

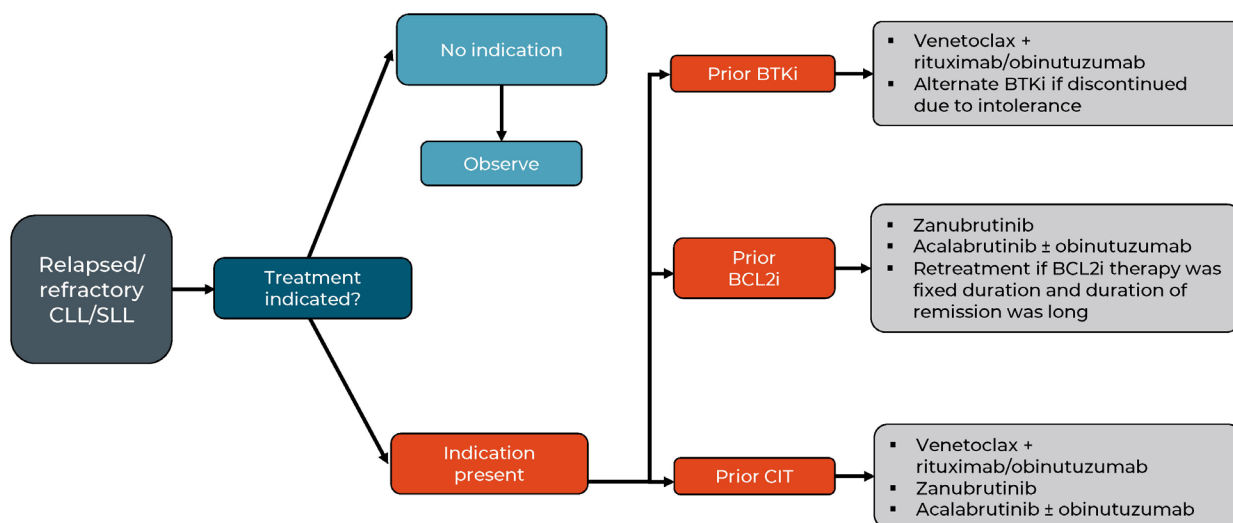
Nursing Considerations for Management of Chronic Lymphocytic Leukemia

- CLL is the most common type of leukemia in the Western world¹
- Typically diagnosed by routine blood work
- Often asymptomatic and does not require immediate treatment; treatment required for symptom management, cytopenias, or bulky lymphadenopathy

Guideline-Recommended First-line Therapy for CLL¹

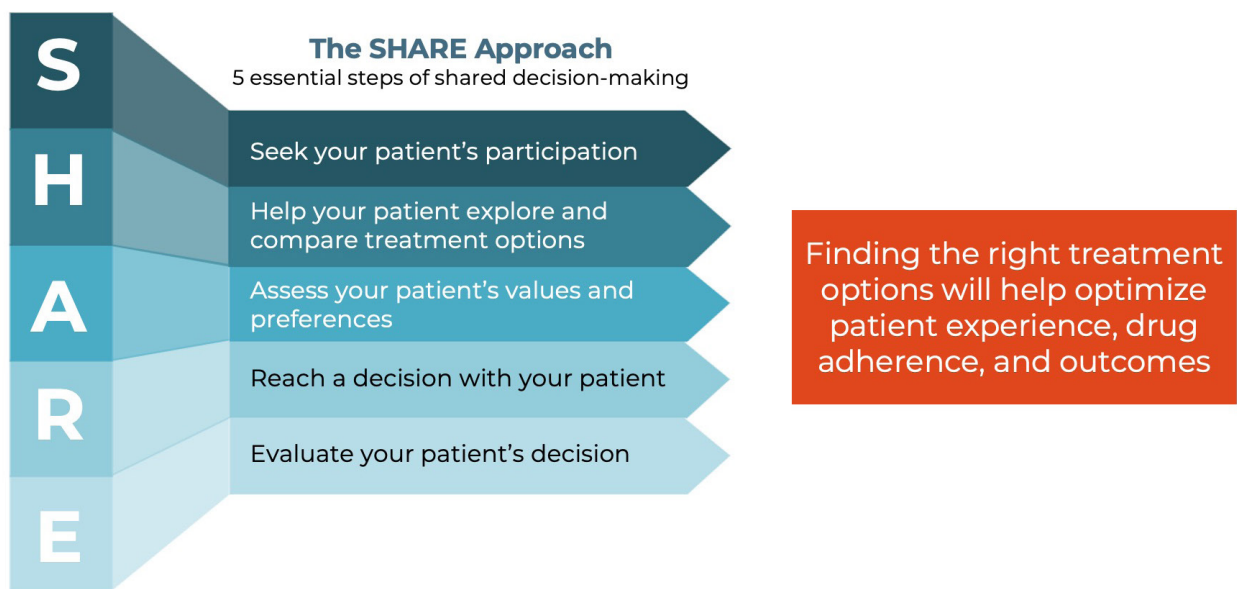
Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Without del(17)p/TP53 mutation		
• Acalabrutinib ± obinutuzumab • Venetoclax + obinutuzumab • Zanubrutinib	• Ibrutinib • Bendamustine + anti-CD20 mAb • Chlorambucil + obinutuzumab • Obinutuzumab • HDMP + rituximab or obinutuzumab • Ibrutinib + obinutuzumab or rituximab or venetoclax	• FCR (consider for <i>IGHV</i>-mutated CLL in patients <65 years of age without significant comorbidities)
With del(17)p/TP53 mutation		
• Acalabrutinib ± obinutuzumab • Venetoclax + obinutuzumab • Zanubrutinib	• Alemtuzumab ± rituximab • HDMP + rituximab • Ibrutinib • Obinutuzumab • Ibrutinib + venetoclax	

Summary of Therapy for Relapsed/Refractory CLL

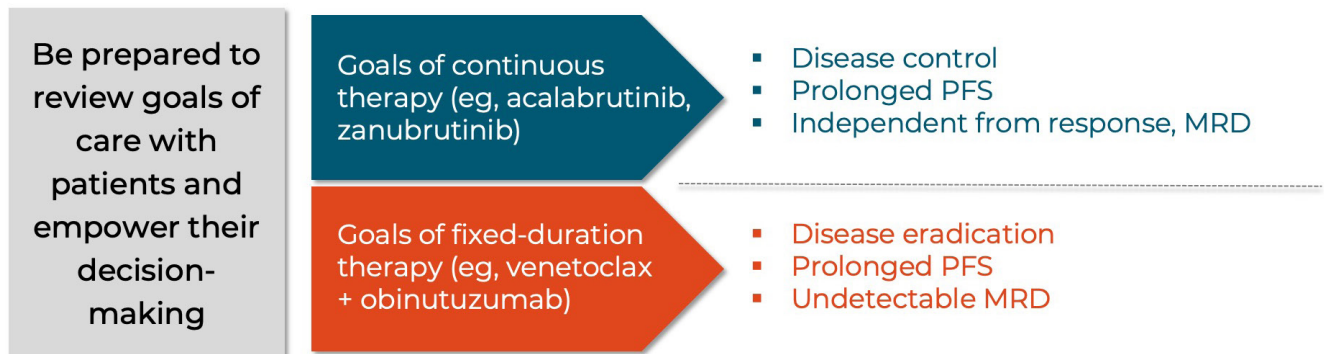


- Useful in certain circumstances (second- or third-line therapy), with/without del(17)p/TP53 mutation: noncovalent (reversible) BTK inhibitor pirtobrutinib (resistance or intolerance to prior covalent BTK inhibitor therapy)

Shared Decision-making²



Goals of Continuous- vs Fixed-Duration Therapy in CLL



Common and Important BTK Inhibitor Toxicities in CLL³

Toxicities of Special Interest	Most Common Toxicities	Other Common Toxicities
• Atrial fibrillation • Ventricular arrhythmia • Bleeding • Hypertension • Infections	• Anemia • Arthralgia/myalgia • Cough • Diarrhea • Fatigue • Headache • Neutropenia	• Cytopenias • Hair/nail changes • Lymphocytosis • Nausea • Rash

Safety Considerations With Covalent BTK Inhibitors⁴⁻⁸

Acalabrutinib	Zanubrutinib
• Head-to-head evidence shows fewer AF/flutter or HTN events with acalabrutinib vs ibrutinib • Headaches commonly occur early in therapy with acalabrutinib and typically resolve in 1-2 months; manage with acetaminophen + caffeine	• Head-to-head data show fewer AF/flutter events with zanubrutinib vs ibrutinib • Neutropenia with zanubrutinib: For first occurrence, dose interruption is recommended • Once toxicity has resolved to grade ≤1 or baseline, resume at 160 mg twice daily or 320 mg once daily • Consider growth factor with G-CSF

- Current guidelines and evidence indicate that sequencing to a second-generation BTK inhibitor can be a useful strategy in settings of ibrutinib intolerance

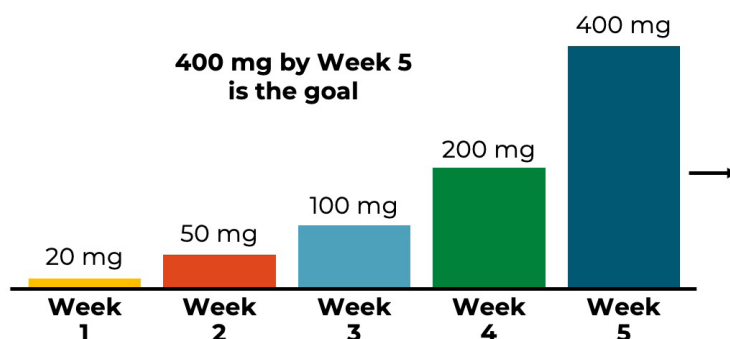
Dosing and Drug Interactions With Covalent BTK Inhibitors^{5,8-10}

BTK inhibitor Dosing in CLL	Coadministration With:			
	Strong CYP3A Inhibitors	Moderate CYP3A Inhibitors	Moderate or Strong CYP3A Inducers	Gastric Acid-Reducing Agents
Ibrutinib 420 mg once daily	Avoid use	Avoid use; if necessary, reduce to 280 mg once daily	Avoid use	No dosage adjustment recommended
Acalabrutinib maleate salt (IR film-coated tablet) 100 mg every 12 hours (capsules discontinued, transition to tablet)	Avoid use	Reduce to 100 mg once daily	Avoid use; if necessary, increase to 200 mg twice daily	Tablets can be used regardless of use of PPIs and ingestion of food
Zanubrutinib 160 mg orally twice daily or 320 mg orally once daily	Reduce to 80 mg once daily; interrupt dose for adverse events	Reduce to 80 mg twice daily; modify for adverse events	Avoid use	No dosage adjustment recommended

Most Frequent Grade ≥3 Adverse Events With Venetoclax + Obinutuzumab¹¹

Grade ≥3 Adverse Event, %	Venetoclax + Obinutuzumab (n = 212)	
	During Treatment	After Treatment
Neutropenia	51.9	4.0
Thrombocytopenia	14.2	0.5
Anemia	7.5	2.0
Febrile neutropenia	4.2	1.0
Leukopenia	2.4	0
Pneumonia	3.8	3.0
Infusion-related reaction	9.0	0
TLS	1.4	0

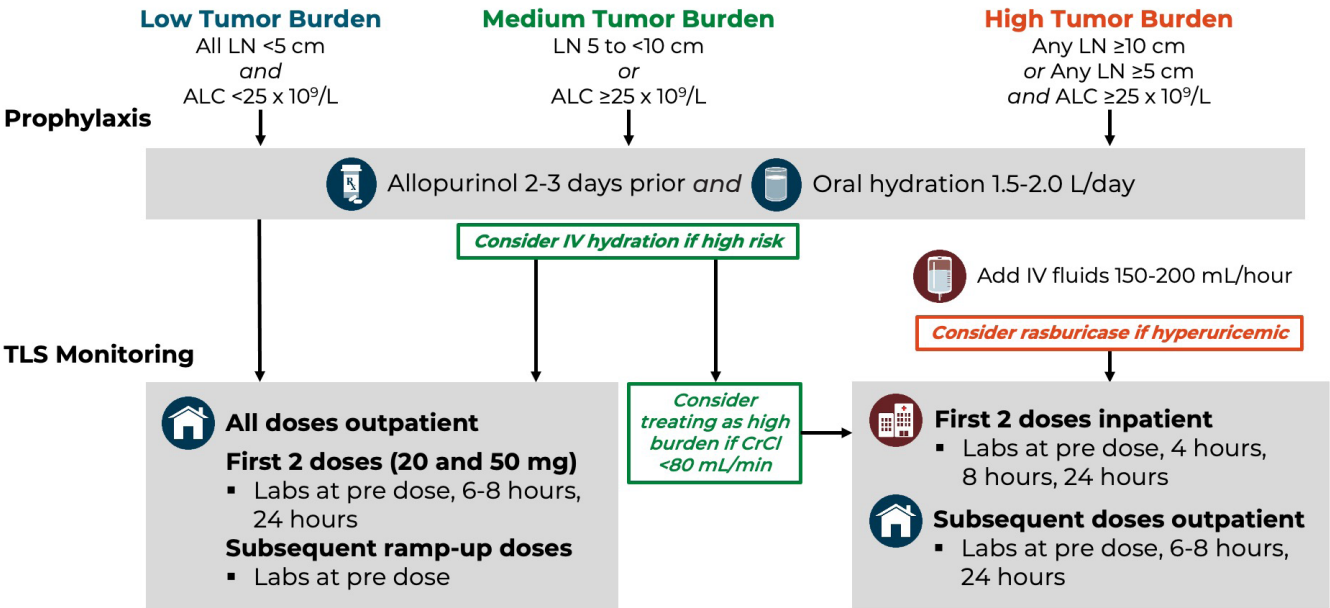
Venetoclax Dosing and Administration¹²



When used with obinutuzumab: Initiate venetoclax (according to 5-week ramp-up dosing) cycle 1, Day 22

When used with rituximab: Start rituximab after the patient has completed venetoclax 5-week ramp-up dosing and has received 400 mg once daily for 7 days

Venetoclax TLS Risk Stratification and Prophylaxis



Emerging Strategies: Managing Patients With CLL Who Have Progressed Following Treatment With a Covalent BTK Inhibitor and Venetoclax

Potential Benefit	Unlikely to Benefit
Noncovalent BTK inhibitors*: initial evidence suggests potent efficacy against resistance mutations (eg, <i>BTK</i> C481) and in the setting of progressive disease CAR T-cell therapy*: highly active in pretreated CLL	PI3K inhibitors: limited benefit in this population and significant toxicity burden Chemoimmunotherapy: limited benefit in this population Covalent BTK inhibitors: patients have already progressed on these agents

*Noncovalent BTK inhibitors and CAR T-cell therapy are not currently approved for treating CLL but are approved for other indications (October 2023). As noted above, pirtobrutinib is listed in national guidelines as a treatment option for specific patients.

Noncovalent BTK Inhibitors: Dosing and Safety of Pirtobrutinib^{13,14}

Dosing	Safety
200 mg orally once daily is approved for MCL and used in phase II BRUIN trial for CLL/SLL	Monitor for arrhythmias, infections, bleeding, and cytopenias

Drug Interactions
- Strong CYP3A inhibitors: Avoid concomitant use; if unavoidable, reduce dose - Strong/moderate CYP3A inducers: Avoid concomitant use; if unavoidable, increase dose

Nursing Take-home Points on Preparing for Noncovalent BTK Inhibitors

- Resistance to covalent BTK inhibitors is a driver of progressive disease/treatment discontinuation
- Patients with double-refractory CLL that has progressed with a covalent BTK inhibitor and venetoclax-based therapy historically have had poor outcomes
- Noncovalent BTK inhibitors represent a significant contribution to CLL care, can overcome BTK resistance, and are effective in double-refractory disease
 - Noncovalent BTK inhibitors are still investigational but available via clinical trial enrollment
 - Pirtobrutinib is approved in MCL and part of national guidelines for CLL; off-label use is a possibility

Clinical Care Options Management Decision Support Tools

- Enter your own case scenarios to get management recommendations from experts
- Assessment and management of BTK inhibitor adverse events: clinicaloptions.com/BTKiTool
- Management of CLL: clinicaloptions.com/CLLTool

AF, atrial fibrillation; ALC, absolute lymphocyte count; BCL2i, BCL2 inhibitor; BTKi, BTK inhibitor; CIT, chemoimmunotherapy; CLL, chronic lymphocytic leukemia; CrCl, creatinine clearance; FCR, fludarabine/cyclophosphamide/rituximab; G-CSF, granulocyte colony-stimulating factor; HDMP, high-dose methylprednisolone; HTN, hypertension; IR, immediate release; LN, lymph node; mAb, monoclonal antibody; MCL, mantle cell lymphoma; MRD, measurable residual disease; PFS, progression-free survival; PPI, proton pump inhibitor; SLL, small lymphocytic lymphoma; TLS, tumor lysis syndrome.

References

1. NCCN. Clinical practice guidelines in oncology: chronic lymphocytic leukemia/small lymphocytic lymphoma. v.3.2023. [nccn.org](https://www.nccn.org).
2. ahrq.gov/health-literacy/professional-training/shared-decision/index.html.
3. Lipsky. Hematology Am Soc Hematol Educ Program. 2020;2020:336.
4. Byrd. JCO. 2021;39:3441.
5. Acalabrutinib PI.
6. Rogers. Haematologica. 2021;106:2364.
7. Brown. NEJM. 2023;388:319.
8. Zanubrutinib PI.
9. Weis. J Oncol Pharm Pract. 2022;28:1411.
10. Ibrutinib PI.
11. Al-Sawaf. Nat Commun. 2023;14:2147.
12. Venetoclax PI.
13. Pirtobrutinib PI.
14. Mato. NEJM. 2023;389:33.



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