

BC Cancer Protocol Summary for Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma using Acalabrutinib

Protocol Code

LYACAL

Tumour Group

Lymphoma

Contact Physician

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ELIGIBILITY:

Patients must have:

- Relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma,
- Received at least one prior systemic therapy, and
- Symptomatic disease requiring therapy

Patients should have:

- Adequate renal and hepatic function

Notes:

- Patients are eligible to receive one of: idelalisib with ritUXimab (LYIDELAR) OR iBRUtinib (LYIBRU) OR acalabrutinib (LYACAL) OR zanubrutinib (LYCLLZANU) in the relapsed/refractory setting. LYIDELAR is not funded as a sequential treatment option for patients who have progressed on iBRUtinib, acalabrutinib, or zanubrutinib, except on a case by case basis as a bridge to allogeneic transplant or other cellular therapy.
- If iBRUtinib (LYIBRU) or zanubrutinib (LYCLLZANU) is discontinued for any reason other than progression, LYACAL may be considered for subsequent treatment regardless of time since discontinuation. **Switching after progression is not funded.**

EXCLUSION:

Patients must not have:

- Previous progression on **BTK inhibitor**

CAUTIONS:

- **Patients at high risk for bleeding complications,**
- **Cardiac risk factors including history of hypertension, diabetes mellitus, cardiac arrhythmia, cardiac failure**

TESTS:

- Baseline (required before first treatment): CBC & Diff, platelets, creatinine, **total** bilirubin, ALT
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with cycle 2): HBsAg, **HBsAb**, HBcoreAb
- **Baseline if clinically indicated: PT, PTT, INR, ECG**
- Each time seen by physician: CBC & Diff, platelets, **total** bilirubin, ALT, **blood pressure**
- If clinically indicated: creatinine, PT, PTT, INR, ECG

PREMEDICATIONS:

- None

SUPPORTIVE MEDICATIONS:

- **Very high risk of hepatitis B reactivation.** If HBsAg or HBcoreAb positive, start [hepatitis B prophylaxis as per current guidelines](#).

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
acalabrutinib	100 mg twice daily	PO

Continuously until disease progression or unacceptable toxicity

DOSE MODIFICATIONS:

Toxicity occurrence	Dose modification after recovery
1 st	Restart at 100 mg twice daily
2 nd	Restart at 100 mg twice daily
3 rd	Restart at 100 mg once daily
4 th	Discontinue

1. Myelosuppression:

Toxicity	Acalabrutinib dose
*Grade 4 neutropenia (ANC less than $0.5 \times 10^9/L$) lasting longer than 7 days	Hold until ANC greater than or equal to $1.5 \times 10^9/L$ or baseline level, then restart at dose indicated above
*Grade 4 thrombocytopenia (platelets less than $25 \times 10^9/L$) or Grade 3 (platelets less than $50 \times 10^9/L$) with significant bleeding	Hold until platelets greater than or equal to $75 \times 10^9/L$ or baseline level, then restart at dose indicated above
Non-hematological toxicity greater than or equal to Grade 3	Hold until improvement to grade 1 toxicity or baseline, restart at dose indicated above

*No dose reduction if decreased counts are due to disease

2. Hepatic Impairment:

- No adjustment recommended in mild or moderate hepatic impairment. Avoid use in patients with severe hepatic impairment (Child-Pugh C or bilirubin >3 x ULN regardless of AST/ALT).

3. Renal impairment:

- No adjustment recommended in mild or moderate renal impairment; no information found for severe renal impairment

PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Hemorrhagic events:** Minor hemorrhagic events including bruising, epistaxis and petechiae occur in approximately half of the patients treated with acalabrutinib. Major hemorrhagic events (serious or Grade 3 or higher bleeding) occur in 3% of patients. Use with caution in patients taking anticoagulants or medications that inhibit platelet function. Hold treatment for 3-7 days pre- and post-surgery; reinstate post-surgery based on the risk of bleeding.
3. **CYP3A4 substrate:** Concomitant therapy with strong or moderate CYP 3A inhibitors may increase acalabrutinib exposure; avoid if possible. Concomitant use of acalabrutinib with strong CYP 3A inducer may decrease acalabrutinib exposure; avoid if possible. If concomitant use cannot be avoided, dose modification may be required.
4. **Hypertension** has been reported in patients taking Bruton's tyrosine kinase (BTK) inhibitors. Blood pressure should be checked at each visit and treated if it develops. Hypertension increases the risk of cardiac complications with BTK inhibitor treatment.
5. **Atrial fibrillation/flutter:** Risk may be increased in patients with cardiac risk factors, preexisting cardiovascular disease, hypertension, previous history of atrial fibrillation, and infection/pneumonia. ECG is recommended in patients who develop arrhythmic symptoms including palpitations and lightheadedness or a new onset of dyspnea.
6. **Lymphocytosis:** Has been reported, usually occurring within the first few weeks of therapy and resolving by 8-23 weeks. Possibly related to the inhibition of BTK-mediated cellular homing and adhesion.
7. **Hepatitis B Reactivation:** See [SCHBV](#) protocol for more details.

Call Dr. Alina Gerrie, Dr. Laurie Sehn or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Ghia P, Pluta A, Wach M, et al. ASCEND: Phase III, randomized trial of acalabrutinib versus idelalisib plus rituximab or bendamustine plus rituximab in relapsed or refractory chronic lymphocytic leukemia. *J Clin Oncol* 2020;38:2849-61.
2. AstraZeneca Canada Inc. CALQUENCE® product monograph. Mississauga, Ontario; 28 November 2019.