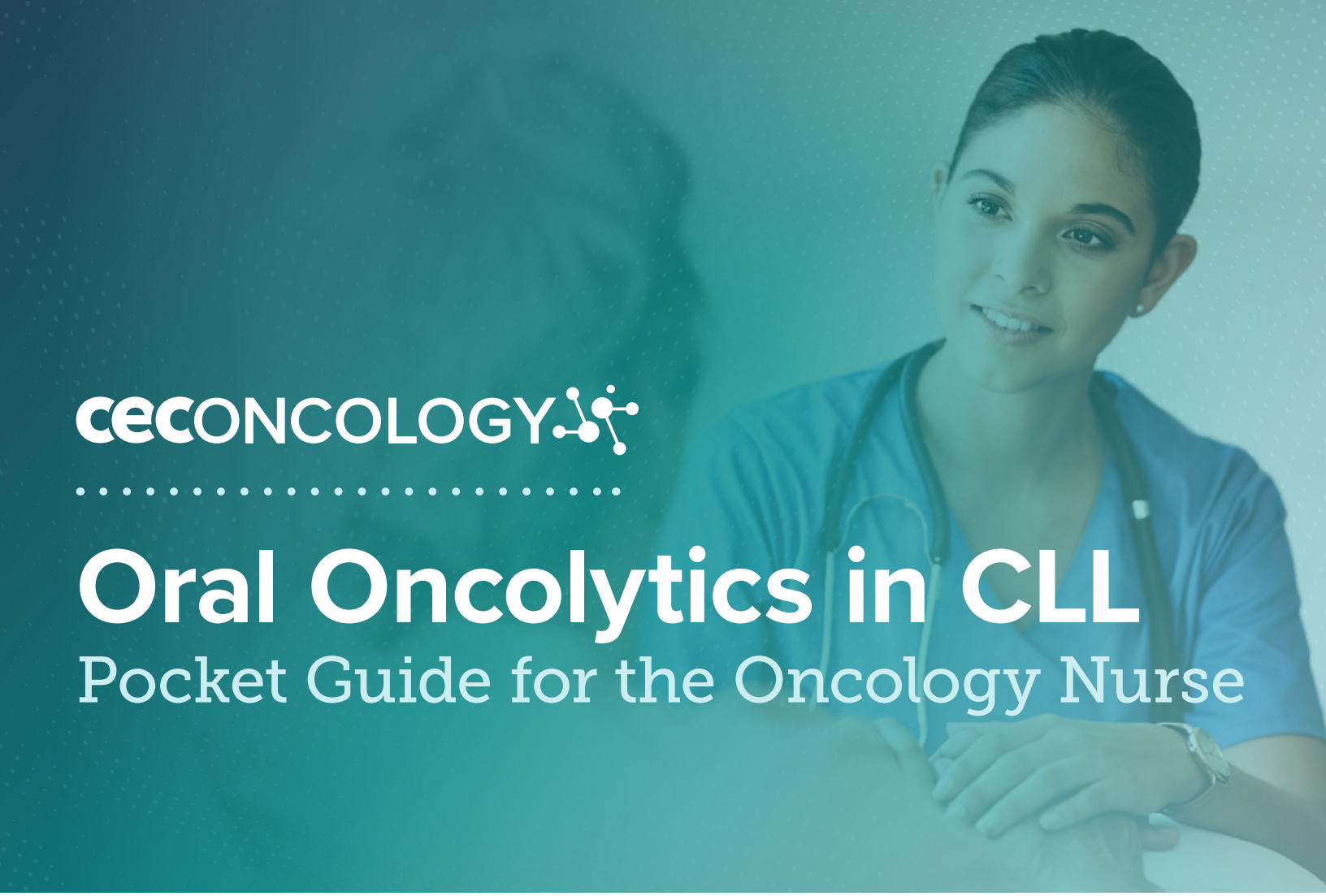

CECONCOLOGY

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	• 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	• 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	• 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(cll)/accc_practiceguide_cll_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	• Dose modifications not required for grade 1/2 events **Suggest:** • 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)	• Evaluate stool for common pathogens • If abdominal discomfort is present, consider CT or X-ray to rule out colitis or overflow diarrhea
Fatigue	• Dose modification typically not needed **Suggest:** • Energy prioritization • Improving sleep quality • Physical activity (e.g., walking, yoga) • Limit stress • Cognitive behavioral therapy • Attention restoring therapy (e.g., games, music)	• If fatigue occurs later in treatment, patient should be evaluated for other potential causes
Headache	• 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 **Suggest:** • Acetaminophen or caffeine • Avoid NSAIDs	• Unresolved and severe headaches should be evaluated at emergency department
Musculoskeletal events	• Dose modifications typically not needed for mild cases; may be required for severe and persistent cases **Suggest:** • Mild stretching/strengthening routines • Hot/cold compresses • Acetaminophen	• Evaluate for electrolyte deficiencies and supplement with sodium, potassium, magnesium as needed
Infection	**Preventative measures:** • Give appropriate non-live vaccines and prophylactic therapies prior to therapy initiation, in consultation with physician **Suggest:** • Drink plenty of fluids • Adhere to prescribed medications • Contact clinic if symptoms worsen/do not improve	• Educate patients to notify clinic upon signs of infection

Adverse Event	Management/Prevention	Monitor/Educate
Hematological toxicity	• 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	• Monitor blood counts monthly until blood is stable and every 3 months thereafter
Rash	• 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 Suggestions for pruritis: • Cold compresses • Lukewarm bath with colloidal oatmeal	• Monitor for signs of severe rash: ◦ Fever ◦ Facial swelling ◦ Cutaneous detachment with blisters or mucosal erosions ◦ Signs of Stevens-Johnson syndrome ◦ Exfoliative rash ◦ Pustules ◦ Lymphadenopathy ◦ Lab abnormalities
Hypertension	• Effectively managed with antihypertensive agents	• 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	• Assess individual stroke/bleeding risk and consult with specialists as needed • BTK inhibitor dose should be interrupted for grade ≥3 events	• Inquire and educate patients on signs of arrhythmias: ◦ Heart racing, fluttering, pounding ◦ Shortness of breath ◦ Easily tired ◦ Faint, dizzy • Teach patients how to take pulse at home
Minor Bleeding (bruising, petechiae)	• Can resolve spontaneously without intervention • Suggest applying ice and moisturizers to affected areas	• Reassure patients that mild bleeding is not a predictor of major hemorrhage
Major Bleeding	Preventative measures: • 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	• Educate on signs of hemorrhage: ◦ 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.jaccao.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	*Mild/moderate:* no dose adjustment needed	*Mild/moderate:* no dose adjustment needed	—	*Severe:* Reduce dose
Hepatic Impairment	*Mild/moderate:* reduce dose *Severe:* avoid	*Severe:* avoid	*Severe:* 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 antinausea agents and non-drug measures to mitigate nausea
Neutropenia (and other cytopenias)	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 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
Tumor lysis syndrome	Prevent TLS: assess risk, institute appropriate prophylaxis, use 5-week dose ramp up Treat TLS: hold treatment, depending on severity and time of resolution, either continue the same dose or reduce dose once resuming venetoclax
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: • 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.venclextahcp.com/content/dam/gene/venclextahcp/cll/pdfs/VENCLEXTA-Treatment-Guide.pdf

Additional CLL Resources

CLL-Specific Patient Support Groups
https://cllsociety.org/programs-and-support/cll-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

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