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

**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 x 10⁹/L

**TESTS:**
- Baseline: CBC & diff, platelets, creatinine, liver function tests
- 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, any initially elevated tumor marker
- Before each subsequent treatment only if clinically indicated: creatinine, liver function tests, potassium, magnesium
- Consider repeating any positive imaging studies after 2 cycles, to assess response

**PREMEDICATIONS:**
- In Cycle 1, 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 together in bag)*
  - ondansetron 8 mg PO 30 minutes pre-CARBOplatin

  *If no paclitaxel hypersensitivity reaction was observed in Cycle 1, then this premedication regime may be modified to omit diphenhydramINE, Ranitidine, and higher-dose Dexamethasone. Note that anti-emetic dose Dexamethasone (8mg PO/IV) will need to be prescribed pre-chemotherapy.

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

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**TREATMENT** (give PACLitaxel first):

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>175 mg/m²&lt;br&gt;(or conservative dosing of 155 mg/ m² or 135 mg/ m²)*</td>
<td>IV in 500 mL NS over 3 hours</td>
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<td></td>
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<td>(use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
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<tr>
<td>CARBOplatin</td>
<td>Dose = AUC 6 x (GFR +25)&lt;br&gt;(or conservative dosing of AUC 5)*</td>
<td>IV in 250 mL NS over 30 minutes</td>
</tr>
</tbody>
</table>

* 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)

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

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

**DOSE MODIFICATIONS:**

1. **Hematological:**
   a) on treatment day (may use results within 96h):

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Doses (both drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1</td>
<td>and</td>
<td>greater than or equal to 100</td>
</tr>
<tr>
<td>less than 1</td>
<td>or</td>
<td>less than 100</td>
</tr>
</tbody>
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   b) at nadir:

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>PACLitaxel</th>
<th>CARBOplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 0.5</td>
<td>and</td>
<td>greater than or equal to 75</td>
<td>100%</td>
</tr>
<tr>
<td>less than 0.5</td>
<td>and</td>
<td>less than or equal to 75</td>
<td>80%</td>
</tr>
<tr>
<td>less than 0.5</td>
<td>and</td>
<td>greater than or equal to 75</td>
<td>80%</td>
</tr>
<tr>
<td>greater than or equal to 0.5</td>
<td>and</td>
<td>less than or equal to 75</td>
<td>100%</td>
</tr>
<tr>
<td>Febrile neutropenia at any time</td>
<td></td>
<td></td>
<td>80%</td>
</tr>
</tbody>
</table>

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/m² or 135 mg/m².

3. **Neuropathy**: Dose modification or discontinuation may be required (see BCCA 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 BCCA CDM).

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 BCCA Hypersensitivity Guidelines

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Measures</th>
</tr>
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</table>
| **mild** symptoms (e.g. mild flushing, rash, pruritus) | ▪ complete PACLitaxel infusion. Supervise at bedside  
▪ no treatment required  
▪ 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  
▪ give IV diphenhydRAMINE 25 to 50 mg and IV hydrocortisone IV 100 mg  
▪ 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.  
▪ if reaction recurs, discontinue PACLitaxel therapy  
▪ 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  
▪ give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated  
▪ discontinue PACLitaxel therapy  
▪ consider GOCXCAD for next cycle |

2. **Extravasation**: PACLitaxel 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. 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: 01 Aug 2014
Date revised: 12 Aug 2016 (Protocol title revised)

References