

Patient Case Study: Treatment Sequencing Considerations for Chronic Lymphocytic Leukemia (CLL)

John and his clinician are considering 3rd-line therapy options for CLL. Here's how they managed his initial treatment:



John

Male
Current age: 78 years



Medical History

- Hypertension
 - Hydrochlorothiazide
- Hyperlipidemia
 - Atorvastatin

CLL Diagnosis – 2014

Primary Care Visit

Routine bloodwork: lymphocytosis

- 24,000 lymphocytes/ μ L

Physical examination: small cervical lymphadenopathy
CLL Confirmed With Flow Cytometry
Prognostic workup

- IGHV molecular assay: negative for mutation
- FISH: del(11q)

Normal hemoglobin and platelet levels

Watch
+
Wait



Tip From an Expert

Most patients diagnosed with CLL will not require immediate treatment. The patient should meet the 2018 iwCLL criteria for active disease to begin treatment.

Symptom Progression – 2016

CLL Symptom Development

- Increasing fatigue
- Worsening lymphadenopathy
- Increasing lymphocytosis
- New anemia

1st Line:
Covalent
BTKi

Treatment Response

- Resolution of lymphadenopathy
- Normalization of hemoglobin

View additional
CLL resources



Tip From an Expert

Work up the patient's symptoms, and confirm that they are attributable to CLL in order to assess for true progression and appropriately time discussions about treatment changes.

Symptom Progression – 2021

CLL Symptom Recurrence

- Increasing lymphocytosis
- Multiple enlarging axillary and inguinal lymph nodes
- Severe fatigue and recurrent anemia

Repeat Prognostic Testing

- FISH: del(11q)
- NGS:
 - TP53 wild type
 - BTKC481S mutation
 - VAF 78%

2nd Line:
BCL-2i
+
Anti-CD20
mAb

Treatment Response

- Resolution of CLL symptoms
- 1 year off CLL treatment



Tip From an Expert

Repeating cytogenetic and molecular testing at each line of therapy may help to prognosticate for patients and identify resistance mechanisms, which can help better inform the next line of therapy.

John's clinician shared that there are treatment options available for patients who have already been exposed to covalent BTK and BCL-2 inhibition.

John expressed a preference for an oral therapy over a cellular treatment due to his lack of family support and distance to a CAR T-cell treatment center.

Symptom Progression – 2024

CLL Symptom Recurrence

- Lymphocytosis and subsequent lymphadenopathy
- Splenomegaly
- Early satiety
- Concurrent anemia and mild thrombocytopenia

Repeat Prognostic Testing

- FISH: del(11q) and del(17p)
- NGS:
 - BTKC481S mutation
 - TP53 mutation

3rd Line:
Non-
Covalent
BTKi

Treatment Response

- Initial treatment-associated lymphocytosis
- Resolution of CLL symptoms

This is a hypothetical patient case.

BCL-2i = BCL-2 inhibitor; BTKi = Bruton tyrosine kinase inhibitor; CAR = chimeric antigen receptor; FISH = fluorescence in situ hybridization; IGHV = immunoglobulin heavy-chain variable region gene; iwCLL = International Workshop on Chronic Lymphocytic Leukemia; mAb = monoclonal antibody; NGS = next-generation sequencing; VAF = variant allele frequency. Shadman M. Diagnosis and Treatment of Chronic Lymphocytic Leukemia: A Review. JAMA. 2023;329(11):918-932.

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