

Clinical Decision Making in CLL: When to Stop and Start Treatment

The principal goal of initiating and discontinuing therapy is to maximize efficacy and minimize adverse events for each individual patient¹

When to initiate therapy



≈2/3 of patients diagnosed with CLL are initially under **active surveillance** and do not need immediate treatment^{2,3}



iwCLL guidelines recommend **initiating** first-line therapy in patients with **symptomatic/active disease** (see criteria below under “When to initiate a new line of therapy”)⁴

Whether to continue or discontinue treatment based on response or AEs⁴⁻⁷

RESPONSE	FIXED-DURATION THERAPIES	CONTINUOUS THERAPIES
CR	STOP THERAPY following completion of the prespecified number of cycles	CONTINUE THERAPY until progression
PR	Treatment will STOP THERAPY after all cycles have been completed or at disease relapse	CONTINUE THERAPY until progression
PD	DISCUSS TREATMENT OPTIONS Therapy may be repeated if relapse occurs 1 to 3 years after treatment-free period	DISCUSS TREATMENT OPTIONS To reduce risk of tumor flare, treatment may overlap a new treatment until disease control is achieved

SAFETY

AEs		Grade 1/2: CONTINUE THERAPY unless patient is unable to tolerate Grade 3/4: INTERRUPT THERAPY OR LOWER DOSE unless the AE persists and/or unable to tolerate, then STOP THERAPY (either can be stopped for an extended period of time or permanently discontinued)
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When to initiate a new line of therapy^{4-6, 8}

Consider initiating a new line of therapy if a patient exhibits symptomatic/active disease defined by the iwCLL 2018 criteria

- ▶ Lymph nodes, liver, and/or spleen size (massive, progressive, or symptomatic)
- ▶ Circulating lymphocyte count*
- ▶ Constitutional disease-related symptoms
- ▶ Worsening anemia and/or thrombocytopenia
- ▶ Progressive marrow failure
- ▶ Extranodal symptoms (eg, skin, kidney, lung)



Key questions to consider when starting the next line of therapy:

Why was the prior therapy discontinued?

What is the patient's preference?

Did the patient respond? If so, for how long?

*Progressive ≥50% over a 2-month period, or lymphocyte doubling time <6 months.

AE, adverse event; CLL, chronic lymphocytic leukemia; CR, complete response; HCPs, healthcare professionals; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; PD, progressive disease; PR, partial response.

1. Molica S. *Expert Rev Hematol*. 2023;16(11):803-806. 2. Leukemia & Lymphoma Society. Accessed April 8, 2025. <https://www.lls.org/leukemia/chronic-lymphocytic-leukemia/treatment/watch-and-wait>. 3. Shadman M. *JAMA*. 2023;329(11):918-932. 4. Hallek M, et al. *Blood*. 2018;131(25):2745-2760. 5. Hallek M, et al. *Am J Hematol*. 2021;96(12):1679-1705. 6. Soumerai JD, et al. *Blood Adv*. 2025;9(5):1213-1229. 7. Jain N, et al. *Lancet*. 2024;404(10453): 694-706. 8. Odetola O, Ma S. *Curr Hematol Malig Rep*. 2023;18(5):130-143.

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