



NCCN Guidelines: Therapeutic Regimens for CLL/SLL and MCL

Full abbreviations, accreditation, and disclosure information available at
[PeerView.com/CLL-MCLTandem25](https://www.peerview.com/CLL-MCLTandem25)

PeerView
Hematology-Oncology



NCCN Guidelines on CLL/SLL¹

Modern Targeted Therapy Regimens As Standards of Care

1L Therapy <u>No del(17p)/TP53 Mutation</u>	1L Therapy <u>With del(17p)/TP53 Mutation</u>
Preferred	
<ul style="list-style-type: none">• Acalabrutinib ± obinutuzumab (category 1)• Venetoclax + obinutuzumab (category 1)• Zanubrutinib (category 1)	<ul style="list-style-type: none">• Acalabrutinib ± obinutuzumab• Venetoclax + obinutuzumab• Zanubrutinib
Other recommended (BTKi-based only)	
<ul style="list-style-type: none">• Ibrutinib (category 1)• Ibrutinib + venetoclax (category 2A)	<ul style="list-style-type: none">• Ibrutinib (category 2A)• Ibrutinib + venetoclax (category 2A)

Sequential Therapy in 2L+ Settings

(CLL/SLL With/Without del(17p)/TP53 Mutation)

Preferred regimens

- Acalabrutinib (category 1)
- Venetoclax + obinutuzumab (category 1)
- Venetoclax (del[17p])
- Zanubrutinib (category 1)

Other recommended regimens

- Ibrutinib (category 1)
- Venetoclax + rituximab (no del[17p]) (category 1)
- Ibrutinib + venetoclax
 - Category 2A for del(17p)
 - Category 2B for no del(17p)
- Venetoclax (no del[17p] only)

Useful in certain circumstances

- Pirtobrutinib (**resistance or intolerance** to prior cBTKi therapy)



NCCN Guidelines: Therapeutic Regimens for CLL/SLL and MCL

Full abbreviations, accreditation, and disclosure information available at
[PeerView.com/CLL-MCLTandem25](https://www.peerview.com/CLL-MCLTandem25)

PeerView
Hematology-Oncology



NCCN Guidelines on CLL/SLL¹ (Cont'd)

Therapy for Relapsed or Refractory Disease After Prior BTKi- and Venetoclax-Based Regimens

Preferred regimens for CLL/SLL with/without del(17p)/*TP53* mutation

- Chimeric antigen receptor (CAR)-T cell therapy: liso-cel
- Pirtobrutinib (if not previously given)

Other recommended options include

- PI3Ki-based treatment, ibrutinib + venetoclax (category 2B), chemoimmunotherapy, CD20 antibody-based treatment, or lenalidomide ± rituximab

Scan to access the complete
NCCN guidelines on chronic
lymphocytic leukemia/small
lymphocytic lymphoma





NCCN Guidelines: Therapeutic Regimens for CLL/SLL and MCL

Full abbreviations, accreditation, and disclosure information available at
[PeerView.com/CLL-MCLTandem25](https://www.peerview.com/CLL-MCLTandem25)

PeerView
Hematology-Oncology



NCCN Guidelines on MCL²

CIT and BTKi-Based Regimens As Frontline Care

Induction Therapy

Aggressive therapy

Preferred regimens

- LyMA regimen: RDHA + platinum followed by R-CHOP for non-PET CR
- NORDIC regimen: dose-intensified rituximab + maxi-CHOP alternating with rituximab + HD cytarabine
- Rituximab + bendamustine followed by rituximab + HD cytarabine
- **TRIANGLE regimen**: alternating R-CHOP + **covalent BTKi**/RDHA + platinum (**category 2A** for ibrutinib; **category 2B** for acalabrutinib or zanubrutinib)

Less aggressive therapy

Preferred regimens

- Bendamustine + rituximab
- VR-CAP
- R-CHOP
- Lenalidomide (continuous) + rituximab

Other recommended regimen

- **Acalabrutinib (continuous)** + rituximab

Acalabrutinib in combination with bendamustine and rituximab has received FDA approval for frontline treatment of adult patients with previously untreated MCL³

Maintenance After HDT/ASCR or Aggressive Induction Therapy

- Covalent BTKi for 2 years (**category 2A** for ibrutinib; **category 2B** for acalabrutinib or zanubrutinib) + rituximab every 8 weeks for 3 years

Maintenance After Less Aggressive Therapy

- Rituximab every 8 weeks for 2-3 years following R-CHOP (category 1) or BR
- Maintenance rituximab following VR-CAP or RBAC500 has not been evaluated



NCCN Guidelines: Therapeutic Regimens for CLL/SLL and MCL

Full abbreviations, accreditation, and disclosure information available at [PeerView.com/CLL-MCLTandem25](https://www.peerview.com/CLL-MCLTandem25)

PeerView
Hematology-Oncology



NCCN Guidelines on MCL² (Cont'd)

Covalent BTKi, Noncovalent BTKi, and CAR-T Are Now Recommended in R/R MCL

Second-Line and Subsequent Therapy

Preferred regimens

- Covalent BTKi (continuous)
 - Acalabrutinib or zanubrutinib
- Lenalidomide + rituximab

Other recommended regimen

- Covalent BTKi (continuous)
 - Ibrutinib ± rituximab

Progressive Disease After Prior cBTKi

- Non-covalent BTKi (continuous)
 - Pirtobrutinib
- Anti-CD19 CAR-T (2 FDA-approved constructs)
 - Brexu-cel or liso-cel

Ibrutinib + venetoclax is now recommended as useful under certain circumstances as 2L and subsequent therapy

Considerations With BTKi From Practice Guidelines

- Patients with ibrutinib intolerance have been successfully treated with acalabrutinib or zanubrutinib without recurrence of symptoms
- Head-to-head clinical trials in other B-cell malignancies have demonstrated a more favorable toxicity profile for acalabrutinib and zanubrutinib versus ibrutinib without compromising efficacy

Scan to access the complete
NCCN guidelines on
B-cell lymphomas



1. NCCN Clinical Practice Guidelines in Oncology. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/clk.pdf.
2. NCCN Clinical Practice Guidelines in Oncology. B-Cell Lymphomas. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf.
3. Calquence (acalabrutinib) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/210259s011lbl.pdf.