## **BC Cancer Protocol Summary for Treatment of Relapsed/Refractory** Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma **Using Venetoclax**

## Protocol Code

**Tumour Group** 

Contact Physicians

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ULYVENETO

Lymphoma

## ELIGIBILITY:

Patients must have:

- Relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma with or without chromosome 17p deletion, who have progressed on or are intolerant to B-cell receptor pathway inhibitors (BTK-inhibitors, such as ibrutinib and/or PI3-kinase inhibitors, such as idelalisib).
- Symptomatic disease requiring systemic therapy, and
- A Compassionate Access Program (CAP) approval is prior to the initiation of treatment

## EXCLUSION:

Patients must not have:

- Inadequate renal function (creatinine clearance less than 30 mL/min per Cockcroft-Gault)\*
- Taken strong CYP3A4 inhibitors within 7 days prior to initiation and during dose ramp-up phase of venetoclax

\*In clinical trials, venetoclax was given to patients with a CrCl  $\geq$  50 mL/min. The Canadian product monograph decreases this threshold to  $\geq$  30 mL/min and mentions that a CrCl < 80 mL/min may be at an increased risk of tumour lysis syndrome (TLS).

## CAUTION:

- Platelet count less than 30 x 10<sup>9</sup>/L unless disease-related
- Absolute neutrophil count (ANC) less than 1.0 x 10<sup>9</sup>/L unless disease-related. Consider giving filgrastim.
- Bilirubin greater than 3 x upper limit of normal (ULN)
- Active and uncontrolled autoimmune cytopenias

## TESTS:

- **Baseline** (required, within 72 h of first treatment); CBC & Diff. potassium, calcium, magnesium, phosphate, uric acid, creatinine, urea, total bilirubin, ALT, LDH, albumin, pregnancy test prior to treatment in females of child-bearing potential
- **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
- Prior to each dose increment during ramp-up phase (weeks 1 to 5): potassium, calcium, phosphate, uric acid, creatinine, LDH, albumin
- Tumour lysis syndrome (TLS) monitoring: 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)
- Each time seen by physician post ramp-up phase (week 6 onwards): CBC & Diff, creatinine, total bilirubin, ALT
- If clinically indicated: HBV viral load, HBsAg (see protocol SCHBV)

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#### PREMEDICATIONS:

Antiemetic protocol for low emetogenic chemotherapy (see SCNAUSEA)

#### SUPPORTIVE MEDICATIONS:

Moderate risk of hepatitis B reactivation. If HBsAg, or HBcoreAb positive, follow hepatitis B prophylaxis as per SCHBV.

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 based on tumour burden:

Tumour Burden		Proj	ohylaxis	Blood chemistry monitoring	
		Hydration	Anti- hyperuricemic	Setting and Frequency of Assessments	
Low	All LN* less than 5 cm AND ALC** less than 25 x 10 <sup>9</sup> /L	Oral: 1.5 to 2 L daily (8 glasses) Start 48 h prior to 1 <sup>st</sup> dose and continue throughout the first 5 weeks of	Allopurinol 300 mg PO daily until dose escalation is complete and at physician discretion Start 72 h prior to 1 <sup>st</sup> dose	<ul> <li>Outpatient:</li> <li>Pre-dose at each dose increment</li> <li>6 h and 24h post first dose of 20 mg and 50 mg</li> </ul>	
Medium	Any LN* 5 cm to less than 10 cm <b>OR</b> ALC** greater than or equal to 25 x 10 <sup>9</sup> /L AND any LN less than 5 cm	therapyOral:1.5 to 2 L daily (8 glasses)Start 48 h prior to 1st dose, and continue throughout the first 5 weeks of therapy.Consider additional IV fluids as needed		<ul> <li>Outpatient:</li> <li>Pre-dose at each dose increment</li> <li>6h and 24h post first dose of 20 mg and 50 mg Consider hospitalization, if CrCl<sup>±</sup> 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)</li> </ul>	

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Tumour Burden		Prophylaxis		Blood chemistry	
		Hydration	Anti- hyperuricemic	Setting and Frequency of Assessments	
High	Any LN* greater than or equal to 10 cm OR ALC** greater than or equal to 25 x 10 <sup>9</sup> /L AND any LN greater than or equal to 5 cm OR CrCl <sup>±</sup> 30-50 mL/min	Oral: 1.5 to 2 L daily (8 glasses) Start 48 h prior to 1 <sup>st</sup> dose, and continue throughout the first 5 weeks of therapy and IV NS (150 to 200 mL/hr, as tolerated)	Allopurinol 300 mg PO daily until dose escalation complete and at physician discretion Start 72 h prior to 1 <sup>st</sup> 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: First dose of 20 mg and 50 mg • Pre-dose, 4h, 8h, 12h and 24h post first dose of 20 mg and 50 mg Outpatient: Subsequent ramp-up doses • Pre-dose, 6h, and 24h post dose	

\*LN= lymph node

\*\*ALC= absolute lymphocyte count

## <sup>±</sup>Cockcroft-Gault Equation:

Estimated creatinine clearance: CrCl (mL/min)

N = 1.23 male

N = 1.04 female

N (140 - age) wt (kg)

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serum creatinine (micromol/L)

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## TREATMENT:

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 dose escalate. Treatment continues until disease progression or unacceptable toxicity.

For low or medium risk TLS patients, the start date must be on a Thursday, and patients must pick up their venetoclax before Thursday.

For high risk TLS patients, start date is not restricted to a Thursday.

#### Ramp-up phase: Weeks 1-5 for low, medium, high risk TLS patients

Week	Drug	Dose	BC Cancer Administration Guideline
1		20 mg once daily	
2		50 mg once daily	
3	Venetoclax <sup>±</sup>	100 mg once daily	PO
4		200 mg once daily	
5		400 mg once daily	

#### Post ramp-up phase: Week 6 onwards for low, medium, high risk TLS patients

Week Drug		Dose	BC Cancer Administration Guideline	
6 onwards	Venetoclax	400 mg once daily	PO	

#### <sup>±</sup> Lab results must be reviewed by pharmacist or MD, at the time points indicated below, before next dose can be authorized in person or by phone (baseline labs reviewed by MD. ramp-up and TLS labs reviewed by pharmacist):

- baseline, within 72h of initiating treatment (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 (24h) and 50 mg dose (24h) increase (weeks 1 and 2)
- for high risk patients only, 24 h 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

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 A pharmacist will contact the patient after the 24h lab results are reviewed for instructions on whether to proceed with the next dose

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

• Treatment is not restricted to a Thursday start date. 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.

#### DOSE MODIFICATIONS:

Venetoclax Dose at Interruption	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 (CrCl ≤ 80 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	Hold venetoclax. Correct abnormalities.
parameters for any of the following:	
Elevated potassium	If resolved within 24-48h, resume at same
<ul> <li>Low calcium (corrected for albumin*)</li> </ul>	dose.
Elevated phosphate	
Elevated uric acid	
• Serum creatinine increase of greater than 20	
micromol/L from baseline	
Abnormal blood chemistry lasting more than	Hold until resolved; then resume at a
48 hours	reduced dose (see Dose Modification table
	above).
OR	
	Continue the reduced dose for 1 week
Clinical TLS (presence of laboratory TLS <sup>†</sup>	before continuing with dose escalation.
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	

\* Corrected calcium (mmol/L) = total calcium (mmol/L) +  $(0.02 \times [40 - \text{albumin in g/L}])$ . Note: Use this formula to correct for calcium only when albumin is low.

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<sup>†</sup>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 and Non-Hematological Toxicities

Toxicity	Venetoclax
ANC less than 1.0 x 10 <sup>9</sup> /L*	Hold until ANC greater than or equal to 1.0 x
	10 <sup>9</sup> /L, then resume at same dose
Platelets less than 30 x 10 <sup>9</sup> /L*	Hold until platelets greater than or equal to 30 x
	10 <sup>9</sup> /L, then resume at same dose
Non-hematological toxicity greater than or	Hold until improvement to grade 1 toxicity or
equal to Grade 3	baseline, then resume at same dose.

\*For 2<sup>nd</sup> and subsequent occurrences, resume treatment at a reduced dose following the above Dose Modification table.

• Consider discontinuing treatment for patients needing dose reduction to less than 100 mg once daily for more than 2 weeks.

Hepatic Impairment	Dosing recommendation
Mild to moderate (total bilirubin greater than 1.5 to less than 3 x ULN)	No dose adjustment
Severe (total bilirubin greater than 3 x ULN)	Discontinue

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## 3. Drug Interactions

Venetoclax is a major CYP3A4 substrate and a substrate of P-glycoprotein. Concurrent administration of drugs which are <u>strong CYP 3A4 inhibitors are contraindicated at</u> <u>initiation and during the dose ramp-up phase</u> due to increased serum concentration of venetoclax and potential increased risk of TLS.

**CYP3A4 inducers** may decrease serum concentration of venetoclax. **P-glycoprotein inhibitors (P-gp)** may increase serum concentration of venetoclax.

Agent Initiated	At initiation and	After dose-ramp up is completed		
Strong CYP3A4 inhibitors	Contraindicated	Reduce venetoclax dose by 75%. Resume standard venetoclax dosing 2 to 3 days after		
Moderate CYP3A4 inhibitors	Avoid if possible, but if unavoidable, reduce venetoclax dose by at least 50%. Monitor patients more closely for signs of toxicities. Resume standard venetoclax dosing 2 to 3 days after CYP3A4 inhibitor is discontinued			
Weak CYP3A4 inhibitors	No dose adjustment needed			
Strong and moderate CYP3A4 inducers	Avoid. Consider alternative treatments with less CYP3A4 induction.			
P-glycoprotein inhibitors	Avoid if possible, but if unavoidable, reduce venetoclax dose by at least 50%. Monitor patients more closely for signs of toxicities. Resume standard dosing one day after discontinuation of P-gp inhibitor. <b>Note:</b> an exception is made for <b>Azithromycin</b> , where dose adjustments of venetoclax are not required			

## **PRECAUTIONS:**

- 1. Tumour lysis syndrome (TLS): TLS has been reported 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 ≤ 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.

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- 4. **Drug interactions:** Venetoclax is a major CYP3A4 substrate and a substrate of Pglycoprotein. 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. See Drug Interactions in Dose Modification section above.
- 5. **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

# 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. Roberts et al. Targeting BCL-2 with venetoclax in relapsed chronic lymphocytic leukemia. NEJM 2016; 374(4):311-322
- 2. Jones JA et al. Venetoclax for chronic lymphocytic leukaemia progressing after ibrutinib: an interim analysis of a multicentre, open-label, phase 2 trial. Lancet Oncol 2018; 19(1):65-75. doi: 10.1016/S1470-2045(17)30909-9
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- 10. Tumor Lysis Syndrome (TLS) in Adult Patients from MD Anderson Centre. <u>https://www.mdanderson.org/content/dam/mdanderson/documents/for-</u> <u>physicians/algorithms/clinical-management/clin-management-tumor-lysis-web-algorithm.pdf</u>
- Agarwal et al. Effect of Azithromycin on Venetoclax Pharmacokinetics in Health Volunteers: Implications for Dosing Venetoclax with P-gp Inhibitors. Advances in Therapy 2018; 35(11):2015-2023

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## **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 guidelines<sup>10</sup>)

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

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

## APPENDIX II.

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

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

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

BC Cancer Protocol Summary ULYVENETO Activated: 1 Sept 2019 Revised: 1 Jul 2024 (Tests, supportive medications and precautions updated, contact pharmacist removed) Warning: The information contained in these documents are a statement of consensus of BC Cancer professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer's terms of use available at www.bccancer.bc.ca/terms-of-use.