Navigate Real-World Treatment Decisions in Chronic Lymphocytic Leukemia (CLL)

A Case-Based Approach

View additional CLL resources.

Jacob and his oncologist are considering therapy options for CLL. Here's how they managed his treatment.

JACOB
Male
Current age: 71 years
Occupation: teacher (retired)
Commutes 2 hours for appointments

Medical History
Hypertension controlled with medication

CLL Diagnosis: Year 0

Primary care visit

Physical examination: asymptomatic, unremarkable

Routine bloodwork:
- Lymphocytosis: 6500 lymphocytes/µL
- Normal hemoglobin and platelet levels

CLL confirmed with flow cytometry

Prognostic workup:
- Unmutated IGHV
- FISH: unremarkable

After discussion with his oncologist, a watch-and-wait approach was taken.

Key Point

Determine need for initial treatment and treatment of disease relapse per iwCLL guideline criteria[1]

Symptom Progression: Years 5-6

- Increasing fatigue
- Bulky lymphadenopathy
- Increasing lymphocytosis: 22,500 lymphocytes/µL
- New anemia: hemoglobin 7.5 g/dL
- Unremarkable cytogenetics
- Unmutated IGHV

First-Line Treatment Options
- Covalent BTKi
- BCL-2i and anti-CD20 mAb

Given Jacob's preference for an all-oral treatment regimen, he and his oncologist selected a covalent BTKi as a more suitable treatment option[3]

With the covalent BTKi, Jacob experienced:
- **Resolution of his anemia and lymphadenopathy**
- **Initial presentation of a treatment-associated rash that quickly resolved**
- **Increase of his anti-hypertensive dose**
- **Occasional headaches and diarrhea**

Key Point

After initiating treatment, evaluate for response and monitor for AEs. Patients should remain on treatment until progression or intolerance indicate a change or the completion of a fixed-duration regimen[3]

Disease Progression on Treatment: Year 12

- Severe fatigue
- Bulky lymphadenopathy
- Increasing lymphocytosis: 44,000 lymphocytes/µL
- Worsening anemia: hemoglobin 7.0 g/dL
- New cytopenia: 15 x 10^8/L
- New del(*11q*) mutation

Second-Line Treatment Options
- Non-covalent BTKi
- BCL-2i and anti-CD20 mAb

Based on his progression on a covalent BTKi, another covalent BTKi was not a viable option for Jacob.[4-6] He and his oncologist discussed options and selected an all-oral, non-covalent BTKi for 2nd-line treatment.

Key Point

Perform molecular/genetic testing at time of treatment initiation and again at progression to inform disease prognosis and individualized treatment options[2]

AE = adverse event; BCL-2i = BCL-2 inhibitor; BTKi = Bruton tyrosine kinase inhibitor; CLL = chronic lymphocytic leukemia; FISH = fluorescence in situ hybridization; IGHV = immunoglobulin heavy-chain variable region gene; iwCLL = International Workshop on CLL; mAb = monoclonal antibody.

1. Hallek M, et al. *Blood*. 2018;131(25):2745-2760. 2. Gaidano G, Rossi D. *Hematology Am Soc Hematol Educ Program (2017)*. 2017(1):329-337. 3. Soumerai JD, et al. *Blood Adv*. 2025;9(5):1213-1229. 4. Fresa A, et al. *Cancers (Basel)*. 2024;16(11):2011. 5. Shadman M. *JAMA*. 2023;329(11):918-932. 6. CGTlive. Accessed October 7, 2025. https://www.cgtlive.com/view/new-agents-and-optimal-patientselection-in-cll-comprise-modern-paradigm