CLL Clinical Decision Making: Patient Case Study

Patient characteristics

Clinical and prognostic factors

- A 72-year-old man, initially diagnosed with Rai stage I CLL
- Unmutated *IGHV*
- Del(17p)

Comorbidities

- Well-controlled hypertension
- Renal insufficiency (eGFR: 52)

Additional considerations

- Lives in a rural area far from the clinic

The patient was initially under watchful waiting. After 2 years, the patient developed symptomatic disease and needed treatment based on iwCLL criteria[1,2]

1L treatment options[3,4]

- Continuous: cBTKi
  –cBTKi ± anti-CD20 mAb

OR

- Time limited
  –BCL-2i ± anti-CD20 mAb



1L treatment decision

- Clinical trials and subgroup analyses of patients with del(17p)/*TP53* mutation treated with a cBTKi have demonstrated durable PFS. Durability of response is less well established with BCL-2i[3]
- Second-generation cBTKi may be an appropriate option given the patient's comorbidities[5,6]
  - While treatment with BTKi may increase the risk of CV AEs, second-generation BTKis are appropriate for patients with well-managed CV risk[5,6]
  - Reduced renal function is a risk factor for TLS. For treatment with BCL-2i, TLS prophylaxis and monitoring may be needed during initial dose ramp-up[5,7]
- During shared decision making, the patient expressed a preference for limited visits/clinical monitoring, thus, oral dosing of cBTKi aligns with patient preferences[3]

Second-generation cBTKi was chosen as 1L therapy

This is a fictional case study to illustrate concepts and considerations for CLL decision making. Individual results may vary.

1L, first line; AE, adverse event; BCL-2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; cBTKi, covalent Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; CV, cardiovascular; eGFR, estimated glomerular filtration rate; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; mAb, monoclonal antibody; PFS, progression-free survival; TLS, tumor lysis syndrome.

1. Hallek M, et al. *Blood*. 2018;131(25):2745-2760. 2. Hallek M, Al-Sawaf O. *Am J Hematol*. 2021;96(12):1679-1705. 3. Soumerai JD, et al. *Blood Adv*. 2025;9(5):1213-1229. 4. Fresa A, et al. *Cancers (Basel)*. 2024;16(11):2011. 5. Galitzia A, et al. *Cancers (Basel)*. 2024;16(11):1996. 6. Awan FT, et al. *Blood Adv*. 2022;6(18):5516-5525. 7. Wanchoo R, et al. *Clin Kidney J*. 2018;11(5):670-680.

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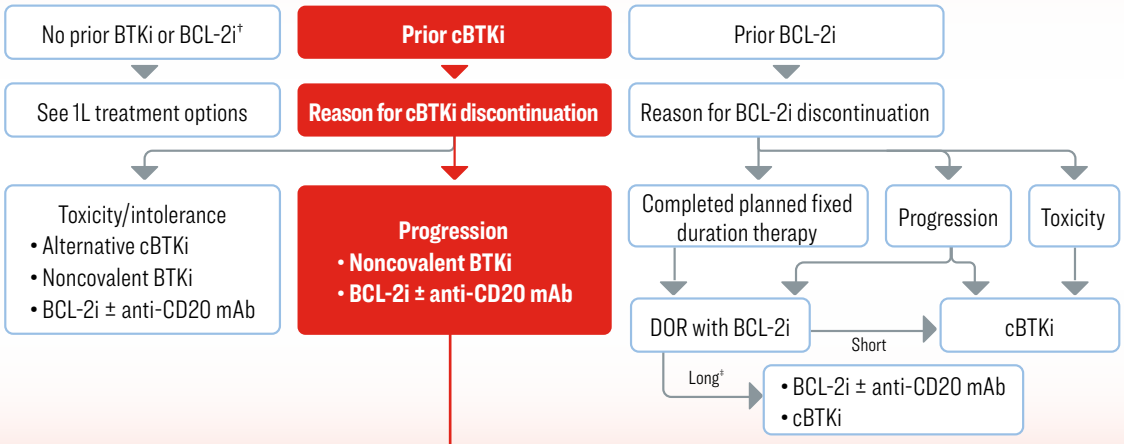
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1L treatment outcome

- The patient achieved PR and did not experience significant AEs on treatment
- 6 years later, the patient developed symptoms of progressive disease per iwCLL criteria including lymphocytosis, night sweats, increased fatigue, and cytopenia[1,2]

When disease progression occurs, a switch to a therapy with a different MOA is recommended due to the potential for overlapping resistance mechanisms[3-5,*]

R/R treatment options[4,5]



2L treatment decision

- The patient's preference for oral medication, along with their prior experience of a cBTK inhibitor without significant AEs, help inform 2L treatment decision making[3]
  - —A noncovalent BTKi allows the patient to continue with familiar dosing and types of side effects[5,6]
- Clinical data show that patients previously treated with a cBTKi respond to noncovalent BTKi[4,5,7]
- Clinical trials and subgroup analyses of patients with del(17p)/*TP53* mutation treated with a cBTKi have demonstrated durable PFS. Durability of response is less well established with BCL-2i[4,8]
- When patients experience disease progression on a cBTKi, abrupt treatment discontinuation may lead to rapid disease flare. It is recommended to continue cBTKi until the next line of therapy is ready[4,9]

Noncovalent BTKi was chosen as 2L therapy

This is a fictional case study to illustrate concepts and considerations for CLL decision making. Individual results may vary.

*Decision to initiate a new line of therapy after disease progression will be based on the iwCLL criteria.[2] †CIT consisting of fludarabine-cyclophosphamide + rituximab, bendamustine-rituximab, and chlorambucil-obinutuzumab was previously the 1L therapy for CLL before the introduction of novel agents.[10] ‡BCL-2i retreatment can be considered for patients with ≥1 year DOR off treatment after prior BCL-2i.[5]

1L, first line; AE, adverse event; BCL-2i, B-cell lymphoma-2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; cBTKi, covalent Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; DOR, duration of response; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; mAb, monoclonal antibody; MOA, mechanism of action; PFS, progression-free survival; PR, partial response ; R/R, relapsed/refractory.

1. Tam CS, et al. *Blood Adv*. 2025 Aug 19:bloodadvances.2025015986. 2. Hallek M, et al. *Blood*. 2018;131(25):2745-2760. 3. Odetola O, Ma S. *Curr Hematol Malig Rep*. 2023;18(5):130-143. 4. Soumerai JD, et al. *Blood Adv*. 2025;9(5):1213-1229. 5. Fresa A, et al. *Cancers (Basel)*. 2024;16(11):2011. 6. Lewis KL, et al. *J Pers Med*. 2021;11(8):764. 7. Mato AR, et al. *N Engl J Med*. 2023;389(1):33-44. 8. Molica S, et al. *Mediterr J Hematol Infect Dis*. 2025;17(1):e2025053. 9. Shadman M, et al. *Blood*. 2025;146(17):2029-2036. 10. Shadman M. *JAMA*. 2023;329(11):918-932.

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