

BC Cancer Protocol Summary for Treatment of Extensive Stage Small Cell Lung Cancer (SCLC) with Atezolizumab, Platinum and Etoposide

Protocol Code

LUSCATPE

Tumour Group

Lung

Contact Physician

Dr. Sophie Sun

ELIGIBILITY:

Patients must have:

- Previously untreated extensive stage small cell lung cancer (ES-SCLC)

Patients should have

- ECOG 0 to 2
- Adequate bone marrow, hepatic and renal function
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of atezolizumab

Notes:

- Patients on active treatment with LUSCPE (less than 4 cycles) and do not have proven progression may switch to LUSCATPE if all other eligibility criteria are met
- Patients previously treated with combined modality therapy for limited stage disease are eligible for LUSCATPE if relapse occurs greater than 6 months after previous treatment
- Patients are eligible to receive either LUSCDURPE or LUSCATPE, but not both

CAUTIONS:

- Active, known or suspected autoimmune disease
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)

TESTS AND MONITORING:

- Baseline: CBC & differential, platelets, creatinine, calcium, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, morning serum cortisol, chest x-ray
- Before each cycle: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH
- If clinically indicated: chest x-ray, ECG, morning serum cortisol, lipase, glucose, calcium, serum or urine hCG (required for women of child bearing potential if pregnancy suspected), free T3 and free T4, serum ACTH levels, testosterone, estradiol, FSH, LH, ECG
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (optional)

PREMEDICATIONS:

For cycles 1 to 4:

- Antiemetic protocol for moderately emetogenic chemotherapy as long as CISplatin dose is not greater than or equal to 50 mg. If CISplatin is greater than or equal to 50 mg, or if giving CARBOplatin, use antiemetic protocol for highly emetogenic chemotherapy (see protocol [SCNAUSEA](#))
- hydrocortisone & diphenhydrAMINE for history of hypersensitivity to etoposide
- If prior infusion reactions to atezolizumab: diphenhydrAMINE 50 mg PO, acetaminophen 325 to 975 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment

For cycles 5 and beyond:

- Antiemetics are not usually required
- Antiemetic protocol for low emetogenicity (see [SCNAUSEA](#))
- If prior infusion reactions to atezolizumab: diphenhydrAMINE 50 mg PO, acetaminophen 325 to 975 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment

TREATMENT:

Cycles 1 to 4:

Drug	Dose	BC Cancer Administration Guideline
atezolizumab	1200 mg on Day 1	IV in 250 mL NS over 1 hour*
CISplatin	25 mg/m ² /day on Days 1 to 3	IV in 100 to 250 mL NS over 30 minutes
etoposide	100 mg/m ² /day on Days 1 to 3	IV in 250 to 1000 mL NS over 45 minutes to 1 hour 30 minutes (use non-DEHP equipment with 0.2 micron in-line filter)

* subsequent infusions may be given over 30 minutes if the first infusion is well-tolerated

In cases of CISplatin toxicity or poorly functioning patients or Age greater than 75:

Drug	Dose	BC Cancer Administration Guideline
CARBOplatin	AUC 5 on Day 1 only Dose = AUC x (GFR** + 25)	IV in 100 to 250 mL NS over 30 minutes

**GFR preferably from nuclear renogram, if not possible use:

$$\text{GFR} = \frac{N \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}} \quad N = 1.04 \text{ (women) or } 1.23 \text{ (men)}$$

The estimated GFR calculated using the Cockcroft-Gault equation should be capped at 125 mL/min when it is used to calculate the initial CARBOplatin dose. When a nuclear renogram is available, this clearance would take precedence

- **Repeat every 3 weeks x 4 cycles**, followed by

Cycle 5 onwards: (to start 3 weeks after cycle 4)

Drug	Dose	BC Cancer Administration Guideline
atezolizumab	1200 mg	IV in 250 mL NS over 30 minutes

- **Repeat every 3 weeks** until disease progression or unacceptable toxicity

DOSE MODIFICATIONS:

1. Other toxicities: for atezolizumab

No specific dose modifications for atezolizumab. Toxicity managed by treatment delay and other measures (see [SCIMMUNE](#) for management of immune-mediated adverse reactions to checkpoint inhibitor immunotherapy:

http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf).

2. Hematology: for etoposide

ANC (X 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
1.0 to less than 1.5	or	75 to less than 100	75%
less than 1.0	or	less than 75	Delay

2. Hepatic dysfunction: for etoposide

Bilirubin (micromol/L)	Dose	
less than 25	100%	100 mg/m ² /day x 3 days
25 to 50	50%	50 mg/m ² /day x 3 days
51 to 85	25%	25 mg/m ² /day x 3 days
greater than 85	Delay	

3. Renal dysfunction:

For CISplatin

Calculated Cr Clearance (mL/min)	Dose
greater than or equal to 60	100%
45 to less than 60	80% CISplatin or go to CARBOplatin option
less than 45	Hold CISplatin or delay with additional IV fluids or go to CARBOplatin option

For etoposide

Initial dose modification to 75% should be considered if creatinine clearance is less than 30 mL/min. Subsequent dosing should be based on patient tolerance and clinical effect.

PRECAUTIONS:

- Serious immune-mediated reactions:** can be severe to fatal and usually occur during the treatment course, but may develop months after discontinuation of therapy. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, pneumonitis, as well as toxicities in other organ systems. Early diagnosis and appropriate management are essential to minimize life-threatening complications (see [SCIMMUNE](http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf) for management of immune-mediated adverse reactions to checkpoint inhibitor immunotherapy: http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf).
- Infusion-related reactions:** isolated cases of severe infusion reactions have been reported. Discontinue atezolizumab for severe reactions (Grade 3 or 4). Patients with mild or moderate infusion reactions may receive atezolizumab with close monitoring and use of premedication.
- Hypersensitivity:** Monitor infusion of etoposide for the first 15 minutes for signs of hypotension. Hypersensitivity reactions have also been reported for CISplatin. Refer to BC Cancer Hypersensitivity Guidelines.
- Extravasation:** CISplatin and etoposide cause irritation if extravasated. Refer to BC Cancer Extravasation Guidelines.
- Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- Infections:** severe infections have been reported. Treat with antibiotics for suspected or confirmed bacterial infections. Hold atezolizumab for Grade 3 or 4 infections. Permanently discontinue for any grade of meningitis or encephalitis.
- Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics.

Contact Dr. Sophie Sun or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.

REFERENCES:

1. Horn L, Mansfield AS, Szczesna A, et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *N Engl J Med* 2018;379(23):2220-2229.
2. Atezolizumab (Tecentriq) CADTH Reimbursement Recommendation. *Canadian Journal of Health Technologies* 2022 2(9):1-18.