Active monitoring of CLL

What it means and why it's important

Includes best practice sharing by
Dr Ali Rismani, consultant haematologist,
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Why active monitoring?

CLL is generally characterised as a **slow-growing** blood cancer.[1]

It is the most prevalent lymphoid malignancy in many parts of the world and **approximately 90%** of patients are diagnosed with asymptomatic, early-intermediate stage (Rai 0–I, Binet A) disease.[2]

More than **1 in 3 patients** never need treatment.[6]

If a patient doesn't need to start treatment, after an initial assessment, the patient can go onto **active monitoring**.[1]

Active monitoring vs 'watch and wait'

Many patients feel confused and worried when they're told they will just be monitored and will not receive treatment at the point of diagnosis. It's hard to understand and explain to others how you can have cancer but not need treatment. It can also cause anxiety as their next check-up comes nearer and they wait for test results.[1]

This approach is called 'watchful waiting' or 'active monitoring'. It is generally agreed that active monitoring is a better description for the approach as it makes it clearer that the doctor is actively involved in patient care, even if the patient doesn't need treatment.[1]

How often should people living with CLL be assessed?[1]

CLL can be treated, and people can live with it for many years. However, it's incurable, and there is no advantage in treating it early if you are otherwise well.[3]

Staging and molecular markers may determine prognosis and how often to assess the patient. The most important factor is likely to be the speed of progression:

6–12 MONTHS

If previous results are available and demonstrate the patient is stable, the patient can be seen **1–2 times per year**

DISCHARGE TO PRIMARY CARE

If the patient is Binet stage A or Rai stage 0–I and has been stable for 2 years, it would be acceptable to **discharge** the patient for the GP to monitor, if both patient and GP are happy

3–4 MONTHS

If no previous results are available, it would be reasonable to review the patient in **3–4 months** and, if stable, to increase the interval to every 6 months

If there is obvious evidence of progression, the intervals of the appointment may need to be reduced

Staging in CLL[4]

There are two staging systems for CLL, the Rai staging system and the Binet staging system:[4]

0–IV

Rai staging system[4]
The Rai system is more common in the US and has 5 stages of CLL – stage 0 to stage IV.

ABC

Binet staging system[4]
Doctors predominantly use the Binet staging system in the UK. This has 3 stages of CLL – stages A, B and C.

2022 statistics

It might help for patients to know that they're not alone – in the UK there are **around 27,000 people** with blood cancer who are on active monitoring.[1]

Links to support groups can be found under 'Useful resources'

Definition of stable and progressing disease in practice

- **Stable disease** – haemoglobin, neutrophils, lymphocytes and platelet count are all stable. No increase in lymphadenopathy or splenomegaly and no new symptoms (specifically B symptoms)
- **Progressive disease** – drop in haemoglobin with no other explanation, rising lymphocyte count (doubling in 6 months), or other new cytopenias. New or enlarging lymphadenopathy or splenomegaly, no B symptoms or uncontrolled haemolytic anaemia or ITP

Useful resources

CLL Support is a patient-led UK charity that aims to empower people affected by CLL and other related conditions through education and access to reliable information. It supports people living with CLL, as well as their carers, by informing them of advancements in treatments and research.

The Leukemia & Lymphoma Society is the world's largest non-profit health organisation dedicated to funding blood cancer research.

Lymphoma Action is the UK's only charity dedicated to lymphoma, ensuring that no patient faces lymphoma alone by providing a support network and information endorsed by medical experts.

Cancer Research UK provides high-quality information to help inform patients and their families, as well as access to support organisations.

Blood Cancer UK is a charity that aims to ensure that everyone affected with blood cancer has access to the right support at the right time.

Macmillan Cancer Support is the UK's leading cancer care charity, which focuses on raising money to provide a range of support services and networks to cancer patients.

Molecular markers in CLL

Many patients have indolent disease and could have a normal life expectancy, whereas others have rapid disease progression and poor outcome.[2] There is no proven survival benefit from early therapy in patients with CLL.[2]

There are now multiple prognostic factors that can be used to predict the risk of disease progression including:[2]

- Serum TK and β2MG levels[2]
- Genomic aberrations assessed by FISH[5]
- ZAP70, CD38, and CD49 expression[5]
- Somatic hypermutation of the *IGHV* genes[5]
- Mutations of other genes, most prominently *TP53*[5]

β2MG, beta-2 microglobulin; CD, cluster of differentiation; CLL, chronic lymphocytic leukaemia; FISH, fluorescence in situ hybridisation; GP, general practitioner; *IGHV*, immunoglobulin heavy chain variable region; ITP, immune thrombocytopenia; TK, thymidine kinase; *TP53*, tumour protein 53; ZAP70, zeta-chain-associated protein kinase 70

1. Blood Cancer UK. Watch and wait for CLL. 2022. https://bloodcancer.org.uk/understanding-blood-cancer/leukaemia/chronic-lymphocytic-leukaemia/cll-watch-wait/. Accessed 9 January 2023; 2. Stilgenbauer S, Furman RR, and Zent CS. Am Soc Clin Oncol Educ Book 2015:35;164–75; 3. Leukemia & Lymphoma Society. Watch and wait. https://www.lls.org/leukemia/chronic-lymphocytic-leukemia/treatment/watch-and-wait. Accessed 9 January 2023; 4. Cancer Research UK. Staging chronic lymphocytic leukaemia. September 2021. https://www.cancerresearchuk.org/about-cancer/chronic-lymphocytic-leukaemia-cll/staging. Accessed 9 January 2023; 5. Yun X, et al. Biomark Res 2020;8:40; 6. Lymphoma action. Chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL). 2020. https://lymphoma-action.org.uk/types-lymphoma/chronic-lymphocytic-leukaemia-cll-and-small-lymphocytic-lymphoma-sll. Accessed 15 February 2023

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Clinic appointments

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Who conducts a clinic appointment?

It's normal for people living with CLL to feel anxious in the months, weeks or days leading up to an appointment, but knowing what to expect from a check-up can help. If people living with CLL feel upset or worried, there's plenty of support available.

Some people living with CLL will go to a clinic or hospital to see a consultant haematologist for their appointments, while others will visit their local GP surgery. At the time of the diagnosis, the haematologist will explain whether the patient will continue to see them or the GP.

What happens at a clinic appointment?

At each appointment, the doctor will check to see if the person living with CLL has developed any new symptoms and will run some tests:

Physical examination

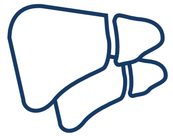
Blood tests

Additional tests

Physical examination[1–3]

The doctor will carry out a full physical examination to check for new symptoms, such as:

Lymphadenopathy



Hepatomegaly

Splenomegaly

Signs of fatigue

Blood tests[1–3]

The doctor will also run a full blood count, test kidney and liver function, and may carry out other routine blood tests:

Full blood count

Liver function test

Urea and electrolytes

Additional tests

If the person living with CLL is starting treatment for blood cancer, infection screening or virology testing to check for conditions such as HIV, hepatitis B and hepatitis C may be performed[4]

A peripheral blood film may be needed to look at the red blood cells, white blood cells and platelets to see whether they are the right size and shape, and whether they look healthy[5]

Genetic testing provides information on gene changes in cancer cells that may help predict which treatments might work best for the person living with CLL, and give a clearer idea of prognosis[6]

Serum protein electrophoresis is sometimes conducted if a paraprotein has been detected previously; paraprotein levels can be used to monitor for signs of progression[7]

X-ray/ultrasound scans may be carried out, and this can give more detailed information about the cancer and check for abnormalities[8,9]

CLL, chronic lymphocytic leukaemia; GP, general practitioner; HIV, human immunodeficiency virus

1. Hallek M, Al-Sawaf O. Am J Hematol 2021;96:1679–1705; 2. CLL Support. About CLL/SLL. https://www.cllsupport.org.uk/information-support/about-cll/. Accessed 9 January 2023; 3. Blood Cancer UK. Watch and wait for CLL. 2022. https://bloodcancer.org.uk/understanding-blood-cancer/leukaemia/chronic-lymphocytic-leukaemia/cll-watch-wait/. Accessed 9 January 2023; 4. Macmillan. Treatment for chronic lymphocytic leukaemia. January 2022. https://www.macmillan.org.uk/cancer-information-and-support/leukaemia/chronic-lymphocytic-leukaemia-cll-treatment. Accessed 9 January 2023; 5. American Cancer Society. How is chronic lymphocytic leukemia diagnosed? May 2018. https://www.cancer.org/cancer/chronic-lymphocytic-leukemia/detection-diagnosis-staging/how-diagnosed.html. Accessed 9 January 2023; 6. Conquer. Genetic testing can help to guide the treatment of patients with chronic lymphocytic leukemia. October 2018. https://conquer-magazine.com/issues/2018/vol-4-no-5-october-2018/792-genetic-testing-can-help-to-guide-the-treatment-of-patients-with-chronic-lymphocytic-leukemia. Accessed 9 January 2023; 7. Hamed HB, et al. Med J Cairo Univ 2018;86:389–94; 8. Cancer Research UK. Chest x-ray for CLL. September 2021. https://www.cancerresearchuk.org/about-cancer/chronic-lymphocytic-leukaemia-cll/getting-diagnosed/tests/chest-x-ray. Accessed 9 January 2023; 9. Cancer Research UK. Ultrasound scan for CLL. September 2018. https://www.cancerresearchuk.org/about-cancer/chronic-lymphocytic-leukaemia-cll/getting-diagnosed/tests/ultrasound-scan. Accessed 9 January 2023

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