

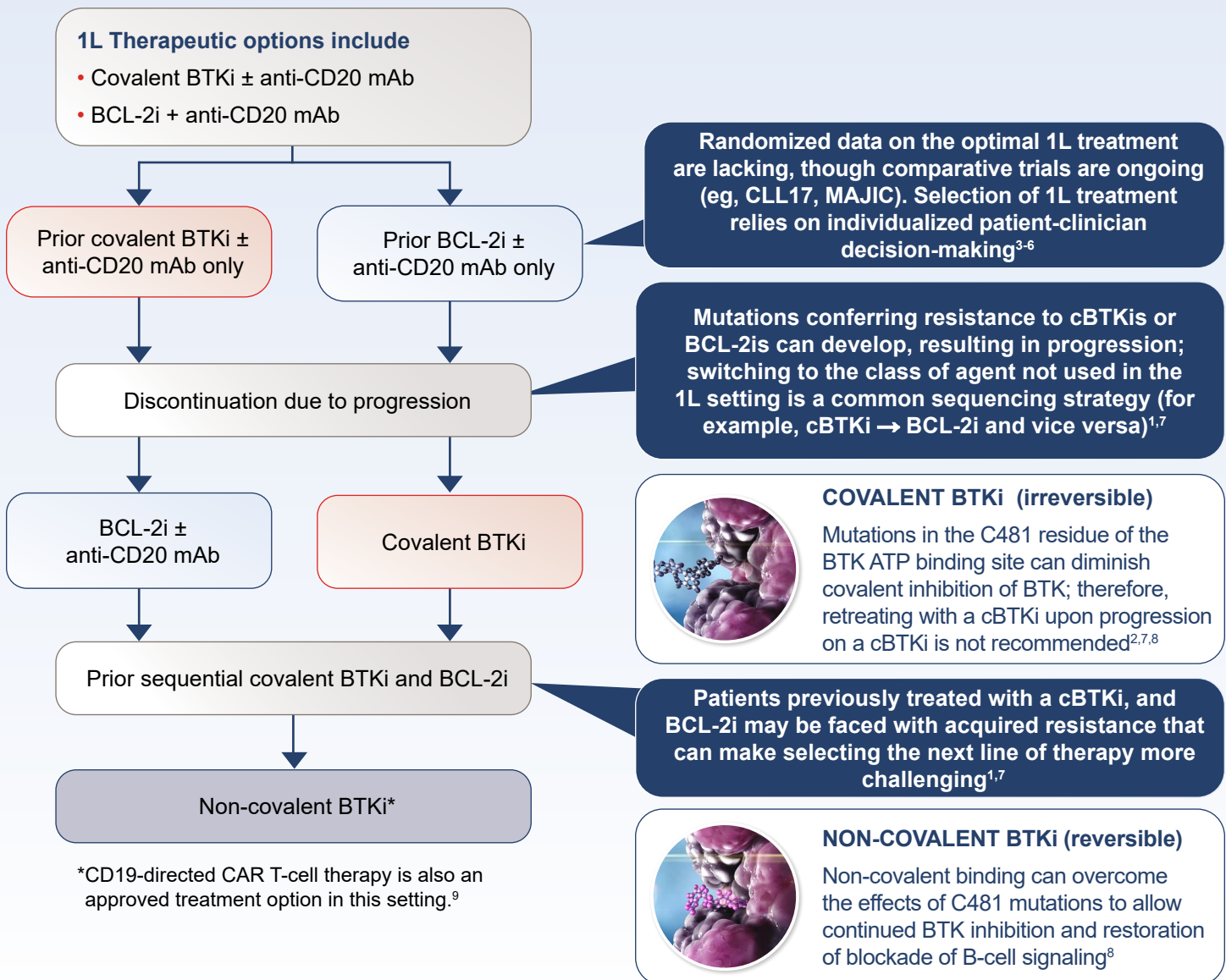
# Sequencing BTK inhibitors in the Treatment of B-Cell Malignancies

## CHRONIC LYMPHOCYTIC LEUKEMIA

### Role of ncBTKis in the Treatment of CLL

- ncBTKis bind **reversibly** to the BTK protein, which may address certain limitations of acquired resistance that occur with cBTKis<sup>1,2</sup>
- ncBTKis may provide an option for patients with CLL requiring treatment after failure on **both** a cBTKi and BCL-2i<sup>2</sup>

## Evidence-Based Approach to Sequencing BTKis in CLL



\*CD19-directed CAR T-cell therapy is also an approved treatment option in this setting.<sup>9</sup>

1L, first line; ATP, adenosine triphosphate; BCL-2i, B-cell lymphoma 2 inhibitor; BTK, Bruton's tyrosine kinase; BTKi, Bruton's tyrosine kinase inhibitor; cBTKi, covalent BTK inhibitor; CAR, chimeric antigen receptor; CLL, chronic lymphocytic leukemia; mAb, monoclonal antibody; ncBTKi, non-covalent BTK inhibitor.

References: 1. Mato AR, et al. *Clin Cancer Res*. 2022;28(4):603-608. 2. Montoya S, Thompson MC. *Cancers (Basel)*. 2023;15(14):3648. 3. Hallek M, Al-Sawaf O. *Am J Hematol*. 2021;96(12):1679-1705. 4. Ahn IE, Brown JR. *Hematology Am Soc Hematol Educ Program*. 2022(1):323-328. 5. ClinicalTrials.gov identifier: NCT04608318. Updated March 6, 2024. <https://clinicaltrials.gov/ct2/show/NCT04608318>. 6. ClinicalTrials.gov identifier: NCT05057494. Updated December 6, 2024. <https://clinicaltrials.gov/study/NCT05057494>. 7. Fresa A, et al. *Cancers (Basel)*. 2024;16(11):2011. 8. Mato AR, et al. *N Engl J Med*. 2023;389(1):33-44. 9. Targeted Oncology. Accessed November 11, 2024. <https://www.targetedonc.com/view/fda-approves-liso-cel-in-relapsed-or-refractory-cll-sll>.

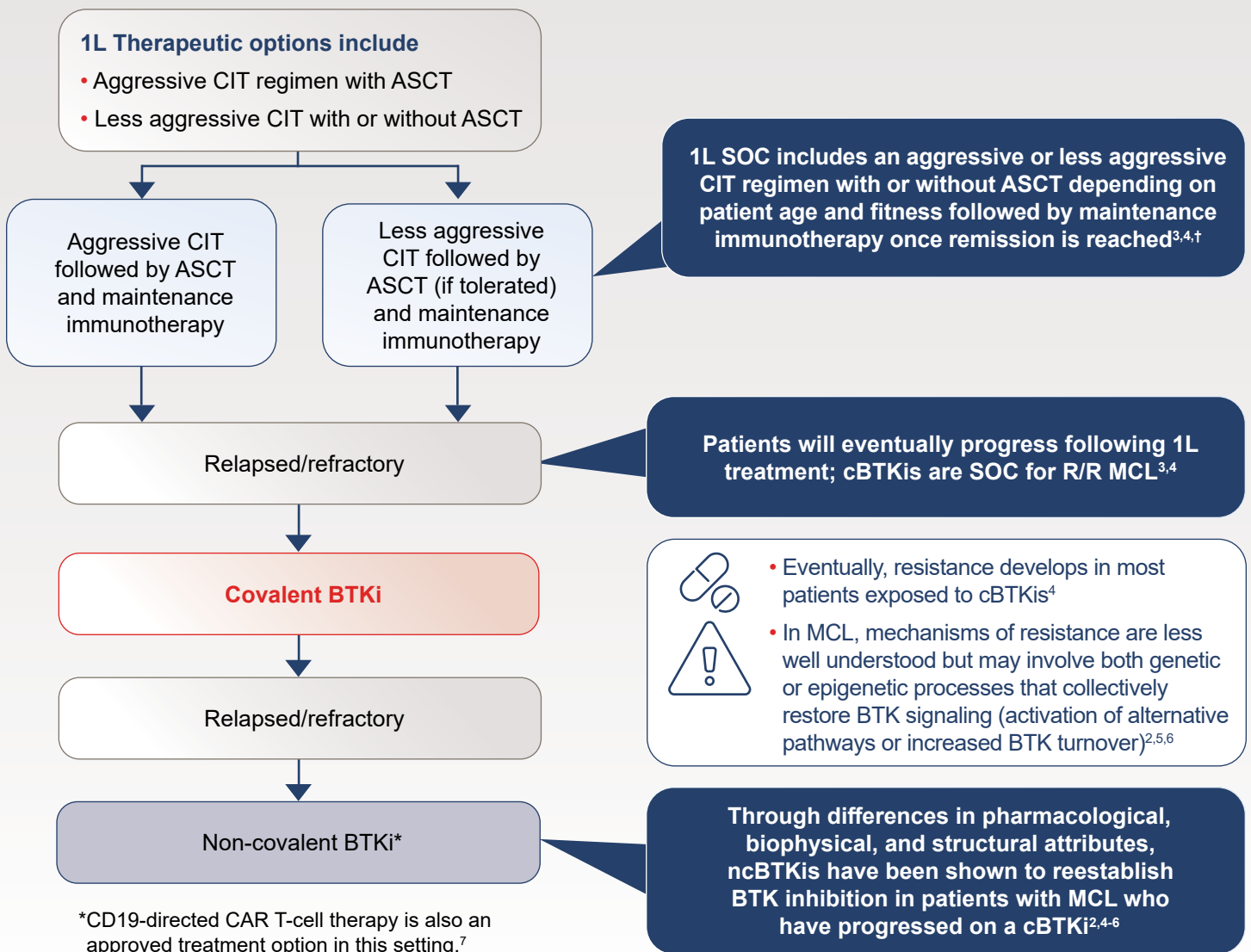
# Sequencing BTK inhibitors in the Treatment of B-Cell Malignancies

## MANTLE CELL LYMPHOMA

### Role of ncBTKis in the Treatment of MCL

- Despite initial efficacy of cBTKis in R/R MCL, resistance or intolerance invariably develops, necessitating a new treatment option<sup>1,2</sup>
- ncBTKis have key differences in structure and MOA compared with cBTKis, including **reversible** binding<sup>1,2</sup>
- ncBTKis may address some of the limitations of resistance cBTKis pose<sup>3</sup>

## Evidence-Based Approach to Sequencing BTKis in CLL



†No regimen has been firmly established as SOC.

1L, first-line; ASCT, autologous stem cell transplant; BTKi, Bruton's tyrosine kinase inhibitor; CAR, chimeric antigen receptor; cBTKi, covalent BTK inhibitor; CIT, chemoimmunotherapy; CLL, chronic lymphocytic leukemia; MCL, mantle cell lymphoma; MOA, mechanism of action; ncBTKi, non-covalent BTKi; R/R, relapsed/refractory; SOC, standard of care.

References: 1. Lewis KL, Cheah CY. *J Pers Med.* 2021;11(8):764. 2. Wang ML, et al. *J Clin Oncol.* 2023;41(24):3988-3997. 3. Jain P, Wang ML. *Am J Hematol.* 2022;97(5):638-656. 4. Jain N. *J Hematol Oncol.* 2023;16(1):99. 5. Gomez EB, et al. *Blood.* 2023;142(1):62-72. 6. Stanchina MD, et al. *Nat Rev Clin Oncol.* 2024;21(12):867-887. 7. FDA. Accessed November 20th, 2024. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lisocabtagene-maraleucel-relapsed-or-refractory-mantle-cell-lymphoma>.

