Systemic Therapy Education Bulletin

BC Cancer news and updates from across the province for Systemic Therapy teams

Immunotherapy

Immunotherapy is a type of biological treatment that boosts the body's immune system to fight cancer. Immunotherapy is used to:

- stop or slow the growth of cancer
- stop cancer from spreading to other parts of the body
- help the immune system work better to destroy cancer cells

Immunotherapy toxicities are different from those encountered with standard chemotherapy or targeted therapy. Management of immune-related adverse events (irAEs) necessitates prompt coordination with a medical oncologist.

The following resources are available on the BC Cancer Website under Immunotherapy:

- Immunotherapy toxicity management algorythms
- Immunotherapy nursing toolkit
- Immunotherapy patient letter
- Immunotherapy patient handout
- Immunotherapy alert card

Provincial Systemic Therapy Drug Programs Under Consideration

Adverse Events

Treatment Programs	Launch Date	Indication (Refer to protocol for more details)	Associated Adverse Events
PACLitaxel plus CARBOplatin plus Bevacizumab		Primary treatment of patients with **invasive epithelial ovarian, fallopian tube and primary peritoneal cancer** with high risk of relapse.	Possible adverse events **(of any grade)**: • Infusion-related reaction • Anemia • Neutropenia • Nausea and vomiting • Arthralgia/myalgia • Peripheral neuropathy • Alopecia • Mucositis • Hypertension • Proteinuria • Poor wound healing
Venetoclax	Possible September 2019	Treatment of patients with **relapsed or refractory chronic lymphocytic leukemia (CLL**) and **small lymphocytic lymphoma (SLL)** who have progressed on Ibrutinib and have failed other standard treatments.	Possible adverse events **(of any grade)**: • Neutropenia • Diarrhea • Nausea • Anemia • Upper respiratory tract infection • Thrombocytopenia • Fatigue Possible adverse events (**of ≥ grade 3**): • Pneumonia • Febrile neutropenia • Autoimmune hemolytic anemia • Tumour Lysis Syndrome (TLS)*

*Tumour Lysis Syndrome (TLS):

Tumour lysis syndrome is an oncological emergency caused by massive and rapid tumour cell breakdown, leading to electrolyte and metabolic abnormalities, including hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. If not treated promptly and appropriately, these electrolyte and metabolic abnormalities can progress to other clinical adverse events, including acute kidney injury, cardiac arrhythmias, seizures, and even death.

Table 1: Prophylaxis and monitoring for Tumour Lysis Syndrome (TLS)

Tumour Lysis Syndrome (TLS) Risk Factors and Venetoclax

1) Tumour Burden - Absolute lymphocyte count and size of lymph node
2) Renal Function - Creatinine clearance <80 ml/min
3) Other Co-morbidities

Low Risk	Medium Risk	High Risk
Prophylaxis and Monitoring	**Prophylaxis and Monitoring**	**Prophylaxis and Monitoring**
Hydration: - Oral 1.5-2 L daily starting 2 days prior to first dose of Venetoclax	**Hydration:** - Oral 1.5-2 L daily starting 2 days prior to first dose of Venetoclax - Consider additional IV hydration	**Hydration:** - Oral 1.5-2 L daily starting 2 days prior to first dose of Venetoclax - IV NS 150-200 mL/hr
Anti-hyperuricemic Agents: - Allopurinol 300 mg PO starting 72 hours prior to first dose of Venetoclax	**Anti-hyperuricemic Agents:** - Allopurinol 300 mg PO starting 72 hours prior to first dose of Venetoclax	**Anti-hyperuricemic Agents:** - Allopurinol 300 mg PO starting 72 hours prior to first dose of Venetoclax - Consider Rasburicase 3 mg IV
Bloodwork Monitoring:* *Venetoclax 20mg & 50mg: Outpatient* - Pre-dose, 6 hours, 24 hours *Venetoclax 100mg & onwards: Outpatient* - Pre-dose	**Bloodwork Monitoring:*** *Venetoclax 20mg & 50mg: Outpatient*** - Pre-dose, 6 hours, 24 hours *Venetoclax 100mg & onwards: Outpatient*** - Pre-dose	**Bloodwork Monitoring:*** *Venetoclax 20mg & 50mg: Inpatient* - Pre-dose, 4 hours, 8 hours, 12 hours, 24hours *Venetoclax 100mg & onwards: Outpatient* - Pre-dose, 6 hours, 24 hours

*TLS Recommended Bloodwork: sodium, potassium, phosphate, calcium, creatinine, uric acid, albumin, LDH

**Consider hospitalization if CrCl 50-80 mL/min

Table 2: Recommended management of TLS

Electrolyte Abnormality	Recommended Management
Hyperkalemia	
Moderate (6-7 mmol/L and asymptomatic)	• Restrict potassium intake • ECG • Kayexalate PO
Severe (Greater than 7 mmol/L and/or symptomatic)	Same as moderate plan plus: • Slow IV infusion of calcium gluconate with ECG monitoring • IV insulin and dextrose, IV sodium bicarbonate, salbutamol nebulizer
Hyperphosphatemia	
Moderate	• Restrict phosphorus intake • Administer phosphate binder
Severe	• Dialysis may be needed in severe cases
Hypocalcemia	
Asymptomatic	• Avoid calcium phosphate
Symptomatic	• Slow IV infusion of calcium gluconate with ECG monitoring
Uremia (Renal Dysfunction) • Fluid and electrolyte management • Uric acid and phosphate management • Adjust doses for renally excreted medications • Dialysis	

Treatment Regimens: Dosing and Administration Schedules

1. PACLitaxel plus CARBOplatin plus Bevacizumab: invasive epithelial ovarian, fallopian tube and primary peritoneal cancer

Dosing and Schedule:

Repeat treatment every 21 days

Cycle 1
IV PACLitaxel[*] 175 mg/m^2 (conservative dosing: 155 mg/ m^2 or 135 mg/ m^2) infuse over 3 hours + **IV CARBOplatin** AUC 6 (if prior pelvic radiation therapy, use AUC of 5) infuse over 30 minutes

⬇

Cycle 2-6[**]
IV PACLitaxel[*] 175 mg/ m^2 (conservative dosing: 155 mg/ m^2 or 135 mg/ m^2) infuse over 3 hours + **IV CARBOplatin** AUC 6 (if prior pelvic radiation therapy, use AUC of 5) infuse over 30 minutes + **IV Bevacizumab** 7.5 mg/kg infuse over 30 minutes[***]

⬇

Maintenance Phase[****]
IV Bevacizumab 7.5 mg/kg infuse over 30 minutes[***]

*use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter

**May extend to 9 cycles if the patient has not achieved a complete response but is continuing to respond

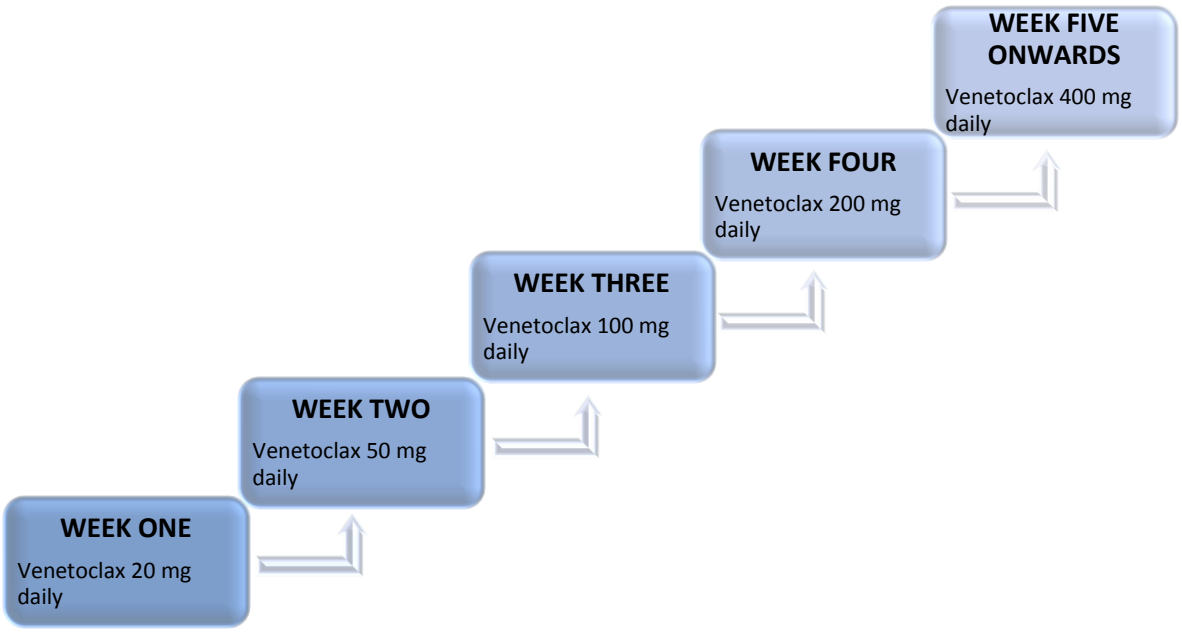
*** First Bevacizumab infusion over 60 minutes

**** Maximum of 17 Bevacizumab doses for the entire treatment

2. Venetoclax: relapsed or refractory chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL)

Dosing and Schedule:

- **Oral Venetoclax** once daily using a stepwise weekly ramp-up schedule (see below) until disease progression.
- Venetoclax must be taken approximately at the same time each day. Venetoclax should not be chewed, crushed, or broken prior to swallowing.



Patient Education:

- Venetoclax is a complex drug, requiring close monitoring. Patient education by a health care professional is essential prior to initiating treatment. Patients require comprehensive teaching around lab monitoring, pre-medication/hydration, and scheduling.

Prophylaxis, Monitoring, and Management of TLS:

- Refer to tables 1 & 2.

Lab results must be reviewed before the next dose can be authorized:

- Before the beginning of treatment (day 1)
- Weeks 1 and 2:
  - 24 hours after the first 20 mg dose and 24 hours after the 50 mg dose increase
- Weeks 2 – 5
  - Before each dose increase to 50 mg, 100 mg, 200 mg, and 400 mg
- Weeks 3 – 5
  - For high risk patients only: 24 hours after each additional dose increase (to 100 mg, 200 mg, and 400 mg).

Website Resources and Contact Information

CONTACT INFORMATION	EMAIL
To subscribe or update contact information, please contact:	
Provincial Systemic Therapy Program	ProvincialSystemicOffice@bccancer.bc.ca