CLINICAL DECISION MAKING IN CLL: WHEN TO STOP AND START TREATMENT

Table of Contents

1 When to Initiate First-Line CLL Treatment

2 Whether to Continue or Discontinue Treatment Based on Response

3 Whether to Continue, Interrupt, or Discontinue Treatment Based on Adverse Events

4 When to Initiate a New Line of Therapy

5 Key Takeaways

CLL, chronic lymphocytic leukemia.

Learning Objectives

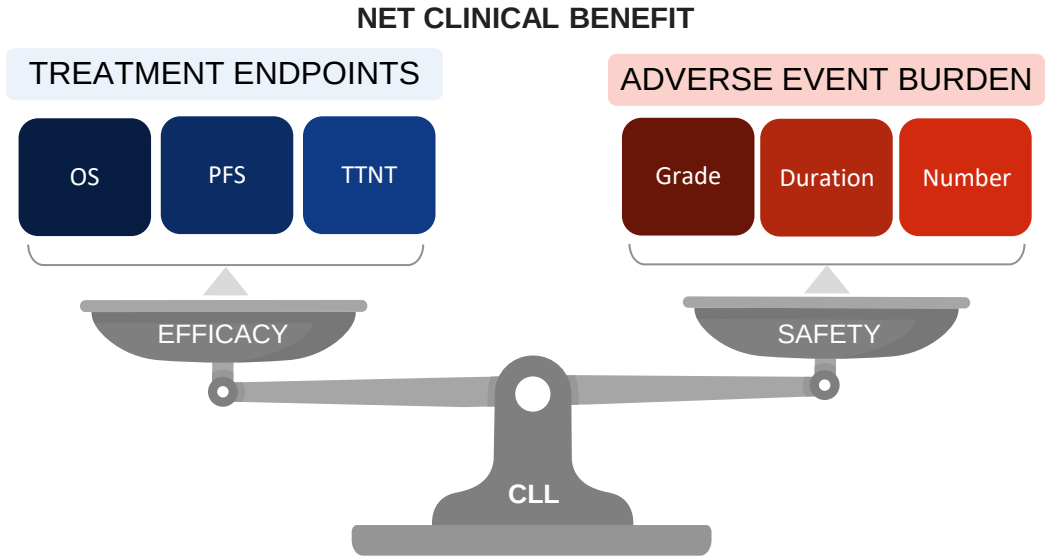
Identify and apply key criteria to determine appropriate time to start, continue, interrupt, or discontinue therapy to maximize efficacy and minimize risk in patients with CLL

Integrate shared decision making and multidisciplinary care to best support patients throughout the treatment journey

1 When to Initiate First-Line CLL Treatment

Before Starting Therapy, the Net Clinical Benefit Needs to Be Considered

- Avoid unnecessary treatment
- Prevent overtreatment
- Ensure timely intervention
- Optimize use of targeted therapies
- Minimize toxicity
- Support patient-centered care
- Adapt to evolving guidelines

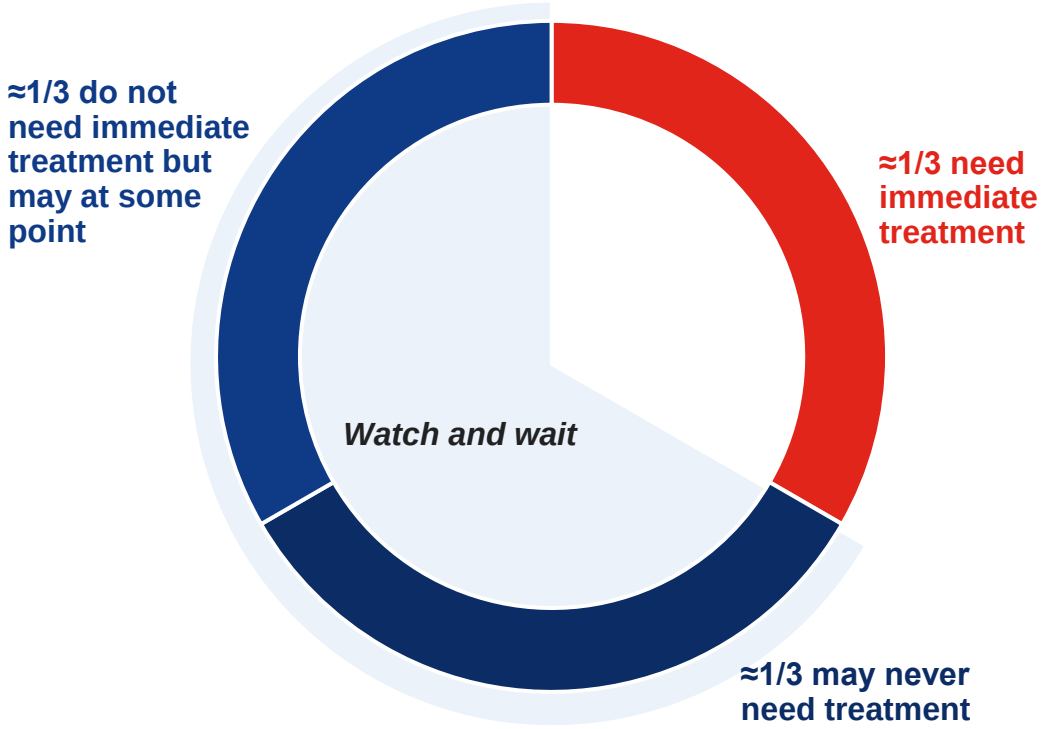


The principal goal of initiating and discontinuing therapy is to maximize efficacy and minimize risk for each patient

CLL, chronic lymphocytic leukemia; PFS, progression-free survival; OS, overall survival; TTNT, time to next treatment.
Figure adapted from Molica S. *Expert Rev Hematol.* 2023;16(11):803-806.
Molica S. *Expert Rev Hematol.* 2023;16(11):803-806.

About One-Third of Patients Diagnosed With CLL Need to Start Immediate Treatment[1,2]

Among patients diagnosed with CLL, most are initially under active surveillance (watch and wait)[1,2]



Impact of unnecessary early treatment includes the following[1]:

- Side effects
- Treatment complications
- Reduced quality of life
- Resistance to therapies

Clinical trials have yet to demonstrate a survival benefit from earlier treatment of CLL in patients in the "watch and wait" category[2-4]

CLL, chronic lymphocytic leukemia.

1. Leukemia & Lymphoma Society. Accessed April 8, 2025. https://www.lls.org/leukemia/chronic-lymphocytic-leukemia/treatment/watch-and-wait 2. Shadman M. *JAMA*. 2023;329(11):918-932. 3. Langerbeins P, et al. *Blood.* 2022;139(2):177-187. 4. Herling CD, et al. *Leukemia.* 2020;34(8):2038-2050.

Multiple Factors Need to Be Considered When Deciding to Start Treatment: Disease Symptoms

iwCLL guidelines recommend initiating **first-line therapy** in patients **with symptomatic/active disease**, which is defined as any of the following[1-3]:

Lymph nodes

- Massive nodes (≥10 cm in longest diameter) **OR**
- Progressive or symptomatic lymphadenopathy

Bone marrow

- Progressive marrow failure (eg, development or worsening of anemia and/or thrombocytopenia) recommended cutoffs: Hb <10 g/dL or platelet counts of <1,000,000/µL
- However, if low platelet counts remain stable then not required to start treatment

Note: Hypogammaglobinemia, monoclonal/oligoclonal paraproteinemia, and elevated leukocyte count do not indicate need for treatment

Liver

- Progressive lymphocytosis (≥50% over a 2-month period or LDT doubling time of <6 months)
- Patients with lymphocyte counts <30,000/µL may require longer observation to determine LDT
- Other factors contributing to lymphocytosis (eg, infections and steroids) should not be considered CLL active disease

Spleen

- Massive spleen (≥6 cm below left costal margin) **OR**
- Progressive or symptomatic splenomegaly

Disease-related symptoms

- Unintentional weight loss ≥10% within previous 6 months
- Significant fatigue (eg, ECOG PS 2 or worse, unable to perform usual activities/work)
- Fever ≥100.5^{o} F for >2 weeks
- Night sweats for ≥1 month without evidence of infection

Extranodal involvement

- Symptomatic or functional extranodal involvement in skin, kidney, lung, or spine

Autoimmune

- Includes anemia or thrombocytopenia poorly responsive to corticosteroids

ECOG PS, Eastern Cooperative Oncology Group performance status; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; Hb, hemoglobin; LDT, lymphocyte doubling time.

1. Hallek M, et al. *Blood.* 2018;131(25):2745-2760. 2. Hallek M, et al. *Am J Hematol.* 2021;96(12):1679-1705. 3. Hampel PJ, Parikh SA. *Blood Cancer J.* 2022;12(11):161.

Multiple Factors Need to Be Considered When Deciding to Start Treatment: Clinical Staging

Clinical staging can help determine **when treatment should be considered** and **how often to monitor patients**[1,2]

Rai[1]	
Low risk (0)	• Lymphocytosis with leukemia cells in blood and/or marrow
Intermediate risk (I or II)	• Peripheral blood lymphocytosis • Enlarged lymph nodes • Splenomegaly and/or hepatomegaly
High risk (III or IV)	• Disease-related anemia (Hb <1 g/dL)* • Thrombocytopenia (platelets <100 × 10^9/L)* • **iwCLL recommends to treat**

Binet[1]	
Areas of involvement	• Head and neck • Axillae • Groin • Palpable spleen • Palpable liver
Stage A	• Hb ≥10 g/dL, platelets ≥100 × 10^9/L, and up to 2 areas
Stage B	• Hb ≥10 g/dL, platelets ≥100 × 10^9/L, and ≥3 lymphoid areas
Stage C	• Hb <10 g/dL or platelets <100 × 10^9/L • **iwCLL recommends to treat**

Note: CLL-IPI is another type of clinical staging that incorporates del17p/*TP53* mutation, *IGHV* genes, serum B2M, Rai stage, and age in the decision whether a patient should be monitored 6 to 12 months vs 3 to 6 months.[2]
*Unrelated causes should be excluded.
B2M, β2 microglobulin; CLL, chronic lymphocytic leukemia; CLL-IPI, Chronic Lymphocytic Leukemia International Prognostic Index; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; Hb, hemoglobin.
1. Hallek M, et al. *Blood.* 2018;131(25):2745-2760. 2. Hampel PJ, Parikh SA. *Blood Cancer J.* 2022;12(11):161.

Multiple Factors Need to Be Considered When Deciding to Start Treatment: Patient-Specific Attributes

Additional factors that impact when to initiate therapy in a patient with active disease include[1-4]:

- Age
- Biomarkers
- General fitness
- Quality of life
- Comorbidities
- Polypharmacy
- Patient's treatment goals

Shared decision making via the SHARE principles can help assess these factors and understand the patient's preferences[5]

Patient-centric care strives for the physician to collaborate with the patient and determine the optimal care plan and timeline based on that patient's specific priorities, as well as evidence-based clinical guidelines[5]

1. Cherny NI, et al. *ESMO Open.* 2025;10(1):104099. 2. Cohen JA, et al. *Cancers (Basel)*. 2020;12(4):894. 3. Galitzia A, et al. *Cancers (Basel).* 2024;16(11):1996. 4. Odetola O, Ma S. *Curr Hematol Malig Rep*. 2023;18(5):130-143. 5. Agency for Healthcare Research and Quality. Accessed May 6, 2025. https://www.ahrq.gov/sites/default/files/publications/files/share-approach_factsheet.pdf

2

Whether to Continue or Discontinue Treatment Based on Response

Efficacy Endpoints Typically Used in Clinical Trials

OS

Time between the first treatment day and death from any cause[1]

PFS

Time between the first treatment day and the first sign of disease progression or death from any cause[1]

TTNT

Time between the first treatment day and when the patient starts a new therapy for progressive CLL[1]

DOR

Time to disease progression or death in patients who achieve CR or PR[2]

Undetectable MRD (MRD-neg)

Defined as <1 CLL cell per 10000 leukocytes in blood or marrow, detected using sensitive multicolor flow cytometry, RQ-PCR, NGF, or NGS[1]

ORR

Proportion of patients who respond to therapy (CR/PR)[2]

Considerations for efficacy endpoints:

- **OS** has been a gold standard endpoint in oncology since the goal of cancer treatment is generally to extend life, but does not distinguish between disease- and non-disease-related deaths[2,3]
- **PFS** has been a gold standard efficacy endpoint in clinical trials, but results in a CLL population can be inconclusive since patients tend to be elderly and have underlying health conditions[4]
- **TTNT** is an emerging marker in CLL studies that may serve as a surrogate for duration of clinical benefit but requires validation before use as a standalone endpoint[3,4]
- **ORR** measures anti-tumor activity and **DOR** assesses how long progression may be delayed but both must use information available at a specific time point[2,3]

CLL, chronic lymphocytic leukemia; CR, complete response; DOR, duration of response; MRD, minimal residual disease; MRD-neg, minimal residual disease-negative; NGF, next-generation flow cytometry; NGS, next-generation sequencing; ORR, overall response rate; PFS, progression-free survival; PR, partial response; OS, overall survival; RQ-PCR, real-time quantitative polymerase chain reaction; TTNT, time to next treatment.

1. Hallek M, et al. *Blood.* 2018;131(25):2745-2760. 2. Brazauskas R, et al. *Best Pract Res Clin Haematol.* 2023;36(3):101479. 3. Delgado A, Guddati AK. *Am J Cancer Res.* 2021;11(4):1121-1131. 4. Molica S. *Expert Rev Hematol.* 2023;16(11):803-806.

The Role of MRD Assessment Is Evolving in CLL

In randomized clinical trials and retrospective studies of **fixed-duration therapies**, **uMRD** has been correlated with **improved PFS and OS** in patients with CLL, making it a useful prognostic factor[1-3]

- For BTKi monotherapy, only about 10% of patients may have had uMRD and the PFS rates did not differ by uMRD status; thus, **MRD assessments are not used for BTKi monotherapies[2]**

The techniques developed to detect MRD are significantly improving; currently a standard panel of **6 markers (MRD6)** is used[1]

- **Bone marrow** and **blood** can be tested; however, both may need to be tested if the blood is MRD-neg because certain therapies preferentially clear the blood and not the marrow[1]

- **MRD assessment** is typically used in **clinical trials for fixed-duration therapies** and may help determine when to discontinue therapy[2-4]
- **MRD assessment** can potentially also be used in **routine clinical practice** for this same purpose[2-5]

BTKi, Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; MRD, minimal residual disease; OS, overall survival; PFS progression-free survival; uMRD, undetectable minimal residual disease.

1. Hallek M, et al. *Blood*. 2018;131(25):2745-2760. 2. Del Giudice I, et al. *Cancers (Basel).* 2024;16(11):2049. 3. Benintende G, et al. *Front Oncol.* 2023;13:1112616. 4. Hallek M, et al. *Am J Hematol.* 2021;96(12):1679-1705. 5. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229

Subsequent Therapy Decisions in Patients With Refractory Disease or Relapse

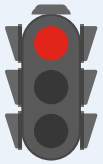
Start CLL treatment ····· 6 months ····· ▶

Refractory disease[1]

Treatment failure or progression **<6 months** from the last dose of therapy (ie, the patient **never responded to therapy**)

Relapse[1]

Evidence of disease progression in a patient who previously achieved **CR or PR** for **≥6 months**



Both refractory disease and relapse should lead to discussion about next treatment options, including when and how current CLL therapy will be discontinued[1-3]

CLL, chronic lymphocytic leukemia; CR, complete response; PR, partial response.

1. Hallek M, et al. *Blood.* 2018;131(25):2745-2760. 2. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229. 3. Jain N, et al. *Lancet*. 2024;404(10453):694-706.

The Type of Therapy Impacts Timing of Discontinuation in Responding Patients[1-4]

Response	Fixed-duration therapies	Continuous therapies
CR	**Stop therapy** following **completion** of the prespecified number of **cycles** or at disease relapse with indications for retreatment	**Continue therapy** until progression
PR	**Additional cycles** may be added but treatment will **stop therapy** after all cycles have been **completed** or at disease relapse	**Continue therapy** until progression
PD	**Discuss treatment options; if relapse occurs after 1 to 3 years* of a treatment-free interval, **therapy may be repeated**	**Discuss treatment options**; to reduce the risk of tumor flare, treatment overlap with a new treatment until disease control is achieved. Switching from a BTKi to a fixed-duration therapy can overlap from 1 week to 2 months

How the treatment is discontinued depends on the specific response and type of therapy (fixed-duration vs continuous)[2,3]

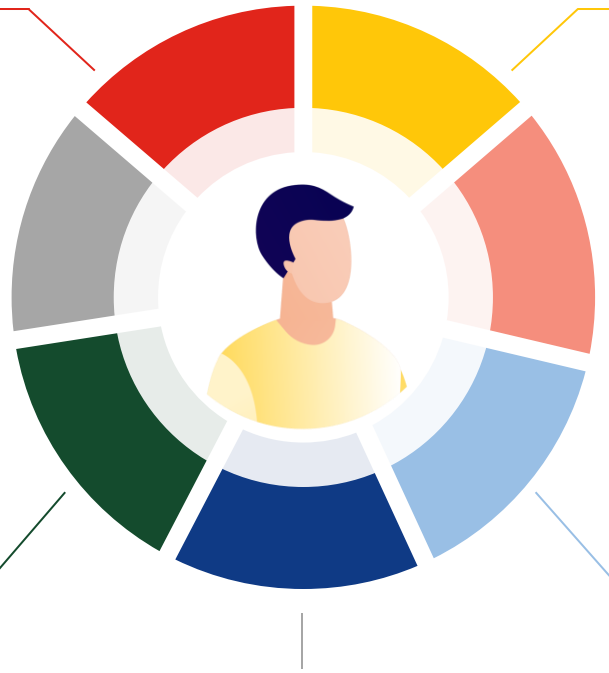
*iwCLL 2018 states that if relapse occurs after 3 years, the fixed-duration therapy can be repeated.[2]
BTKi, Bruton's tyrosine kinase inhibitor.
1. Hallek M, et al. *Blood.* 2018;131(25):2745-2760. 2. Hallek M, et al. *Am J Hematol.* 2021;96(12):1679-1705. 3. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229. 4. Jain N, et al. *Lancet*. 2024;404(10453):694-706.

Patients Who Discontinue Therapy May Need Additional Support[1,2]

Offer patients therapists/counselors who specialize in long-term illnesses, which can help with the emotional load

Share complementary therapies (eg, acupuncture, yoga, meditation) to aid patients' sense of control over their health

Advise patients to give their family members/friends specific ways they can support them



Provide information on support groups and educational resources to help address patient fears and misconceptions

Promote a healthy lifestyle, including nutritious, balanced meals, staying active, making rest a priority, and protecting against infection

Collaborate with therapists/counselors who specialize in long-term illnesses to support your patients

Suggest focusing on other things beyond the illness (eg, hobbies, being in nature)

1. Cleveland Clinic. Accessed June 2, 2025. https://my.clevelandclinic.org/health/diseases/22883-blood-cancer 2. Leukemia & Lymphoma Society. Accessed June 3, 2025. https://www.lls.org/sites/default/files/2021-05/PS67_EachNewDay_2020_FINAL.pdf.

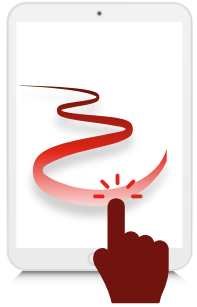
Shared Decision Making Can Help Manage Patients' Misconceptions About Stopping Therapy

Engage in shared decision making to **help manage patients' misconceptions** when they are no longer responding to CLL therapy[1]

Image adapted from: LUNGevity Transforming Lunch Cancer. Accessed August 3, 2023.
https://www.lungevity.org/research/patient-focused-research-center-patient-force/shared-decision-making

Provide education on the CLL treatment journey and avoid the term "treatment failure"[2]

Emphasize how most patients with CLL require multiple lines of therapy, and provide education on their treatment options



Provide patient case studies to demonstrate typical treatment journeys in patients with progressive disease, highlighting they are not alone

For more information on shared decision making, please see medical.lilly.com

CLL, chronic lymphocytic leukemia.
1. LUNGevity Transforming Lunch Cancer. Accessed June 30, 2025. https://www.lungevity.org/research/patient-focused-research-center-patient-force/shared-decision-making 2. Kranzler EC, et al. *J Patient Exp.* 2021;8:23743735211034967.

3

Whether to Continue, Interrupt, or Discontinue Based on Adverse Events

Differentiating Between Intolerance and Disease Progression Is Essential for Determining Whether to Continue Therapy

Disease progression and treatment intolerance may present with similar symptoms (eg, cytopenia)[1-4]

Intolerance

Inability of the patient to endure adverse events associated with a treatment[5]

VS

Progression

Worsening of disease as it continues to spread in the body[6]

To avoid early discontinuation, dose adjustments should be made according to recommendations in the associated PI, along with prescription of symptom-targeted measures when a patient is experiencing an AE that is difficult to tolerate[3]

For more information on intolerance vs disease progression, please see medical.lilly.com

AE, adverse event; PI, prescribing information.

1. Hallek M, et al. *Blood*. 2018;131(25):2745-2760. 2. Hallek M. *Am J Hematol*. 2025;100(3):450-480. 3. Galitzia A, et al. *Cancers (Basel).* 2024;16(11):1996. 4. Upchurch MD, et al *Expert Rev Clin Pharmacol.* 2024;17(5-6):467-475. doi:10.1080/17512433.2024.2344665 5. Flannery MA, et al. *J Clin Oncol.* 2021;39(19):2150-2163. 6. National Cancer Institute. Accessed May 2, 2025. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/progression

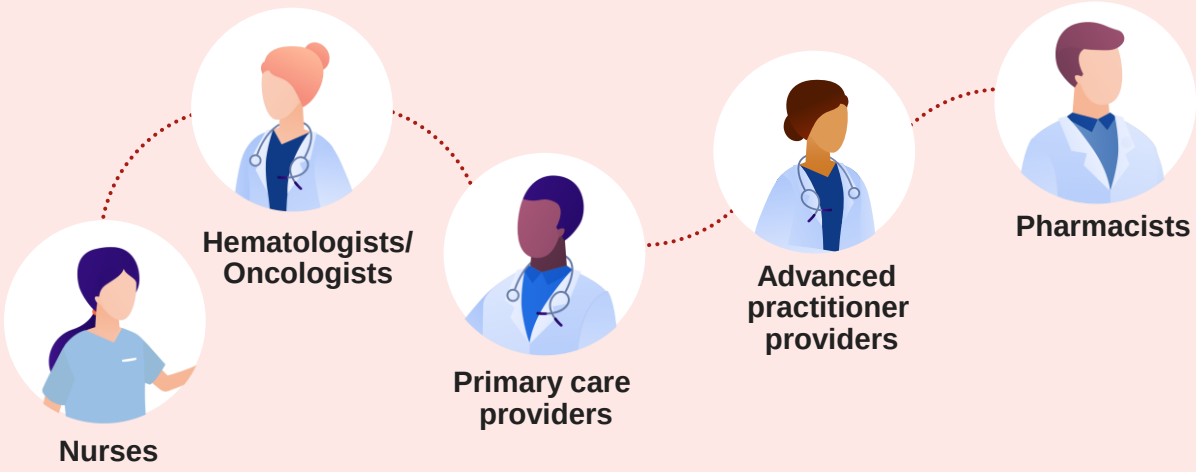
Treatment-Related Toxicities Require Careful Consideration When Deciding to Continue, Interrupt, or Discontinue Therapy

Thorough monitoring for AEs, including patient-reported signs and symptoms, is necessary throughout the course of treatment

Different **drug classes** are associated with **specific AEs:**

- For instance, BCL-2i are associated with TLS, whereas covalent BTKi are associated with cardiotoxicity*
- In general, combination therapies have similar safety profiles as the composite of their respective single agents

Employ an **MDT approach** to help manage AEs and patient expectations



The goal of managing AEs is to maximize adherence to enhance survival rate, while maintaining quality of life

*Especially first-generation covalent BTKi.
AE, adverse event; BCL-2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; MDT, multidisciplinary team; TLS, tumor lysis syndrome.
Galitzia A, et al. *Cancers (Basel).* 2024;16(11):1996.

Consider the Severity and Type of AE When Deciding if Treatment Can Continue

Select AE	Consider continuing treatment	Consider interrupting treatment*	Consider treatment discontinuation
Hematologic toxicity	Grade 1/2	Grade 3/4	Persistent cytopenia or onset of cytopenia after 6 months of therapy may require marrow assessment to detect hematologic disorders
Infections†	Grade 1/2	Grade 3/4, interrupt/modify dose until infection is mild/resolves	Infection worsens or continues to return
Secondary primary malignancies	Screen, monitor, manage with targeted therapies		
GI events	Grade 1/2	Grade 3/4	Persistent cases may require temporary discontinuation or initiation of an alternative treatment in the same drug class
TLS (more common with BCL-2i)	Lab abnormalities resolve within 24 to 48 hours	Lab abnormalities take more than 48 hours to resolve (effects amplified with combination therapies)	
Cardiotoxicity‡ (more common with BTKi)	Grade 1/2	Grade 3/4	Recurrent, severe episodes

*Skipping a dose and/or reducing dose. †No consensus on managing infectious events. ‡Cardiotoxicity includes atrial fibrillation/flutter, hypertension, heart failure, ventricular arrythmias, and bleeding. For patients who experience grade 2 heart failure using a first generation covalent BTKi, the dose should be reduced or treatment discontinued. For bleeding, patients with minor events can continue treatment, but any major bleeding or life-threatening hemorrhage should prompt discontinuation of treatment.

BCL-2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; GI, gastrointestinal; TLS, tumor lysis syndrome.

Galitzia A, et al. *Cancers (Basel).* 2024;16(11):1996.

Factor In the Patient's Quality of Life and Mental Health When Determining if a Treatment Should Continue[1,2]

- **Bothersome, long-term, treatment-related AEs** (eg, fatigue, headaches, arthralgias) can impact many aspects of the **patient's everyday life** and may prompt discussions on whether to interrupt or discontinue treatment
  - **More serious, acute, treatment-related AEs** may necessitate rapid management, independent of shared decision making

Engage in shared decision making when deciding if treatment interruptions or discontinuation may be necessary for your patient

Topics to discuss with patients relating to their treatment:

- Quality of life
- Cognitive and psychological health
- Patient preferences
- Patient treatment goals

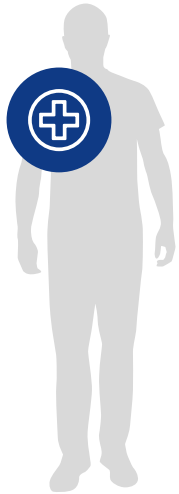
AE, adverse event.

1. Galitzia A, et al. *Cancers (Basel).* 2024;16(11):1996. 2. Agency for Healthcare Research and Quality. Accessed June 30, 2025. https://www.ahrq.gov/sites/default/files/publications/files/share-approach_factsheet.pdf

4 When to Initiate a New Line of Therapy

Not All Patients With CLL Who Discontinue Therapy Need to Immediately Start the Next Line of Therapy

When to consider active surveillance on a current line of therapy[1-3]

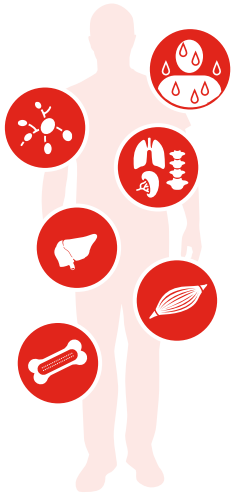


If a responding patient with CLL experiences intolerance (an AE that leads to treatment discontinuation) but does not have symptomatic disease

A **drug with a similar MOA** may be considered if a patient was **intolerant** to treatment and begins to **exhibit disease symptoms**

VS

When to consider starting a new line of therapy[1-3]



If a patient exhibits active disease, defined by the iwCLL 2018 criteria (for more details, see **Disease Symptoms slide**)[1]

A **drug with a different MOA** is usually recommended if the disease **relapsed*** or was **refractory**

Similar to initiating first-line therapy, deciding the optimal treatment plan is based on that patient's specific priorities, as well as evidence-based clinical guidelines[4]

*If the relapse occurs in a **treatment-free interval following fixed-duration therapy** then **retreatment** can be considered.

AE, adverse event; CLL, chronic lymphocytic leukemia; ; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; MOA, mechanism of action.

1. Hallek M, et al. *Am J Hematol.* 2021;96(12):1679-1705. 2. Hampel PJ, Parikh SA. *Blood Cancer J.* 2022;12(11):161. 3. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229. 4. Agency for Healthcare Research and Quality. Accessed May 6, 2025. https://www.ahrq.gov/sites/default/files/publications/files/share-approach_factsheet.pdf

Additional Factors Need to Be Considered When a Patient Is Ready for the Next Line of Therapy

Prior therapy discontinuation

- If **PD** occurs while on a **BTKi**, **continue** the BTKi until the **next therapy is ready** to be administered, at the appropriate dose to reduce the risk of tumor flare[1,2]
- If **intolerance** occurs with no PD symptoms, a treatment holiday can be considered[1]

Acquired resistance

- Acquired resistance may ultimately lead to disease progression but does not always require immediate treatment discontinuation[1]
- If **drug resistance** occurs with **disease symptoms**, consider a different MOA for the next line of treatment[1,3]

Response timing

- **Outcomes of the previous lines** of therapy can impact the next line of therapy[1,3,4]
  - If relapse occurs after an extended (eg, 3 years) BCL-2i treatment-free period, retreatment can be considered
  - If refractory disease or relapse on a covalent BTKi or BCL-2i, a different MOA should be considered

Questions to consider

- Why was the prior therapy discontinued?
- Should I test for resistance mutations?
- Did the patient respond? If so, for how long?

BCL-2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; MOA, mechanism of action; PD, progressive disease.

1. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229. 2. Jain N, et al. *Lancet*. 2024;404(10453):694-706. 3. Odetola O, Ma S. *Curr Hematol Malig Rep.* 2023;18(5):130-143. 4. Hallek M, et al. *Am J Hematol.* 2021;96(12):1679-1705.

5 Key Takeaways

Key Takeaways

- Approximately one-third of patients diagnosed with CLL present with **active disease,** defined by iwCLL criteria, and **need immediate treatment**[1-3]
- **Refractory disease** or **relapse** may lead to discussions between HCPs and patients about when to discontinue therapy and next treatment options[3-5]
- Different drug classes are associated with specific AEs but, in general for moderate to severe AEs, **dose adjustments** or **interruptions** may help to **avoid early discontinutaion**[4,6,7]
- **Shared decision making** can help determine patient preferences regarding CLL treatment, manage patients' misconceptions about stopping therapy, and determine if therapy should continue when they experience a long-term AE such as fatigue or headache[6,8]
- Determining how and when to start the **next line of therapy** in patients with **active disease** depends on careful consideration of numerous factors, including washout period, acquired resistance, and depth and duration of response to previous lines of therapy[3,4,9,10]

AE, adverse event; CLL, chronic lymphocytic leukemia; iwCLL, International Workshop on Chronic Lymphocytic Leukemia.

1. Leukemia & Lymphoma Society. Accessed April 8, 2025. https://www.lls.org/leukemia/chronic-lymphocytic-leukemia/treatment/watch-and-wait 2. Shadman M. *JAMA*. 2023;329(11):918-932. 3. Hallek M, et al. *Blood.* 2018;131(25):2745-2760. 4. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229. 5. Jain N, et al. *Lancet*. 2024;404(10453):694-706. 6. Galitzia A, et al. *Cancers (Basel).* 2024;16(11):1996. 7. CGTlive. Accessed May 2, 2025. https://www.cgtlive.com/view/new-agents-and-optimal-patient-selection-in-cll-comprise-modern-paradigm 8. Agency for Healthcare Research and Quality. Accessed June 30, 2025. https://www.ahrq.gov/sites/default/files/publications/files/share-approach_factsheet.pdf 9. Odetola O, Ma S. *Curr Hematol Malig Rep.* 2023;18(5):130-143. 10. Hallek M, et al. *Am J Hematol.* 2021;96(12):1679-1705.