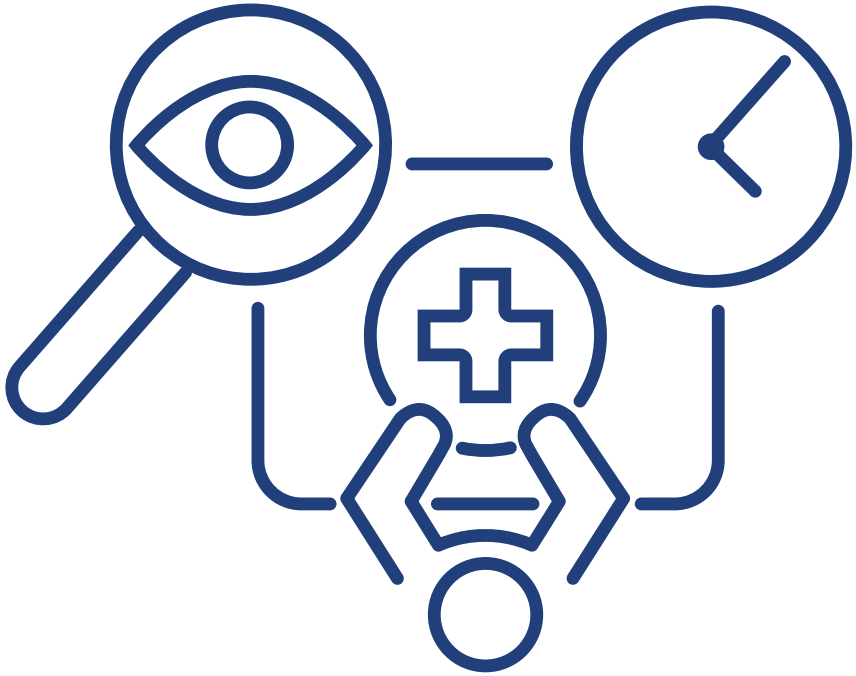
Rai Stage	Findings
0	Asymptomatic lymphocytosis
I	Lymphocytosis and lymphadenopathy
II	Lymphocytosis and lymphadenopathy, orgainomegaly*
III	Lymphocytosis and anemia, with or without lymphadenopathy and/or organomegaly
IV	Lymphocytosis and thrombocytopenia, with or without lymphadenopathy, organomegaly, and/or anemia

*Organomegaly = enlargement of organs, such as liver (hepatomegaly) and/or spleen (splenomegaly).

Rai Stage	Findings
A	No anemia or thrombocytopenia and <3 involved areas*
B	No anemia or thrombocytopenia and ≥3 involved areas
C	Anemia and/or thrombocytopenia, an any number of involved areas

*Areas considered are head and neck including the Waldeyer ring (counts as I area), axilla, groin/superficial femoral, palpable spleen and palpable liver.

Therapeutic approaches



WATCH and WAIT

Because CLL is a slow-growing type of blood cancer, most patients **do not require treatment immediately after diagnosis**, and some may never need it.

The approach of not having treatment until you need it is called **'Watch and wait'**. It is a way of **monitoring asymptomatic patients** with regular check-ups and blood tests.

If patients have very early-stage CLL, doctors usually wait until there are signs of progression before suggesting treatment. There is no evidence that starting treatment earlier helps and may cause side effects

Therapeutic approaches

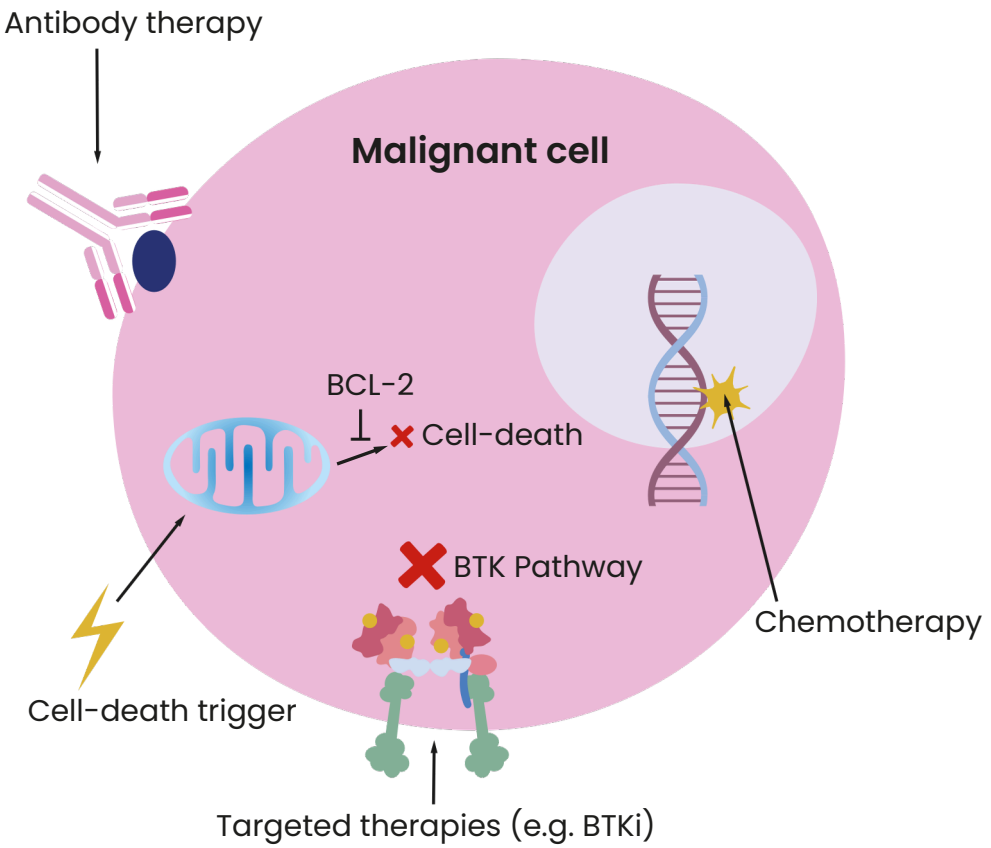
Treatment should be started when a patient has an **advanced or symptomatic disease**.

The choice of treatment will depend on several aspects: the **patient's age and fitness level, disease progression, genetic test results, previous CLL treatment,** and **comorbidities (in particular cardiac and renal disease).**

Most patients are treated with a combination of 2 types of treatment. These are:

- **chemotherapy,**
- **targeted therapy.**

The aim of treatment is to reduce the number of CLL cells to as few as possible **(remission)**. It is not usually possible to cure CLL, but it can be well controlled for many years. Most patients with CLL have long periods of time when they have a normal life with no symptoms.



Notes

Useful links and contacts

lymphome.ch

Weidenweg 39
4147 Aesch BL

+41 (0)61 421 09 27
info@lymphome.ch
www.lymphome.ch

Krebsliga Switzerland

Effingerstrasse 40
P.O. box
3001 Bern

+41 (0)31 389 91 00
www.krebsliga.ch

HOPOS Umbrella Organization of Hemato-Oncological Patient Organizations Switzerland

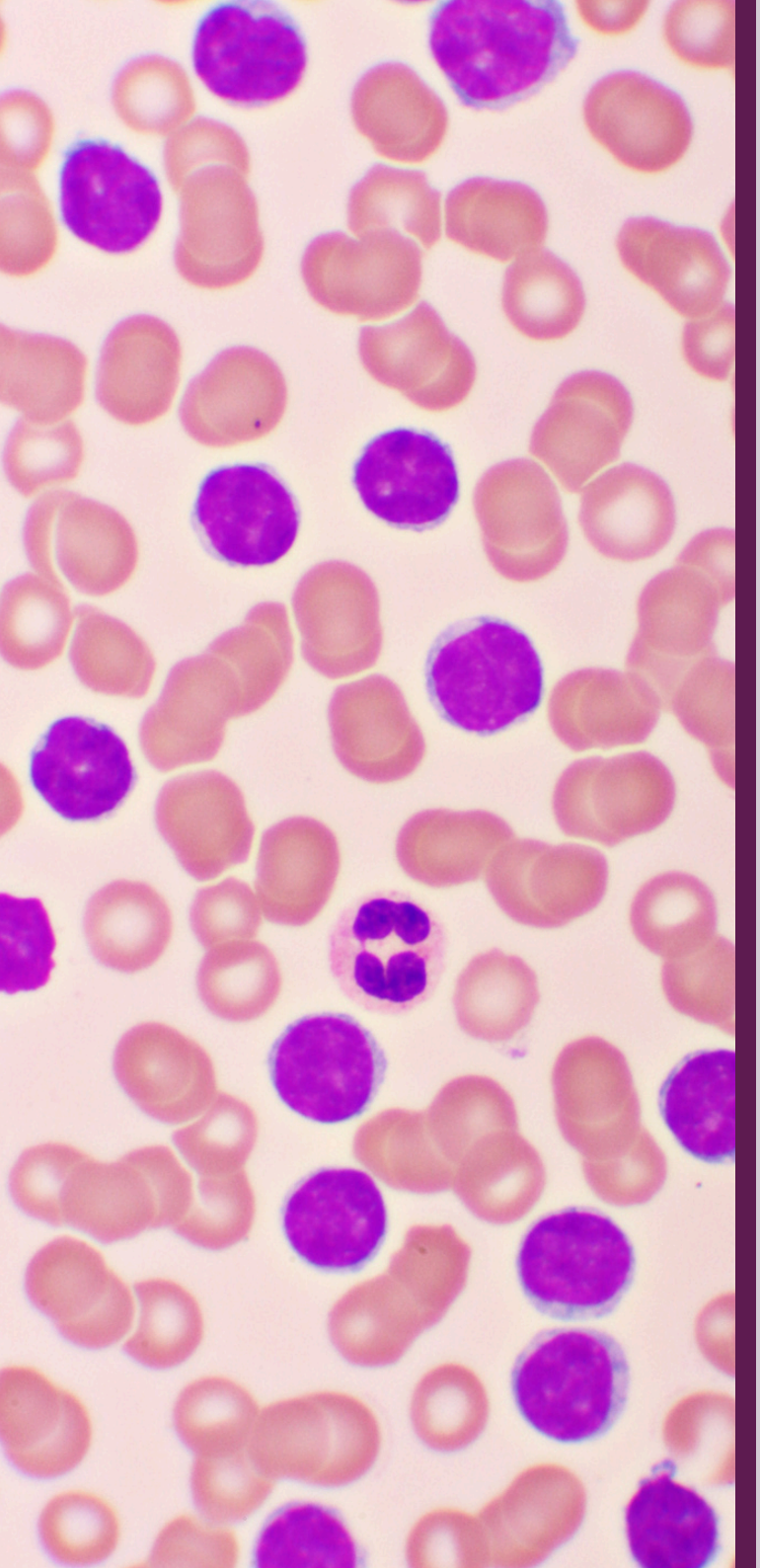
Weidenweg 39
4147 Aesch BL

+41 (0)76 296 06 55
Info@hopos.ch
www.hopos.ch

SCI - Swiss Cancer Institute

Effingerstrasse 33
3008 Bern

+41 (0)31 389 91 91
info@swisscancerinstitute.ch
www.swisscancerinstitute.ch



In collaboration with:

Dr. med. Nathan Cantoni
Kantonsspital Aarau

Dr. med. Mitja Nabergoj
Hôpital du Valais, Sion

Rosmarie Pfau
lymphome.ch

BeOne

0224-BGB-3111-MRC-007