

BC Cancer Protocol Summary for Treatment of Previously Untreated Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma Using Acalabrutinib and Venetoclax

Protocol Code

LYCLLACALV

Tumour Group

Lymphoma

Contact Physicians

LY Systemic Therapy

ELIGIBILITY:

Patients must have:

- Chronic lymphocytic leukemia or small lymphocytic lymphoma with no prior therapy,
- Symptomatic disease requiring therapy

Patients should have:

- Good performance status
- Adequate hematologic, hepatic and renal function

Notes:

- Retreatment is allowed at time of disease progression if the progression-free interval was greater than 1 year following completion of therapy
- Patients are eligible to receive either iBRUtinib with venetoclax OR acalabrutinib with venetoclax, but not sequential use of these regimens.

EXCLUSION:

Patients must not have:

- Richter's syndrome,
- CNS involvement

CAUTIONS:

- Cardiac risk factors including history of hypertension, diabetes mellitus, cardiac arrhythmia, cardiac failure,
- Patients at high risk for bleeding complications,
- Platelet count less than 30×10^9 /L unless disease-related,
- Absolute neutrophil count (ANC) less than 1.0×10^9 /L unless disease-related. Consider giving filgrastim (G-CSF).
- Total bilirubin greater than 3 x upper limit of normal (ULN),
- Active and uncontrolled autoimmune cytopenias

TESTS:

- Baseline: CBC & Diff, creatinine, total bilirubin, ALT, PTT, INR
- 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: ECG
- Prior to Cycle 2: CBC & Diff, total bilirubin, ALT, blood pressure
- Prior to Cycle 3: CBC & Diff, total bilirubin, ALT, creatinine, potassium, calcium, magnesium, phosphate, uric acid, urea, LDH, albumin, blood pressure
- Prior to each dose increment during venetoclax ramp-up phase (Cycle 3, Weeks 1 to 5): CBC & Diff, potassium, calcium, phosphate, uric acid, creatinine, LDH, albumin
- Tumour lysis syndrome (TLS) monitoring during venetoclax ramp-up phase (Cycle 3, Weeks 1 to 5): potassium, calcium, phosphate, uric acid, creatinine, LDH, albumin based on tumour burden/TLS risk (See Table 1 below). TLS labs must be drawn STAT at a laboratory capable of rapid turnaround time (e.g. BC Cancer or hospital laboratory)
- Cycle 4 onwards, prior to each cycle: CBC & Diff, creatinine, total bilirubin, ALT, blood pressure
- If clinically indicated: creatinine, PTT, INR, ECG, HBV viral load (see protocol SCHBV)

PREMEDICATIONS:

- Antiemetic protocol for low emetogenic chemotherapy (see SCNAUSEA)

SUPPORTIVE MEDICATIONS:

- Very high risk of hepatitis B reactivation. If HBsAg or HBcoreAb positive, start hepatitis B prophylaxis as per SCHBV.
- Consider antimicrobial prophylaxis for patients at increased risk of opportunistic infections:
 - valACYclovir 500 mg PO BID
 - cotrimoxazole 1 DS tab PO 3 times each week (Monday, Wednesday and Friday)
- Tumour lysis syndrome (TLS), including fatal events and renal failure requiring dialysis, has been reported in patients with medium or high tumour burden, but the incidence is reduced when the venetoclax dose is gradually increased. It is mandatory that electrolytes are monitored as recommended as TLS requires prompt management (see Appendix I). TLS can occur as early as 6-8 hours after the first dose and after each dose increase.

Table 1: Recommended TLS monitoring and prophylaxis during venetoclax ramp-up phase, based on tumour burden:

Tumour Burden		Prophylaxis		Blood Chemistry Monitoring
		Hydration	Anti-hyperuricemic	Setting and Frequency of Assessments
Low	All LN* less than 5 cm AND ALC** less than $25 \times 10^9/L$	Oral: 1.5 to 2 L daily (8 glasses) Start 48 h prior to 1 st dose, and continue throughout the first 5 weeks of therapy. Consider additional IV fluids as needed	Allopurinol 300 mg PO daily until dose escalation is complete and at physician discretion. Start 72 h prior to 1 st dose	Outpatient: - Pre-dose at each dose increment 6 hours and 24 hours post first dose of 20 mg and 50 mg
	Any LN* 5 cm to less than 10 cm OR ALC** greater than or equal to $25 \times 10^9/L$ AND any LN less than 5 cm			Outpatient: - Pre-dose at each dose increment 6 hours and 24 hours post first dose of 20 mg and 50 mg Consider hospitalization, if CrCl [±] 50-80 mL/min or if patient unable to drink 2L of oral fluids at first dose of 20 mg and 50 mg (see High Risk category)
High	Any LN* greater than or equal to 10 cm OR ALC** greater than or equal to $25 \times 10^9/L$ AND any LN greater than or equal to 5 cm OR CrCl [±] 30-50 mL/min	Oral: 1.5 to 2 L daily (8 glasses) Start 48 h prior to 1 st dose, and continue throughout the first 5 weeks of therapy and IV NS (150 to 200 mL/h, as tolerated)	Allopurinol 300 mg PO daily until dose escalation complete and at physician discretion. Start 72 h prior to 1 st dose Consider rasburicase 3 mg IV x 1, may repeat q24h PRN For patients on rasburicase, blood sample for uric acid must be placed on ice while awaiting assay	Inpatient: <u>First dose of 20 mg and 50 mg</u> - Pre-dose, 4h, 8h, 12h and 24h post first dose of 20 mg and 50 mg Outpatient: <u>Subsequent ramp-up doses</u> - Pre-dose, 6h, and 24h post dose

*LN= lymph node

**ALC= absolute lymphocyte count

***Cockcroft-Gault Equation:**

Estimated creatinine clearance:
CrCl (mL/min)

$N = 1.23 \text{ male or } 1.04 \text{ female}$

$= \frac{N (140 - \text{age}) \text{ wt (kg)}}{\text{serum creatinine (micromol/L)}}$

TREATMENT:

Cycles 1 to 2:

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

- Acalabrutinib should start on a Thursday for Cycles 1 to 2 to match the Thursday start date of venetoclax and for correct timing of bloodwork.
- Repeat every 28 days for 2 cycles, then proceed to Cycle 3

Cycle 3:

Due to the risk of TLS, venetoclax dosing must be initiated carefully according to a 5-week ramp-up schedule up to the recommended dose of 400 mg PO once daily. Patients who show signs of TLS should have their dose held or if appropriate, kept the same for more than one week, until it is safe to escalate dose.

For patients considered low or medium risk for TLS after completion of Cycle 2, the start date must be on a Thursday, and patients must pick up their venetoclax supply before Thursday (unless an alternate date is agreed upon by provider and pharmacy/team for monitoring venetoclax ramp up labs).

For patients considered at high risk for TLS after completion of Cycle 2, start date is not restricted to a Thursday as treatment will be delivered in an inpatient setting.

Week	acalabrutinib PO	venetoclax [±] PO	Cycle length
1	100 mg twice daily	20 mg once daily x 7 days	35 days (5 weeks)
2		50 mg once daily x 7 days	
3		100 mg once daily x 7 days	
4		200 mg once daily x 7 days	
5		400 mg once daily x 7 days	

[±] Lab results must be reviewed by pharmacist or prescriber, at the time points indicated below, before next dose can be authorized in person or by phone (baseline labs reviewed by prescriber; ramp-up and TLS labs reviewed by pharmacist):

- Baseline: within 72 hours of Cycle 3 Week 1 Day 1
- Before each dose increase at 50 mg, 100 mg, 200 mg and 400 mg (Weeks 2 to 5)
- The day after the first 20 mg dose (24 h) and 50 mg dose (24 h) increase (Weeks 1 and 2)
- For high-risk patients only, 24 hours after each additional dose increase (100 mg, 200 mg, and 400 mg, at Weeks 3, 4 and 5)

For **low or medium risk TLS** patients, see **Appendix II, Table 1** for frequency of laboratory monitoring by pharmacist and patient follow-up schedule.

- If baseline labs adequate to proceed, patient to take first dose at **6 am on a Thursday in order for labs and RN phone call to not fall on a statutory holiday or weekend.**
- Outpatient STAT **TLS labs** at **6 h** (12 noon) and at approximately **24 h** (8 am the second day)
- Results must be reviewed immediately by the pharmacist to assess for signs of TLS and determine whether prompt management or admission is required
- A pharmacist will contact the patient **after the 24h lab results are reviewed** for instructions on whether to proceed with the next dose

For **high-risk TLS** patients, see **Appendix II, Table 2** for frequency of laboratory monitoring by pharmacist and patient follow-up schedule.

- Treatment is not restricted to a Thursday start date as treatment will be delivered in an inpatient setting. When patients are discharged home, supply enough tablets so that the start day of a new dose occurs on a Thursday, to ensure that labs will be monitored by pharmacy.

Cycle 3 to 14:

Drug	Dose	BC Cancer Administration Guideline
acalabrutinib	100 mg twice daily	PO
venetoclax	400 mg once daily	PO

- Repeat every 28 days for 12 cycles (i.e. Cycles 3 to 14)

DOSE MODIFICATIONS:

Venetoclax Dose Reductions for Toxicity:

Venetoclax Dose at Interruption	Venetoclax Recommended Restarting Dose
20 mg once daily	10 mg once daily
50 mg once daily	20 mg once daily
100 mg once daily	50 mg once daily
200 mg once daily	100 mg once daily
300 mg once daily	200 mg once daily
400 mg once daily	300 mg once daily

1. Tumour Lysis Syndrome (TLS)

- Changes in blood chemistries that require prompt management can occur as early as 6-8 hours after the first dose of venetoclax and after each dose increase
- Reduced renal function ($\text{CrCl} \leq 80 \text{ mL/min}$) increases the risk for TLS
- Electrolytes must be corrected to within normal limits prior to proceeding with next dose of venetoclax or any dose increases during the 5-week ramp-up phase
- See **Appendix I** for TLS management strategies

Event	Action
Abnormal blood chemistry outside normal parameters for any of the following: • Elevated potassium • Low calcium (corrected for albumin*) • Elevated phosphate • Elevated uric acid • Serum creatinine increase of greater than 20 micromol/L from baseline	Hold venetoclax and acalabrutinib. Correct abnormalities. If resolved within 24-48h, resume treatment at same dose.
Abnormal blood chemistry lasting more than 48 hours OR Clinical TLS (presence of laboratory TLS [†] plus any of the following): • cardiac arrhythmia, symptomatic hypocalcemia, seizures, increased creatinine level of 26.5 micromol/L or single value greater than 1.5 times ULN	Hold venetoclax and acalabrutinib until resolved; then resume treatment. Venetoclax should be resumed at a reduced dose (see Dose Modification table below). When resuming treatment, monitor for TLS and provide adequate prophylaxis. Continue the venetoclax reduced dose for 1 week before continuing with dose escalation.

* Corrected calcium (mmol/L) = total calcium (mmol/L) + (0.02 x [40 – albumin in g/L]).

Note: Use this formula to correct for calcium only when albumin is low.

[†] **Laboratory TLS** (2 or more metabolic abnormalities during the same 24-hour period):

- Uric acid greater than or equal to 476 micromol/L
- Phosphate greater than or equal to 1.45 mmol/L
- Potassium greater than or equal to 6 mmol/L
- Corrected calcium less than or equal to 1.75 mmol/L

2. Hematological Toxicity:

Neutropenia:

ANC (x 10 ⁹ /L)	Occurrence	Doses
Greater than or equal to 1.0	--	100%
Less than 1.0	1 st	Hold one or both drugs and consider filgrastim (G-CSF) if clinically indicated. Once ANC recovers to greater than or equal to 1.5 x 10 ⁹ /L or baseline, restart treatment with one or both drugs at the same dose.
	2 nd	Hold one or both drugs and consider filgrastim (G-CSF) if clinically indicated. Once ANC recovers to greater than or equal to 1.5 x 10 ⁹ /L or baseline, resume treatment as follows: ▪ acalabrutinib: restart at the same dose ▪ venetoclax: restart at next lower dose level
	Subsequent	Hold one or both drugs until ANC recovers to greater than or equal to 1.5 x 10 ⁹ /L or baseline. Consider filgrastim (G-CSF) if clinically indicated. Further management should be guided by the clinical judgement of the treating healthcare provider, based on an individual patient benefit-risk assessment.

Thrombocytopenia:

Platelets (x 10 ⁹ /L)	Occurrence	Doses
Greater than or equal to 50	--	100%
Less than 50 and/or bleeding	1 st	Hold one or both drugs. Once bleeding resolves and platelets recover to greater than or equal to 75 x 10 ⁹ /L or baseline without transfusion support for 5 consecutive days, restart one or both drugs at the same dose.
	2 nd	Hold both drugs until bleeding resolves and platelets recover to greater than or equal to 75 x 10 ⁹ /L or baseline without transfusion support for 5 consecutive days, then: ▪ acalabrutinib: restart at the same dose, and/or ▪ venetoclax: restart at next lower dose level
	Subsequent	Hold both drugs until bleeding resolves and platelets recover to greater than or equal to 75 x 10 ⁹ /L or baseline without transfusion support for 5 consecutive days, then: ▪ acalabrutinib: restart at 100 mg once daily, and/or ▪ venetoclax: restart at next lower dose level For recurrent severe thrombocytopenia despite dose reduction and/or symptomatic bleeding, management should be guided by the clinical judgement of the treating healthcare provider, based on an individual patient benefit-risk assessment.

2. Other Non-Hematological Toxicities:

Severity	Occurrence	Doses
Grade 3	1 st	Hold one or both drugs until toxicity resolves to less than or equal to Grade 1* then restart treatment with one or both drugs at same dose.
	2 nd	Hold one or both drugs until toxicity resolves to less than or equal to Grade 1*. Further management should be guided by the clinical judgement of the treating healthcare provider, based on an individual patient benefit-risk assessment.
Grade 4	1 st	Hold one or both drugs until toxicity resolves to less than or equal to Grade 1*, then: ▪ acalabrutinib: restart at 100 mg once daily, and/or ▪ venetoclax: restart at next lower dose level
	2 nd	Hold one or both drugs until toxicity resolves to less than or equal to Grade 1*. Further management should be guided by the clinical judgement of the treating healthcare provider, based on an individual patient benefit-risk assessment.

*Certain treatment-emergent non-hematologic adverse events may be managed and become clinically stable following medical intervention but may not improve to less than or equal to Grade 1. In such cases, if a patient is clinically stable, resumption of treatment should be guided by the clinical judgement of the treating healthcare provider.

3. Hepatic Impairment:

acalabrutinib: No dose adjustment is recommended in patients with mild or moderate hepatic impairment. Avoid administration of acalabrutinib in patients with severe hepatic impairment (Child-Pugh C or total bilirubin greater than 3 times upper limit of normal).

Venetoclax: No dose adjustment is recommended in patients with mild or moderate hepatic impairment; however, patients should be monitored more closely for signs of toxicity at initiation and during the dose ramp-up phase. In patients with severe hepatic impairment, a 50% dose reduction is recommended during initiation and ramp-up phase, and at steady state.

PRECAUTIONS:

1. **Tumour lysis syndrome (TLS):** TLS has been reported with venetoclax and the risk is greatest during the dose ramp-up phase. Patients should be stratified as low, medium, or high risk based on their lymph node size (LN), absolute lymphocyte count (ALC), and comorbidities including renal dysfunction. All patients require prophylaxis for TLS using hydration beginning 48 hours and anti-hyperuricemic agents beginning 72 hours prior to initiation of therapy. Hospitalization is recommended for high-risk patients, medium risk patients with abnormal CrCl and any risk patients with CrCl $\leq$ 50 mL/min. Hospitalization may be considered for those with additional risk factors for TLS (CrCl $\leq$ 80 mL/min, unable to drink 1.5-2 L per day, unsuitable for outpatient treatment and lab monitoring, or at physician discretion). It is mandatory that electrolytes are monitored as TLS requires prompt management (see [Appendix I](#) for management recommendations). **For outpatients, TLS labs must be reviewed at 6 hours and 24 hours after the first 2 dose escalations (20 mg and 50 mg) for low or medium risk patients and after all dose escalations for high-risk patients (100 mg, 200 mg, and 400 mg). Patients must be instructed to wait to take the second dose until approval is given (by phone). See Appendix II, Tables 1 and 2 for frequency of laboratory monitoring and patient follow-up schedule.**
2. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
3. **Hepatitis B Reactivation:** See [SCHBV](#) protocol for more details.
4. **Drug interactions:** Venetoclax is a major CYP3A4 substrate and a substrate of P-glycoprotein. Concurrent administration of drugs which are strong CYP 3A4 inhibitors is contraindicated at initiation and during the dose ramp-up phase, due to increased serum concentration of venetoclax and potential increased risk of TLS. acalabrutinib is a CYP3A substrate and 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. See BC Cancer Cancer Drug Manual for more information.
5. **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; reinstitute post-surgery based on the risk of bleeding.
6. **Pregnancy:** Venetoclax is not recommended for use in pregnancy. Fetotoxicity is likely. Women of childbearing potential should undergo pregnancy testing before initiating

treatment and use adequate contraception during treatment and for at least 30 days after the last dose.

7. **Renal impairment:** While no dose adjustments are required for patients with creatinine clearance of 30 to 60 mL/min, renal impairment increases TLS risk. Monitor patients closely.
8. **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.
9. **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.
10. **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.

Call the LY Systemic Therapy physician at your regional cancer centre or LY Systemic Therapy Chair with any problems or questions regarding this treatment program.

REFERENCES:

1. Brown JR, Seymour JF, Jurczak W et al. Fixed-Duration Acalabrutinib Combinations in Untreated Chronic Lymphocytic Leukemia. N Engl J Med 2025 Feb 20; 392(8): 748-7623.
2. Acalabrutinib (Calquence) Canada's Drug Agency (CDA-AMC) Reimbursement Recommendation. Canadian Journal of Health Technologies Jan 2026; 6(1): 1-24.

APPENDIX I:

Manage Tumour Lysis Syndrome (TLS) according to institution guidelines. If no local guidelines, may use the following. Consider hospital admission, if needed for cardiac monitoring or IV medications/hydration.

Suggested Guide for Management of Tumour Lysis Syndrome (TLS) (adapted from MD Anderson TLS guidelines¹⁰)

Electrolyte Abnormality	Management Recommendations
Hyperkalemia	
Mild (greater than upper limit of normal to less than 6 mmol/L)	• Restrict potassium intake (avoid IV and PO potassium, limit dietary intake) • Sodium polystyrene (Kayexalate®) ○ 15-30 grams PO ○ Repeat as needed depending on follow-up potassium levels • Consider ECG and cardiac rhythm monitoring at physician discretion
Moderate (6-7 mmol/L) and asymptomatic	• Restrict potassium intake (avoid IV and PO potassium, limit dietary intake) • ECG and cardiac rhythm monitoring • Sodium polystyrene (Kayexalate®) ○ 15-30 grams PO ○ Repeat every 4 to 6 hours depending on follow-up potassium levels
Severe (greater than 7 mmol/L and/or symptomatic)	Same as moderate plan plus: • Concurrent ECG changes: calcium gluconate 1 g via slow IV infusion; may be repeated after 5-10 minutes if ECG changes persist • To temporarily shift potassium intracellularly: • IV insulin and dextrose ➢ Give 10 units of regular insulin in 500 mL of D10W infused IV over 60 minutes ➢ Monitor blood glucose closely • Sodium bicarbonate ➢ Give 50 mEq via slow IV infusion ➢ Can be used if patient is acidemic; however sodium bicarbonate and calcium should not be administered through the same lumen • Salbutamol ➢ Give 10-20 mg in 4 mL saline via nebulizer over 20 minutes or 10-20 puffs via inhaler over 10-20 minutes ➢ Avoid in patients with acute coronary disease

Electrolyte Abnormality	Management Recommendations
Hyperphosphatemia	
Moderate (greater than or equal to 1.94 mmol/L)	• Restrict phosphorus intake (avoid IV and PO phosphorus; limit dietary sources) • Administer phosphate binder: ○ Sevelamer (Renagel®, Renvela®) 800-1600 mg PO three times a day with meals ○ Lanthanum carbonate (Fosrenol®) 500-1000 mg PO three times a day with meals ○ Aluminum hydroxide tablet 300 mg PO three times a day with meals, may increase dose to 600 mg PO three times a day (avoid in patients with renal dysfunction) ○ Aluminum hydroxide 64 mg/mL suspension 15 mL PO three times a day with meals, may increase dose to 30 mL four times a day based on phosphate level (avoid in patients with renal dysfunction)
Severe	Dialysis may be needed in severe cases
Hypocalcemia (calcium less than or equal to 1.75 mmol/L or ionized calcium less than or equal to 0.8 mmol/L)	
Asymptomatic	• No therapy • To avoid calcium phosphate precipitation, asymptomatic patients with acute hypocalcemia and hyperphosphatemia should not be given calcium repletion until phosphorous level has normalized
Symptomatic	Calcium gluconate 1 g via slow IV infusion with ECG monitoring
Uremia (renal dysfunction)	
	• Fluid and electrolyte management • Uric acid and phosphate management • Adjust doses for renally excreted medications • Dialysis

APPENDIX II.

Table 1. Monitoring for Low or Medium Risk TLS Patients. Pharmacist reviews labs in Cycle 4 and contacts patient to take venetoclax dose.

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Week 1 20 mg ▪ baseline lab	6 AM dose ▪ lab at 12 noon ▪ review bloodwork and notify MD if abnormal	▪ lab at 8 am ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 1 day 2 dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose ▪ RN call to remind patient to go for lab the next day (pre ramp-up lab)	8 AM dose ▪ lab before 12 noon ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 2 day 1 dose (50 mg) the following day
Week 2 50 mg	6 AM dose ▪ lab at 12 noon ▪ review bloodwork and notify MD if abnormal	▪ lab at 8 am ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 2 day 2 dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose ▪ RN call to remind patient to go for lab the next day (pre ramp-up lab)	8 AM dose ▪ lab before 12 noon ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 3 day 1 dose (100 mg) the following day
Week 3 100 mg	8 AM dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose ▪ RN call to remind patient to go for lab the next day (pre ramp-up lab)	8 AM dose ▪ lab before 12 noon ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 4 day 1 dose (200 mg) the following day
Week 4 200 mg	8 AM dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose ▪ RN call to remind patient to go for lab the next day (pre ramp-up lab)	8 AM dose ▪ lab before 12 noon ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 5 day 1 dose (400 mg) the following day
Week 5 onwards 400 mg	8 AM dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose

Table 2. Monitoring for High Risk TLS patients. Unless otherwise specified, Cycle 3 lab review is done by pharmacist and pharmacist contacts patient to take venetoclax dose.

	<u>Day 1</u>	<u>Day 2</u>	<u>Day 3</u>	<u>Day 4</u>	<u>Day 5</u>	<u>Day 6</u>	<u>Day 7</u>
Week 1 20 mg ▪ baseline lab	Inpatient ▪ labs 4h, 8h, 12h and 24 h post dose (monitoring done by ward)	Inpatient for 2 nd dose ▪ ward team to review 24h lab post 20 mg dose and notify MD if abnormal. If normal, give patient week 1 day 2 dose and may be discharged home or at MD discretion	8 AM dose	8 AM dose	8 AM dose	8 AM dose ▪ RN call to remind patient to go for lab the next day (pre ramp-up lab)	8 AM dose ▪ lab before 12 noon ▪ review bloodwork and notify MD if abnormal.
Week 2 50 mg	Inpatient ▪ labs 4h, 8h, 12h and 24 h post dose (monitoring done by ward)	Inpatient for 2 nd dose ▪ ward team to review 24h lab post 50 mg dose and notify MD if abnormal. If normal, give patient week 2 day 2 dose and may be discharged home or at MD discretion	8 AM dose	8 AM dose	8 AM dose	8 AM dose ▪ RN call to remind patient to go for lab the next day (pre ramp-up lab)	8 AM dose ▪ lab before 12 noon ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 3 day 1 dose (100 mg) the following day
Week 3 100 mg	6 AM dose ▪ lab at 12 noon ▪ review bloodwork and notify MD if abnormal	▪ lab at 8am ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 3 day 2 dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose ▪ RN call to remind patient to go for lab the next day (pre ramp-up lab)	8 AM dose ▪ lab before 12 noon ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 4 day 1 dose (200 mg) the following day
Week 4 200 mg	6 AM dose ▪ lab at 12 noon ▪ review bloodwork and notify MD if abnormal	▪ lab at 8am ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 4 day 2 dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose ▪ RN call to remind patient to go for lab the next day (pre ramp-up lab)	8 AM dose ▪ lab before 12 noon ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 5 day 1 dose (400 mg) the following day
Week 5 onwards 400 mg	6 AM dose ▪ lab at 12 noon ▪ review bloodwork and notify MD if abnormal	▪ lab at 8am ▪ review bloodwork and notify MD if abnormal. If normal, contact patient to take week 5 day 2 dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose	8 AM dose