

BCCA Protocol Summary for Treatment of Small Cell or Neuroendocrine Carcinoma of Gynecologic System Origin using PACLitaxel, CISplatin, Etoposide and CARBOplatin with Radiation (GO 95 02)

Protocol Code: GOSMCCRT

Tumour Group: Gynecology

Contact Physician: Dr. Paul Hoskins

ELIGIBILITY:

- small cell or neuroendocrine cancer (pure or mixed)
- **administration of this protocol is restricted to BCCA Cancer Centres**

EXCLUSIONS:

- age greater than 70 (unless physiologically younger)
- creatinine greater than 150 micromol/L (after hydration and/or stenting)
- partial deafness
- inability to tolerate fluid load

RELATIVE EXCLUSIONS:

- disease not radio-encompassable
- (in this situation cure is unlikely therefore can use either this protocol or lung small cell protocols)

Note: if disease is localized but radiation therapy is contra-indicated, consider surgery to replace radiation therapy.

TESTS:

- Baseline: CBC & diff, creatinine, Magnesium, Calcium, phosphate, bilirubin, AST, LDH, alk. phos., gamma GT, tumour marker screen (CEA, CA199, CA125, CA15-3, SCC), chest X-ray, CT scan of abdomen/pelvis, CT scan of brain if clinically indicated.
- Before each treatment: blood work as at baseline, best tumour marker.
- Before Cycle D: nuclear renogram

PRE-MEDICATIONS:

PACLitaxel must not be started unless the following drugs have been given:

- 45 minutes prior to PACLitaxel:
 - Dexamethasone 20 mg IV in 50 mL NS over 15 minutes
- 30 minutes prior to PACLitaxel:
 - DiphenhydrAMINE 50 mg IV and Ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in bag)

HYDRATION:

- Hydration pre-CISplatin:
 - Cycle A: NS 500 mL piggy-back with PACLitaxel, begin 1 hour after PACLitaxel infusion starts
 - Cycle B: 2/3D5W-1/3NS 1000 mL with potassium chloride 20 mEq and magnesium sulfate 2 g IV over 3 hours; begin on admission; repeat x 1 prn to ensure urine output greater than 100 mL/h
 - Cycle C: (optional) 2/3D5W-1/3NS 1000 mL with potassium chloride 20 mEq and magnesium sulfate 2 g IV over 1 hour.
- Hydration post-CISplatin:
 - Cycle A: 2/3D5W-1/3NS 1000 mL with potassium chloride 20 mEq and magnesium sulfate 2 g IV over 3 hours; on day 1, continue at 100 mL/h until day 2 therapy begins
 - Cycle B: after completion of Etoposide infusion on day 1, resume pre-CISplatin hydration solution at 100 mL/h until day 2 therapy begins; after completion of Etoposide infusion on day 2, resume pre-CISplatin hydration solution 500 mL over 2 hours

ANTIEMETIC THERAPY:

- Ondansetron 8 mg PO and Dexamethasone 8 mg PO 30 minutes before CISplatin, CARBOplatin or Etoposide
- Dexamethasone 4 mg PO/IV on any day CISplatin administered
- Dexamethasone 4 mg PO/IV q12h x 3 days after each cycle
- additional antiemetics as required for highly emetogenic chemotherapy (see SCNAUSEA protocol)

TREATMENT:

CYCLE DAY	A		B					C					D	E				
	1	2	21	22	23	24	25	42	49	56	63	70	98	126	127	128	129	130
¹ PACLitaxel 175 mg/m ² IV	X												X					
² CISplatin 60 mg/m ² IV	X	X	X	X														
² CISplatin 40 mg/m ² IV								X	X	X	X	X						
³ etoposide 75 mg/m ² IV			X	X														
etoposide 100 mg PO					X	X	X							X	X	X	X	X
⁴ CARBOplatin AUC x (25+GFR) IV													X	X				
⁵ pelvic/para-aortic XRT 4000 cGy in 25#; selectron x2 or lat. pelvis 1000 cGy in 5#																		

¹**PACLitaxel:** - IV in 500 mL NS over 3 hours; use non-PVC equipment, in-line filter; give **before** CISplatin or CARBOplatin

²**CISplatin:** - IV in 500 mL NS with 30 g mannitol and 2 g magnesium sulfate, over 1 hour
 - due to its use as a radio-sensitizing agent in Cycle C, CISplatin should be given on a Monday or Tuesday of the week, before radiation, and each subsequent weekly CISplatin should be on that same day of the week. The RT booking on those days should be within two hours of the completion of the CISplatin infusion.

³**Etoposide:** - IV in 500 mL NS (non-PVC bag), over 45 minutes (use non-PVC tubing); give **after** CISplatin or CARBOplatin

⁴**CARBOplatin:** - use AUC of 6 for Cycle D, AUC of 5 for Cycle E
 - **Measured GFR** (e.g. nuclear renogram) is preferred whenever feasible, **particularly** in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR; the estimated GFR reported by the lab or 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.

Cockcroft-Gault Formula

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

Note: The same method of estimation should be used throughout the treatment course (i.e., if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft-Gault estimate).

- IV in 250 mL D5W over 30 minutes

⁵radiation therapy:

- pelvic/para-aortic radiation therapy for non-progressors only; if progression, discontinue protocol
- if radiation is delayed, delay CISplatin in parallel; delay Cycle D & E by amount of radiation delay
- on days with concurrent CISplatin infusion, RT should be booked within two hours of the completion of the CISplatin infusion.

DOSE MODIFICATIONS:

1. Hematological (on treatment day):

Day	ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Doses (both drugs)
21, 98 and 126	less than 1	or	less than 100	delay till recovery, then full dose

2. **Neuropathy:** Modification or discontinuation of doses may be required (contact Dr. Hoskins)
3. **Arthralgia and/or myalgia:** If arthralgia and/or myalgia of grade 2 (moderate) or higher is not relieved by adequate doses of NSAIDs or acetaminophen with codeine (e.g., **TYLENOL #3®**), a limited number of studies report a possible therapeutic benefit using:
- Prednisone 10 mg po bid x 5 days starting 24 hours post-PACLI taxel
 - Gabapentin 300 mg po on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 7-10 days
- If arthralgia and/or myalgia persists, reduce subsequent PACLI taxel doses to 135 mg/m².

PRECAUTIONS:

1. **Hypersensitivity:** Reactions to IV Etoposide are possible. Reactions to PACLI taxel are common. See BCCA Hypersensitivity Guidelines and table below.

<i>mild</i> symptoms (e.g. mild flushing, rash, pruritus)	<ul style="list-style-type: none"> • complete PACLI taxel infusion. Supervise at bedside • no treatment required
<i>moderate</i> symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension)	<ul style="list-style-type: none"> • stop PACLI taxel infusion • give IV DiphenhydrAMINE 25-50 mg and Hydrocortisone IV 100 mg • after recovery of symptoms resume PACLI taxel infusion at 20 mL/h for 5 minutes, 30 mL/h for 5 minutes, 40 mL/h for 5 minutes, then 60 mL/h for 5 minutes. If no reaction, increase to full rate. • if reaction recurs, discontinue PACLI taxel therapy
<i>severe</i> symptoms (i.e. <i>one</i> or more of respiratory distress requiring treatment, generalized urticaria, angioedema, hypotension requiring therapy)	<ul style="list-style-type: none"> • stop PACLI taxel infusion • give IV antihistamine and steroid as above. Add Epinephrine or bronchodilators if indicated • discontinue PACLI taxel therapy

2. **Extravasation:** PACLI taxel causes pain and tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.
3. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **Hypotension:** Rapid administration of IV Etoposide may cause transient hypotension (Faintness, shortness of breath, lightheadedness, or restlessness).
5. **Renal toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycosides.

Call Dr. Paul Hoskins or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: N/A (as GOSMCC2)

Date revised: 01 June 2011 (Infusion section revised)