

# BCCA Protocol for Primary Treatment of Advanced/Recurrent Non-Small Cell Cancer of the Cervix with CARBOplatin and PACLitaxel in Ambulatory Care Settings

<b>Protocol Code</b>	GOCXCAT
<b>Tumour Group</b>	Gynecology
<b>Contact Physician</b>	Dr. Ken Swenerton

## ELIGIBILITY:

- non-small cell cancer of the cervix (squamous, adenocarcinoma or mixed)
- recurrent or IIIb, IVa or IVb
- ineligible for GOCXRADC
- Note: The GOCXCAT and GOCXCAD regimens are alternatives. The clinician's selection should be based upon the patient's circumstances. The docetaxel-containing combination produces more neutropenic complications, diarrhea, edema and hypersensitivity; the PACLitaxel-containing combination produces more peripheral neurotoxicity, arthralgia, myalgia, and alopecia. Physician may choose between PACLitaxel (GOCXCAT) and docetaxel (GOCXCAD). A maximum of 6 cycles\* of taxane treatment will be reimbursed for each line of therapy. However, a patient who had previously responded to 6 cycles\* of say, a PACLitaxel-based regimen may be retreated with another 6 cycles\* of a taxane-based regimen.

\* may extend to 9 cycles if the patient has not achieved a complete response but is continuing to improve

## EXCLUSIONS:

- any small cell component
- creatinine greater than 150 micromol/L
- neutrophils less than  $1 \times 10^9/L$
- performance status greater than ECOG2

## RELATIVE CONTRAINDICATIONS:

- pre-existing motor or sensory neuropathy greater than grade 2

## TESTS:

- Baseline: CBC & diff, platelets, creatinine, tumor marker (CA 125, CA 15-3, CA 19-9), liver function tests, chest X-ray, abdominopelvic imaging, camera nuclear renogram for GFR (if available)
- Day 14 and 21 after first cycle (and in subsequent cycle if dose modification made): CBC & diff; once nadir pattern established, check CBC & diff at that point only
- Before each treatment: CBC & diff, creatinine, any initially elevated tumor marker, liver function tests (if clinically indicated)

## PREMEDICATIONS:

- **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)
- Ondansetron 8 mg po 30 minutes pre-CARBOplatin

**ANTIEMETIC THERAPY POST-CHEMOTHERAPY:**

- Dexamethasone 4 mg po BID for 2 days and DimenhyDRINATE 50-100 mg prn after treatment is usually adequate

**TREATMENT** (give PACLitaxel first):

Drug	Starting Dose	BCCA Administration Guideline
PACLitaxel	175 mg/m <sup>2</sup> (or conservative dosing of 155 mg/ m <sup>2</sup> or 135 mg/ m <sup>2</sup> )**	IV in 500 mL NS over 3 hours (use non-PVC equipment, in-line filter)
CARBOplatin	Dose = AUC* x (GFR +25)	IV in 250 mL D5W over 30 minutes

\* use AUC of 6; if extensive prior radiation therapy, use AUC of 5

\*\* Conservative dosing may be considered in the following cases: existing or potential myelosuppression; existing or potential arthralgia and myalgia; prior radiotherapy, particularly to the pelvic region; reduced bone marrow capacity. An initial dose of 135 mg/m<sup>2</sup> is recommended in patients greater than 75 years of age, with escalation to 155 mg/m<sup>2</sup> and then 175 mg/m<sup>2</sup> if tolerated.

*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).

Repeat every 28 days up to a maximum of 6 cycles. Following administration of cycle 2, treatment interval may be changed to 21 days if hematologic recovery meets or exceeds values necessary for retreatment at full doses.

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

## DOSE MODIFICATIONS:

### 1. Hematological:

a) on treatment day:

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	Doses (both drugs)
greater than or equal to 1.0	and	greater than or equal to 100	treat as per nadir
less than 1.0	or	less than 100	delay until recovery

b) at nadir:

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	PACLitaxel	CARBOplatin
greater than or equal to 1.5	and	greater than or equal to 100	100%	120%*
0.5-1.4	and	75-99	100%	100%
less than 0.5	and	less than or equal to 75	80%	80%
less than 0.5	and	greater than or equal to 75	80%	100%
greater than or equal to 0.5	and	less than or equal to 75	100%	80%
Febrile neutropenia at any time			80%	80%

\*no escalation above 120% of cycle 1 dose

- 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-PACLitaxel
  - 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 PACLitaxel doses to 135 mg/m<sup>2</sup>.
- Neuropathy:** Dose modification or discontinuation may be required (see BCCA Cancer Drug Manual).
- Renal dysfunction:** If significant increase (greater than 20%) in creatinine, repeat nuclear renogram (if available) and recalculate CARBOplatin dose using new GFR.
- Hepatic dysfunction:** Dose reduction may be required for PACLitaxel (see BCCA Cancer Drug Manual)

## PRECAUTIONS:

- Hypersensitivity:** Reactions are common. See BCCA Hypersensitivity Guidelines

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

2. **Extravasation:** **PACLI**taxel causes pain and may, rarely, cause tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.
3. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.

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

Date activated: 01 Jul 2000

Date revised: 01 Apr 2011 (estimated GFR capped, reformatted with TALLman lettering)

**Reference<sup>1,2</sup>:**

1. Vasey PA. Role of docetaxel in the treatment of newly diagnosed advanced ovarian cancer. *J Clin Oncol* 2003;21(90100):136s-44s.
2. Moore DH, McQuellon RP, Blessing JA, et al. A randomized phase III study of cisplatin versus cisplatin plus paclitaxel in stage IVB, recurrent or persistent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group Study. *Proc Am Soc Clin Oncol* 2001;20:(abstract 801).