

BC Cancer Protocol Summary for Second-Line Treatment of Extensive Stage Small Cell Lung Cancer (SCLC) with Irinotecan With or Without Platinum

Protocol Code: LUSCPI

Tumour Group: Lung

Contact Physician: Dr. Christopher Lee

ELIGIBILITY:

- Recurrent/progressive small cell lung cancer following first-line therapy
- ECOG performance status 0-2
- In any one patient either LUSCTOP or LUSCPI (i.e. – one or the other, **but not both**) will be reimbursed

EXCLUSIONS:

- ECOG performance status 3 to 4
- Inadequate hepatic function (bilirubin greater than or equal to 35 micromol/L; ALT/ Alkaline Phosphatase greater than or equal to 5 x ULN)
- Greater than 3 loose stools per day in patients without colostomy or ileostomy

TESTS:

- Baseline: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin and LDH
- Before each treatment:
 - Day 1 – CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin and LDH
 - Day 8 – CBC & differential, platelets

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA) if using CISplatin
- Antiemetic protocol for moderate emetogenic chemotherapy (see protocol SCNAUSEA) if using irinotecan alone or in combination with CARBOplatin
- Prochlorperazine should be avoided on the same day as irinotecan treatment due to the increased incidence of akathisia
- Atropine may be required for treatment or prophylaxis of diarrhea (see precautions)

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
irinotecan	50 mg/m ² /day on day 1 and day 8	IV in D5W 250 to 500 mL over 30 minutes to 1 hour

Optional:

CISplatin	75 mg/m ² /day on day 1	Prehydrate with NS 1000 mL over 1 hour, then CISplatin IV in NS 500 mL with potassium chloride 20 mEq, magnesium sulfate 1 g, mannitol 30 g over 1 hour
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OR

CARBOplatin	AUC 5 DAY 1 only Dose = AUC 5 x (GFR* + 25)	IV in NS 100 to 250 mL over 30 minutes.
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Repeat every 21 days until disease progression, unacceptable toxicity or 6 cycles

All patients should be advised to obtain an adequate supply of loperamide (IMODIUM®) with explicit instructions for the management of diarrhea.

*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 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.

DOSE MODIFICATIONS:**1. Hematology:****Day 1 of each cycle:**

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose (both drugs)
greater than or equal to 1.5	and	greater than or equal to 100	100%
less than 1.5	or	less than 100	Delay*

* If ANC less than 1.0 or platelets less than 75, consider dose reduction to 75%

Day 8 of each cycle:

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Irinotecan 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	85%
0.5 to less than 1.0	or	50 to less than 75	70%
less than 0.5	or	less than 50	Omit

2. **Neutropenic Fever:** Delay, then consider dose reduction to 75% when resolved

3. Renal Dysfunction:

Calculated Cr Clearance (mL/min)	CISplatin dose
greater than or equal to 60	100%
45 to less than 60	80% CISplatin (same prehydration as 75 mg/m ² dose) or go to CARBOplatin option
less than 45	Hold CISplatin or delay with additional IV fluids or go to CARBOplatin option
less than 30	Omit

4. Diarrhea:

Grade	Diarrhea	Irinotecan Dose
1 to 2	Increase of up to 6 stools/day, or nocturnal stools or moderate increase in loose watery colostomy output	100%
3 to 4	Increase of 7 or more stools/day or incontinence, malabsorption, severe increase in loose water, colostomy output, grossly bloody diarrhea, may require parenteral support	Delay until Grade 2 or less, then reduce dose to 75%

PRECAUTIONS:

1. **Diarrhea** may be life-threatening and requires prompt, aggressive treatment.

- **Early diarrhea** or abdominal cramps occurring within the first 24 hours is treated with **atropine** IV or SC 0.3 to 1.2 mg. Prophylactic atropine may be required for subsequent treatments.
- **Late diarrhea** must be treated with **loperamide** (eg, IMODIUM®). The loperamide dose is higher than recommended by the manufacturer. Instruct patient to have loperamide on hand and start treatment at the first poorly formed or loose stool, or earliest onset of more frequent stool than usual:
 - **4 mg stat**
 - **then 2 mg every 2 hours until diarrhea-free for 12 hours**
 - may take 4 mg every 4 hours at night

2. **Other cholinergic symptoms** may occur during or shortly after infusion of irinotecan, including rhinorrhea, increased salivation, lacrimation, diaphoresis and flushing. These should be treated with atropine IV or SC 0.3 mg to 0.6 mg. This dose may be repeated at the physician's discretion. Blood pressure and heart rate should be monitored. Prophylactic atropine may be required for subsequent treatments.
3. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Use caution with pre-existing renal dysfunction.
5. **Gilbert's Syndrome** increases the risk of irinotecan-induced toxicity (Ann Oncol 1997;8:1049-51). A screen for Gilbert's Syndrome using direct/indirect serum bilirubin is recommended.
6. **Hepatic Dysfunction:** irinotecan has not been studied in patients with bilirubin greater than 35 micromol/L or ALT greater than 3x the upper limit of normal if no liver metastases, or ALT greater than 5x the upper limit of normal with liver metastases.
7. **Pulmonary Toxicity:** Severe pulmonary toxicity has been reported rarely. Supportive care is required.

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

References:

1. Schmittel A et al. A randomized phase II trial of irinotecan plus carboplatin vs etoposide plus carboplatin treatment in patients with extended disease SCLC. Ann Oncol 2006;17:663-7.
2. Noda K et al. Irinotecan plus cisplatin compared to etoposide plus cisplatin for extensive small-cell lung cancer. N Engl J Med 2002;346:75-81.
3. BCCA protocol summary and doctor's orders for LUTCAIRI: A Phase II trial of carboplatin and irinotecan (CPT-11) as first-line therapy for patients with extensive stage small cell lung cancer, 2006.