**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

**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 10^9/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, creatinine, any initially elevated tumor marker
- Before each subsequent treatment only if clinically indicated: 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
TREATMENT (give PACLitaxel first):

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>175 mg/m²</td>
<td>IV in 500 mL NS over 3 hours</td>
</tr>
<tr>
<td></td>
<td>(or conservative dosing of 155 mg/m² or</td>
<td>(use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
</tr>
<tr>
<td></td>
<td>135 mg/m²)*</td>
<td></td>
</tr>
<tr>
<td>CARBOplatin</td>
<td>Dose = AUC 6 x (GFR +25)</td>
<td>IV in 250 mL NS over 30 minutes</td>
</tr>
<tr>
<td></td>
<td>(or conservative dosing of AUC 5)*</td>
<td></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 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Doses (both drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1 and greater than or equal to 100</td>
<td>treat as per nadir</td>
<td></td>
</tr>
<tr>
<td>less than 1 or less than 100</td>
<td>delay until recovery</td>
<td></td>
</tr>
</tbody>
</table>

b) at nadir:

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>PACLitaxel</th>
<th>CARBOplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 0.5 and greater than or equal to 75</td>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>less than 0.5 and less than or equal to 75</td>
<td>80%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>less than 0.5 and greater than or equal to 75</td>
<td>80%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>greater than or equal to 0.5 and less than or equal to 75</td>
<td>100%</td>
<td>80%</td>
<td></td>
</tr>
</tbody>
</table>

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/m² or 135 mg/m²

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 pretreatment 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

| **mild** symptoms (e.g. mild flushing, rash, pruritus) | ▪ complete PACLtaxel 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 PACLtaxel infusion (in place of usual 20 mg IV dose 45 minutes prior to PACLtaxel infusion) |
| --- | --- |
| **moderate** symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension) | ▪ stop PACLtaxel infusion
▪ give IV diphenhydRAMINE 25 to 50 mg and IV hydrocortisone IV 100 mg
▪ after recovery of symptoms resume PACLtaxel 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 PACLtaxel therapy
▪ consider altering Dexamethasone premedication in next cycle to 20 mg PO 12 hours and 6 hours prior to PACLtaxel infusion (in place of usual 20 mg IV dose 45 minutes prior to PACLtaxel infusion) |
| **severe** symptoms (i.e. one or more of respiratory distress requiring treatment, generalized urticaria, angioedema, hypotension requiring therapy) | ▪ stop PACLtaxel infusion
▪ give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated
▪ discontinue PACLtaxel therapy
▪ consider GOCXCAD for next cycle |

2. **Extravasation**: PACLtaxel 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**