# BC Cancer Protocol for Primary Adjuvant Treatment of Adenocarcinoma/Adenosquamous Cancer of the Cervix with CARBOplatin and PACLitaxel Preceding or Following Irradiation with or without CISplatin

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| ***Protocol Code*** | *GOCXAJCAT* |
| ***Tumour Group*** | *Gynecology* |
| ***Contact Physician*** | *Dr. Paul Hoskins* |

**ELIGIBILITY**:
- Adenocarcinoma or adenosquamous histology
- Stage 1a if node-positive and patient will be receiving RT +/- GOCXCRT
- Stage 1b to 4a and will be receiving RT +/- GOCXCRT

**EXCLUSIONS**:
- any small cell or neuroendocrine component
- pure squamous cell histology
- Stage 4b or recurrent cancer – use GOCXCAT

**RELATIVE CONTRAINDICATIONS**:
- pre-existing motor or sensory neuropathy greater than grade 2
- creatinine greater than 150 micromol/L
- neutrophils less than 1.0 x $10^9$/L

**TESTS**:
- Baseline: CBC & diff, platelets, creatinine, bilirubin, ALT, alkaline phosphatase, GGT
- Optional at baseline: tumor marker(s) as appropriate e.g., CA 125, CA 15-3, CA 19-9, CEA, SCC
- *Optional*: Day 14 (and Day 21 if using 28-day interval) after first cycle (and in subsequent cycle if dose modification made): CBC & diff
- Before each subsequent treatment: CBC & diff, creatinine, any initially elevated tumor marker
- Before each subsequent treatment *only if clinically indicated:* bilirubin, ALT, alkaline phosphatase, GGT, LDH, total protein, albumin, potassium, magnesium
- Consider repeating any positive imaging studies after 2 cycles, to assess response

**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 in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)

- ondansetron 8 mg PO 30 minutes pre-CARBOplatin

**ANTIEMETIC THERAPY POST-CHEMOTHERAPY**:
- Antiemetic protocol for moderate emetogenic chemotherapy protocols (see SCNAUSEA)
- dexamethasone 4 mg PO BID for 4 doses

**TREATMENT** (give PACLitaxel first):

| Drug | Starting Dose | BC Cancer Administration Guideline |
|---|---|---|
| PACLitaxel | 175 mg/m$^2$<br><br>(or conservative dosing of 155 mg/ m$^2$ or 135 mg/ m$^2$)* | IV in 250 to 500 mL NS over 3 hours<br><br>(use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter) |
| CARBOplatin | Dose = AUC 6 x (GFR +25)<br><br>(or conservative dosing of AUC 5)* | IV in 100 to 250 mL NS over 30 minutes |

* Conservative dosing may be considered in the following cases: existing or potential myelosuppression; existing or potential arthralgia and myalgia; reduced bone marrow capacity, age greater than 75 years.

Cockcroft-Gault Formula (cap at 125 mL/min)

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

Repeat every 21 (preferred) or 28 days, for 3 cycles.

**DOSE MODIFICATIONS**:

1. **Hematological**:

a) on treatment day (may use results within 96h):

| ANC (x $10^9$/L) | | Platelets (x $10^9$/L) | Doses (both drugs) |
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| 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 $10^9$/L) | | Platelets (x $10^9$/L) | PACLitaxel | CARBOplatin |
|---|---|---|---|---|
| greater than or equal to 0.5 | and | greater than or equal to 75 | 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% |

2. **Arthralgia and/or myalgia**: If arthralgia and/or myalgia of grade 2 (moderate) or higher, a limited number of studies report a possible preventative therapeutic benefit using:
   - (*Preferred option*) gabapentin 300 mg PO on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 5 to 10 days – to match the duration of arthromyalgia symptoms.
   - (*Alternate option*) predniSONE 10 mg PO bid x 5 days starting 24 hours post-PACLitaxel

   If arthralgia and/or myalgia persists, reduce subsequent PACLitaxel doses to 155 mg/m$^2$ or 135 mg/m$^2$
3. **Neuropathy**: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).
4. **Renal dysfunction**: If significant increase (greater than 20%) in creatinine, recalculate CARBOplatin dose using new GFR.
5. **Hepatic dysfunction**: Dose reduction may be required for PACLitaxel (see BC Cancer Drug Manual)

6. **Severe Paclitaxel hypersensitivity/allergy** thought to be not manageable with increased pre-treatment Dexamethasone, switch to GOCXCAD.
7. **Vomiting**: consider adding a NK1 receptor antagonist e.g., aprepitant.

**PRECAUTIONS**:

1. **Hypersensitivity**: Reactions are common. See BC Cancer Hypersensitivity Guidelines

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| *mild* symptoms (e.g. mild flushing, rash, pruritus) | ▪ complete PACLitaxel infusion. Supervise at bedside<br>▪ no treatment required<br>▪ consider altering Dexamethasone premedication in next cycle to 20 mg PO 12 hours and 6 hours prior to PACLitaxel infusion (in place of usual 20 mg IV dose 45 minutes prior to PACLitaxel infusion) |
| *moderate* symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension | ▪ stop PACLitaxel infusion<br>▪ give IV diphenhydrAMINE 25 to 50 mg and IV hydrocortisone IV 100 mg<br>▪ after recovery of symptoms resume PACLitaxel 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.<br>▪ if reaction recurs, discontinue PACLitaxel therapy<br>▪ consider altering Dexamethasone premedication in next cycle to 20 mg PO 12 hours and 6 hours prior to PACLitaxel infusion (in place of usual 20 mg IV dose 45 minutes prior to PACLitaxel infusion) |
| *severe* symptoms (i.e. *one* or more of respiratory distress requiring treatment, generalized urticaria, angioedema, hypotension requiring therapy) | ▪ stop PACLitaxel infusion<br>▪ give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated<br>▪ discontinue PACLitaxel therapy<br>▪ consider GOCXCAD for next cycle |

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

**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.**

**References**

Tang J, et al. Chemoradiation and adjuvant chemotherapy in advanced cervical adenocarcinoma. Gynecol Oncol 2012;125:297-302.