BC Cancer Protocol Summary for Alternative Treatment of Gynecological Malignancies Using CIPlatin and PACLitaxel

Protocol Code: GOCISP
Tumour Group: Gynecologic Oncology
Contact Physician: Dr. Anna Tinker

ELIGIBILITY:
- Previous non-life threatening allergic reactions to CARBOplatin
- Eligible for the following protocols
  - GOOVCATM, GOOVCATR, GOOVCATX, GOOVDCCAT
  - GOCXCAT, GOCXCATB
  - GOENDCAT

EXCLUSIONS:
- Creatinine clearance less than 45 mL/min at baseline

TESTS:
- Baseline: CBC & diff, platelets, creatinine, electrolytes, magnesium, tumour marker (CA 125, CA 15-3, CA 19-9), liver function tests (if abnormal liver function is a potential concern)
- Before each treatment: CBC & diff, platelets, creatinine, any initially elevated tumour 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)
- Antiemetic protocol for highly emetogenic chemotherapy protocols (see SCNAUSEA)

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>175 mg/m² * on day 1</td>
<td>IV in 500 mL NS over 3 hours (use non-DEHP equipment, in-line filter)</td>
</tr>
<tr>
<td>CISplatin</td>
<td>75 mg/m²/day on day 1</td>
<td>Prehydrate with 1000 mL NS over 1 hour, then CISplatin IV in 500 mL NS with potassium chloride 20 mEq, magnesium sulfate 1 g, mannitol 30 g over 1 hour</td>
</tr>
</tbody>
</table>

- Repeat every 21 days to complete total number of cycles in original CARBOplatin/PACLitaxel protocol
DOSE MODIFICATIONS:

1. Hematology

<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 1.0 and greater than or equal to 100</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>less than 1.0 or less than 100</td>
<td>Delay</td>
<td></td>
</tr>
</tbody>
</table>

2. Renal Dysfunction

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>CISplatin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 60</td>
<td>75 mg/m^2</td>
</tr>
<tr>
<td>45 to 59</td>
<td>35 mg/m^2</td>
</tr>
<tr>
<td>less than 45</td>
<td>Delay</td>
</tr>
</tbody>
</table>

3. Arthralgia and/or myalgia: If arthralgia and/or myalgia of grade 2 (moderate) or higher was not adequately relieved by 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 5 to 15 days days (based on duration of arthromyalgia)
If arthralgia and/or myalgia persists, reduce subsequent PACLitaxel doses to 135 mg/m^2 or switching to an alternate taxane may be considered

4. Neuropathy: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

5. Renal dysfunction: If significant increase (greater than 20% or rises above the upper limit of normal) in creatinine, recheck/recalculate GFR and recalculate CARBOplatin dose using new GFR.

6. Hepatic dysfunction: Dose reduction may be required for PACLitaxel.

<table>
<thead>
<tr>
<th>ALT</th>
<th>Bilirubin</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 10 x ULN and less than or equal to 1.25 x ULN</td>
<td>175 mg/m^2</td>
<td></td>
</tr>
<tr>
<td>less than 10 x ULN and 1.26-2 x ULN</td>
<td>135 mg/m^2</td>
<td></td>
</tr>
<tr>
<td>less than 10 x ULN and 2.01-5 x ULN</td>
<td>90 mg/m^2</td>
<td></td>
</tr>
<tr>
<td>greater than or equal to 10 x ULN and/or greater than 5 x ULN</td>
<td>not recommended</td>
<td></td>
</tr>
</tbody>
</table>
**PRECAUTIONS:**

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

| **Mild** symptoms (e.g. mild flushing, rash, pruritus) | ▪ complete PACLitaxel infusion. Supervise at bedside  
▪ no treatment required |
|-----------------|--------------------------------------------------|
| **Moderate** symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension) | ▪ stop PACLitaxel infusion  
▪ give IV diphenhydrAMINE 25 to 50 mg and 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 |
| **Severe** symptoms (i.e. one or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy) | ▪ stop PACLitaxel infusion  
▪ give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated  
▪ discontinue PACLitaxel therapy |

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.

4. **Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Use caution with pre-existing renal dysfunction.

5. **Drug Interactions:** PACLitaxel is a CYP 2C8/9 and CYP 3A4 substrate. Drug levels may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

Call Dr. Anna Tinker or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.

Date activated:

Date revised:

References: