

# Exploring Treatment Sequencing Strategies in Chronic Lymphocytic Leukemia



Multiple clinical, disease, and patient factors influence treatment selection and sequencing<sup>1,2</sup>

## Medicines for the treatment of CLL<sup>3-6</sup>



- Covalent BTKi ± anti-CD20 mAb
- BCL-2i ± anti-CD20 mAb
- CIT\*



- BCL-2i + anti-CD20 mAb
- Covalent BTKi ± anti-CD20 mAb
- Non-covalent BTKi



- Non-covalent BTKi
- CAR T-cell therapy



Laboratory evaluations such as testing for del(17p)/TP53 mutations and IGHV mutational status can help inform treatment decisions and predict likely response to therapy<sup>7,8</sup>

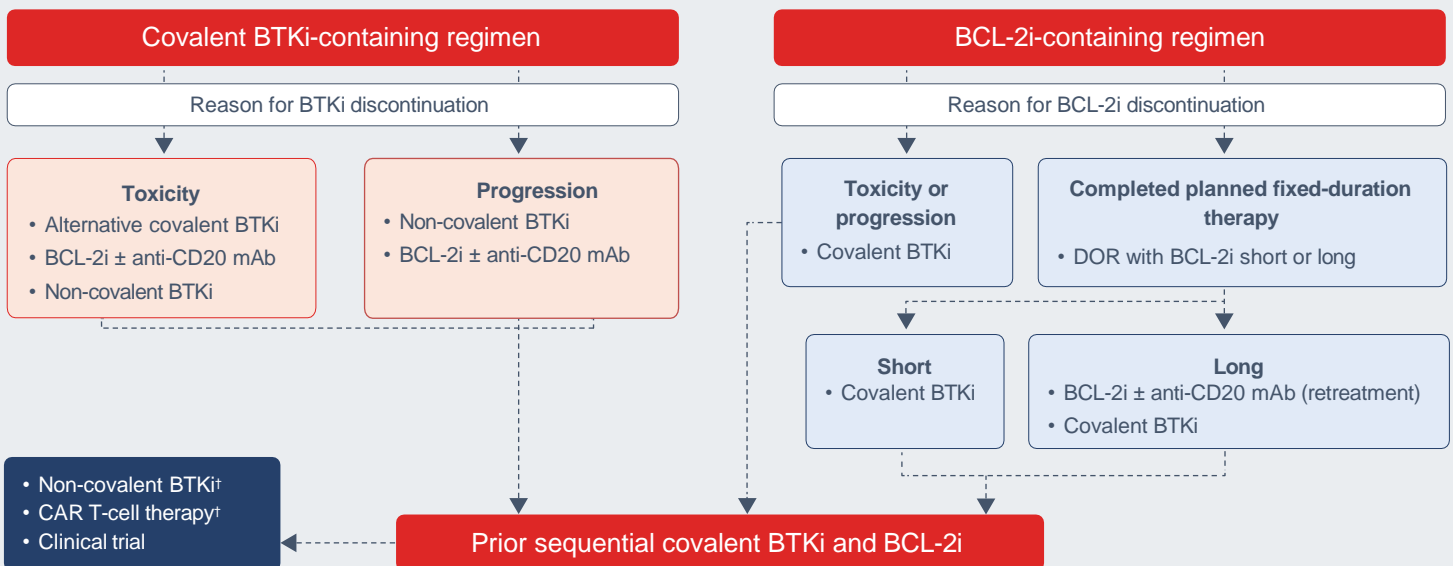


Signs of disease progression and/or treatment intolerance may indicate the need to switch therapies.<sup>3</sup> Switching between drug classes (eg, a BTKi and a BCL-2i) is a common strategy in the 2L setting<sup>3</sup>



Because CLL is a progressive disease, patients will likely require multiple therapies through the course of the disease to continue to achieve a response<sup>1</sup>

## Treatment Sequencing Approaches for Previously Treated Patients With CLL<sup>3-6</sup>



## Treatment requirements and patient preferences can influence treatment selection<sup>3,4,9</sup>



Patients may perceive different administration routes as more or less convenient<sup>4</sup>



Due to having similar resistance mechanisms, sequencing covalent BTK inhibitors after progression should be avoided. A non-covalent BTKi can be used after progression on a covalent BTKi<sup>3</sup>



Patients may have preferences between continuous oral therapy administered at home vs fixed-duration oral and IV therapy with frequent office visits and increased monitoring<sup>4,9</sup>

\*Due to its inferior efficacy when compared to targeted therapies, CIT is appropriate only for select patients.<sup>3,4</sup>

†Optimal sequencing of CAR T-cell therapy and non-covalent BTKi therapy is yet to be determined.<sup>3,4</sup>

1L, first line; 2L, second line; 3L+, third line or greater; BCL-2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; CAR, chimeric antigen receptor; CIT, chemoimmunotherapy; CLL, chronic lymphocytic leukemia; DOR, duration of response; IGHV, immunoglobulin heavy chain variable region genes; mAb, monoclonal antibody.

1. Odetola O, Ma S. *Curr Hematol Malig Rep.* 2023;18(5):130-143. 2. Hallek M, Al-Sawaf O. *Am J Hematol.* 2021;96(12):1679-1705. 3. Shadman M. *JAMA.* 2023;329(11):918-932. 4. Jain N. *Lancet.* 2024;404(10453):694-706. 5. Sharman JP et al. *J Clin Oncol.* 2025;43(22): 2538-2549. 6. Hallek M. *Am J Hematol.* 2025;100:450-480. 7. Heerema NA, et al. *Haematologica.* 2021;106(6):1608-1615. 8. Campo E, et al. *Haematologica.* 2018;103(12):1956-1968. 9. González-Gascón-Y-Marín I, et al. *Cancers (Basel).* 2023;15(17):4391.

