



Oral Oncolytics in CLL

Pocket Guide for the Oncology Nurse

Understanding patient and/or caregiver goals for CLL treatment encompasses more than discussions regarding treatment efficacy. Discussion points to consider with patients:

What are your goals for treatment? Priorities to consider:

- Living as long as possible
- Having a high quality of life
- The safest treatment – low risk for severe side effects
- The most effective treatment
- Keeping out-of-pocket costs affordable
- Fewer trips to the hospital or cancer center

How will this treatment affect day-to-day life?

Health-Related Social Needs Assessment

Assess and Evaluate the Patient's:

Lifestyle and Economic Situation	<ul style="list-style-type: none">• Do they live alone or with a family member/partner?• Do they work or are they retired? What is their financial situation?• What is their daily activity level?
Social Situation	<ul style="list-style-type: none">• What kind of help and support do they need with daily activities and management of their condition?• Do they have a dedicated caregiver?• Would they like help connecting to resources for additional social support?• What is their education level? What is their English language proficiency? What is their health literacy level?• What is the preferred language for communication for the patient and caregiver?
Transportation	<ul style="list-style-type: none">• Do they drive or have a caregiver with reliable transportation?• Do they have trouble getting transportation to medical or laboratory appointments?• How far do they live from the clinic?• Are there health care facilities for laboratory monitoring close to the patient's home?• Provide recommendations for support services, including navigation and/or advocacy organization resources.

During the Initial Patient Education Session:

- Review patient-specific goals of treatment
- Provide medication-specific education:
 - What AEs to expect and how to manage AEs if they occur (including OTC remedies)
 - Safe medication handling and disposal of unused medication
- Discuss the overall treatment plan and review the patient calendar:
 - How it works, how to take it (dose and frequency), and duration of therapy
 - Follow-up appointments (clinic and laboratory)
- Discuss plan and strategies for patient medication adherence and persistency
- Educate on emergency management (where/whom to call, contact list)
- Develop a comprehensive educational binder for the patient to take home:
 - Include disease and drug information, glossary of cancer medical terms, patient calendar
 - Utilize translation services to provide educational materials in the patient's preferred language
- If oral oncolytic medication is not available for 1st oral education session:
 - Utilize manufacturer-provided education kits
 - Educate about the logistics of obtaining the medication (i.e., expected timeline, reasons for potential delay)
 - Give instructions on what to do when the patient receives medication (i.e., call the clinic before starting)

Pulled from: [https://www.accc-cancer.org/docs/projects/chronic-lymphocytic-leukemia\(cil\)/accc_practiceguide_cil_flowchart.pdf?sfvrsn=93ae91dd_2&](https://www.accc-cancer.org/docs/projects/chronic-lymphocytic-leukemia(cil)/accc_practiceguide_cil_flowchart.pdf?sfvrsn=93ae91dd_2&)

SUMMARY TABLE
Management of BTKi AEs (Adapted from Nixon S., et al. 2023)

Adverse Event	Management/Prevention	Monitor/Educate
Diarrhea	<ul style="list-style-type: none"> • Dose modifications not required for grade 1/2 events <p>Suggest:</p> <ul style="list-style-type: none"> • Increase fluid intake • Small frequent meals • Eat low-fiber, high-calorie food (BRAT diet) • Topical barrier cream for perianal area • Take anti-diarrheal medication (e.g., loperamide) 	<ul style="list-style-type: none"> • Evaluate stool for common pathogens • If abdominal discomfort is present, consider CT or X-ray to rule out colitis or overflow diarrhea
Fatigue	<ul style="list-style-type: none"> • Dose modification typically not needed <p>Suggest:</p> <ul style="list-style-type: none"> • Energy prioritization • Improving sleep quality • Physical activity (e.g., walking, yoga) • Limit stress • Cognitive behavioral therapy • Attention restoring therapy (e.g., games, music) 	<ul style="list-style-type: none"> • If fatigue occurs later in treatment, patient should be evaluated for other potential causes
Headache	<ul style="list-style-type: none"> • Dose modification not needed • Prior to treatment initiation, advise patients that headaches should abate quickly, are easily managed, and are not a long-term consequence of treatment <p>Suggest:</p> <ul style="list-style-type: none"> • Acetaminophen or caffeine • Avoid NSAIDs 	<ul style="list-style-type: none"> • Unresolved and severe headaches should be evaluated at emergency department
Musculoskeletal events	<ul style="list-style-type: none"> • Dose modifications typically not needed for mild cases; may be required for severe and persistent cases <p>Suggest:</p> <ul style="list-style-type: none"> • Mild stretching/strengthening routines • Hot/cold compresses • Acetaminophen 	<ul style="list-style-type: none"> • Evaluate for electrolyte deficiencies and supplement with sodium, potassium, magnesium as needed
Infection	<p>Preventative measures:</p> <ul style="list-style-type: none"> • Give appropriate non-live vaccines and prophylactic therapies prior to therapy initiation, in consultation with physician <p>Suggest:</p> <ul style="list-style-type: none"> • Drink plenty of fluids • Adhere to prescribed medications • Contact clinic if symptoms worsen/do not improve 	<ul style="list-style-type: none"> • Educate patients to notify clinic upon signs of infection

Adverse Event	Management/Prevention	Monitor/Educate
Hematological toxicity	<ul style="list-style-type: none"> Consider supportive care with G-CSF for patients with grade ≥ 3 neutropenia For grade 3/4 neutropenia and thrombocytopenia that is persistent or is associated with significant bleeding, fever, or infection, follow dose modifications outlined in the product monographs 	<ul style="list-style-type: none"> Monitor blood counts monthly until blood is stable and every 3 months thereafter
Rash	<ul style="list-style-type: none"> Dose modifications typically not needed for mild cases; may be required for severe and persistent cases Generally requires dermatology referral and treatment with topical corticosteroids and antihistamines <p>Suggestions for pruritis:</p> <ul style="list-style-type: none"> Cold compresses Lukewarm bath with colloidal oatmeal 	<ul style="list-style-type: none"> Monitor for signs of severe rash: <ul style="list-style-type: none"> Fever Facial swelling Cutaneous detachment with blisters or mucosal erosions Signs of Stevens-Johnson syndrome Exfoliative rash Pustules Lymphadenopathy Lab abnormalities
Hypertension	<ul style="list-style-type: none"> Effectively managed with antihypertensive agents 	<ul style="list-style-type: none"> Regularly monitor blood pressure at clinic and at home where possible Educate patient to seek emergency care if systolic/diastolic pressure is ≥ 180 mmHg/≥ 120 mmHg
Atrial Fibrillation	<ul style="list-style-type: none"> Assess individual stroke/bleeding risk and consult with specialists as needed BTK inhibitor dose should be interrupted for grade ≥ 3 events 	<ul style="list-style-type: none"> Inquire and educate patients on signs of arrhythmias: <ul style="list-style-type: none"> Heart racing, fluttering, pounding Shortness of breath Easily tired Faint, dizzy Teach patients how to take pulse at home
Minor Bleeding (bruising, petechiae)	<ul style="list-style-type: none"> Can resolve spontaneously without intervention Suggest applying ice and moisturizers to affected areas 	<ul style="list-style-type: none"> Reassure patients that mild bleeding is not a predictor of major hemorrhage
Major Bleeding	<p>Preventative measures:</p> <ul style="list-style-type: none"> Assess concomitant medication and reduce nonessential drugs that may contribute to bleeding risk Pause BTK inhibitor 3-7 days before and after surgical procedure depending on bleeding risk 	<ul style="list-style-type: none"> Educate on signs of hemorrhage: <ul style="list-style-type: none"> Localized pain Severe bruising Blood in vomit, urine, or stool Shortness of breath Dizziness, altered mental state Thirst, decreased urination Cold, clammy skin Increased heart rate Decreased blood pressure

Additional Resource: *Cardiotoxicities in Patients Treated with BTK Inhibitors*
<https://www.jacc.org/doi/10.1016/j.jacc.2023.09.002>

SUMMARY TABLE

Management of Drug-Drug Interactions with BTKis (Adapted from Nixon S, et al. 2023)

	Ibrutinib	Acalabrutinib	Zanubrutinib	Pirtobrutinib
Strong CYP3A Inhibitors	Avoid	Avoid	Reduce dose	Avoid
Moderate CYP3A Inhibitors	Reduce dose	Reduce dose	Reduce dose	—
CYP3A Inducers	Avoid	Avoid	Avoid	Avoid
Warfarin/Vitamin K antagonists	Avoid	—	—	—
Proton pump inhibitors	Avoid only with capsule formulation	—	—	—
Renal impairment	<i>Mild/moderate:</i> no dose adjustment needed	<i>Mild/moderate:</i> no dose adjustment needed	—	<i>Severe:</i> Reduce dose
Hepatic Impairment	<i>Mild/moderate:</i> reduce dose <i>Severe:</i> avoid	<i>Severe:</i> avoid	<i>Severe:</i> reduce dose	—
Administer w/ caution	Drugs that prolong the PR interval Anticoagulants/ antiplatelets BCRP and P-gp substrates	BCRP and MATE1 substrates Consider the risk/benefit of anticoagulants or antiplatelets	Consider the risk/benefit of anticoagulants or antiplatelets	Sensitive CYP2C8, CYP2C19, CYP3A, P-gp, or BCRP Substrates Consider the risk/benefit of anticoagulants or antiplatelets

SUMMARY TABLE
Management of Venetoclax AEs

Adverse Event	Management Strategy
Diarrhea	Rule out possible infectious causes; treat with loperamide or temporary dose reductions
Edema	Elevate the feet, use of compression socks, low sodium intake, and diuretics if needed
Myalgia	Use over-the-counter pain relievers
Nausea	Use anti-nausea agents and non-drug measures to mitigate nausea
Neutropenia (and other cytopenias)	<p>Expert recommendations: use G-CSF to maintain dose intensity during ramp up; treat any infections that occur while considering drug-drug interactions; consider reducing the venetoclax dose if there is recurrent neutropenia beyond the first 3-4 months despite G-CSF, or if G-CSF does not improve ANC</p> <p>Package insert: grade 3 neutropenia with fever or grade 4 hematologic toxicity (other than lymphopenia): hold the dose, then depending on how many times it has occurred, the dose may need to be reduced once the toxicity has resolved to grade 1 or baseline</p>
Tumor lysis syndrome	<p>Prevent TLS: assess risk, institute appropriate prophylaxis, use 5-week dose ramp up</p> <p>Treat TLS: hold treatment, depending on severity and time of resolution, either continue the same dose or reduce dose once resuming venetoclax</p>
URTI, cough	Treat any infectious causes while considering drug-drug interactions; dose reductions, if needed, depending on the severity and frequency of recurrence

For any grade 3-4 non-hematologic toxicities, interrupt venetoclax dose. Resume venetoclax when the toxicity resolves to grade 1 or baseline.

- For 1st occurrence, resume the same dose of venetoclax
- For 2nd or subsequent occurrence, reduce the dose of venetoclax (per the dose reduction table or a larger dose reduction per physician discretion)

SUMMARY TABLE

Managing Drug Interactions with Venetoclax

Concomitant Agent	Recommendations
Strong CYP3A4 inhibitor (azole antifungals, clarithromycin, nirmatrelvir + ritonavir, others)	Concomitant use is contraindicated during the dose ramp up phase due to TLS risk Dose reductions if the patient is at steady daily dosing: <ul style="list-style-type: none"> • Use with posaconazole: decrease to venetoclax 70 mg PO daily • Use with other strong CYP3A4 inhibitor: decrease to venetoclax 100 mg PO daily
Moderate CYP3A4 inhibitor (erythromycin, diltiazem, verapamil, others)	Reduce the dose of venetoclax by at least 50%; resume the previous dose of venetoclax 2-3 days after discontinuation of the CYP3A4 inhibitor
Strong CYP3A4 inducer	Avoid concomitant use
P-gp inhibitor (amiodarone, azole antifungals, others)	Reduce the dose of venetoclax by at least 50%; resume the previous dose of venetoclax 2-3 days after discontinuation of the P-gp inhibitor
P-gp substrates (dabigatran, digoxin, methotrexate)	Avoid concomitant use; if concomitant use cannot be avoided, separate the dosing of the P-gp substrate by at least 6 hours before venetoclax administration
Warfarin	Monitor INR more frequently when used with venetoclax

Additional Venetoclax Resource: Preventing TLS on Venetoclax
<https://www.venclxthcp.com/content/dam/gene/venclxthcp/cll/pdfs/VENCLEXTA-Treatment-Guide.pdf>

Additional CLL Resources



CLL-Specific Patient Support Groups

<https://cllsociety.org/programs-and-support/ctl-specific-patient-support-groups/>



The CLL Guide: Information for Patients and Caregivers

https://www.lls.org/sites/default/files/2023-06/PS48_CLL_Guide_2023.pdf



Steps To Success: Implementing Oral Oncolytics

https://www.accc-cancer.org/docs/projects/pdf/implementing-oral-oncolytics-final.pdf?sfvrsn=274a112_0

Citations

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