Identifying Disease Progression Versus Treatment Intolerance in CLL

In CLL, **disease progression** and **treatment intolerance** are the primary reasons for treatment discontinuation but may be challenging to differentiate as they could present with similar symptoms (eg, cytopenia).¹⁻⁴



When assessing treatment response and PD, physical examination and evaluation of blood and bone marrow should be performed^{4,5}



Timing of response assessment4,5

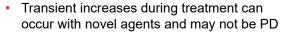
- Fixed-duration therapies: at least
 2 months after completing therapy
- Continuous therapies: at least
 2 months after maximum response

Assessment of CLL disease progression or treatment intolerance

PD during or after therapy is characterized by at least one of the parameters below4

1. Lymphadenopathy4







2. Hepatomegaly/splenomegaly⁴

Increase ≥50% from BL or from response

 Hepatomegaly must be attributable to lymphoid involvement to count as PD

3. Constitutional symptoms^{2,4,6}



▶ Some can also be an AE of CLL therapies



4. Cytopenia^{4,*}

Decrease in platelet count of ≥50% from BL, or in hemoglobin of ≥2 g/dL from BL*

► Can be an AE of many CLL therapies



Increase ≥50% over BL[†]

► Can be an AE of certain therapies



6. Marrow infiltration⁴

Increase of CLL cells by ≥50% on successive biopsies



Treatment Sequencing Considerations for PD and Intolerance

- If a patient experiences intolerance, it may be possible to try a different agent from the same drug class^{7,8}
- In contrast, when disease progression occurs, a therapy with a new MOA is recommended^{7,8,¶}



Differentiating between **disease progression** and **treatment intolerance** is essential to ensure patients maximize adherence to therapy and overall treatment journey to optimize outcomes, as each has distinct implications for subsequent therapy selection.^{3,7,8}

*Secondary to CLL. To define PD, cytopenia cannot be attributable to AIC and must progress at least 3 months after treatment.⁴ †A temporary increase in lymphocyte count can also be associated with certain therapies so lymphocytosis alone may not be a sign of treatment failure or PD.⁴ †Intolerance with active disease. §Noncovalent BTKi therapy is indicated after at least two prior lines of therapy, including a BTKi and a BCL-2i.⁹ ¶f disease progression occurs during a treatment-free interval after completion of fixed-duration therapy (eg, BCL-2i), a re-challenge with the same MOA is an option.⁷

AE, adverse event; AIC, autoimmune cytopenia; BCL-2i, B-cell lymphoma 2 inhibitor; BL, baseline; BTKi, Bruton's tyrosine kinase inhibitor; cBTKi, covalent Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; MOA, mechanism of action; ncBTKi, noncovalent Bruton's tyrosine kinase inhibitor; PD, progressive disease.

1. Shadman M, et al. Clin Lymphoma Myeloma Leuk. 2023;23(7):515-526. 2. Hallek M. Am J Hematol. 2025;100(3):450-480. 3. Galitzia A, et al. Cancers (Basel). 2024;16(11):1996. 4. Hallek M, et al. Blood. 2018;131(25):2745-2760. 5. Del Giudice I, et al. Cancers (Basel). 2024;16(11):2049. 6. CLL Society.

https://cllsociety.org/cll-sll-patient-education-toolkit/cancer-related-fatigue/ 7. Fresa A, et al. *Cancers (Basel)*. 2024;16(11):2011. 8. Hampel PJ, Parikh SA. *Blood Cancer J*. 2022;12(11):161. 9. Soumerai JD, et al. *Blood Adv*. 2025;9(5):1213-1229.

VV-MED-173798 06/2025 © 2025 Lilly USA, LLC. All rights reserved.

