BC Cancer Protocol Summary for Treatment of Relapsed/Progressing Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using PACLitaxel

**Protocol Code**
GOOV TAX3

**Tumour Group**
Gynecologic Oncology

**Contact Physician**
Dr. Anna Tinker

**PREFACE:**
- In **platinum sensitive** disease: patients should be considered for doublet therapy consisting of carboplatin plus either a taxane or gemcitabine or DOXOrubicin pegylated liposomal (e.g., GOOV CATR, GOOVCAD, GOOV CAG, GOOV PLDC)
- In **platinum resistant** disease (i.e., cancer progresses within six months of completing a platinum-containing treatment protocol): patients will ideally receive single agent carboplatin, as it is the least toxic and most convenient choice of the equally efficacious agents available (i.e., GOOVCARB)
- In **platinum refractory** disease (i.e., cancer progresses while being treated with a platinum) choose between available agents based upon toxicity profile and convenience of dosing regimen. Options include: GOOVTOP, GOOLDOX, GOOV GEM, GOOOETO, GOOV VIN, GOOV TAX3, GOOVD OC. If gemcitabine (GOOV GEM), topotecan (GOOVTOP) or DOXOrubicin pegylated liposomal (GOOVLDOX) is used, only one of these options will be reimbursed in any one patient. Subsequently, if a patient is thought likely to benefit from one of the other two, a request should be submitted to the BC Cancer Compassionate Access Program (CAP).
- Patients who will not benefit from further therapy after second or subsequent rounds of chemotherapy can be identified by the following formula: “day 1 of treatment N to day of progression on treatment N+1 is less than or equal to 6 months.” They should be offered symptomatic management or investigational protocols.

**ELIGIBILITY:**
- Platinum refractory ovarian, primary peritoneal or Fallopian tube carcinoma
- Platinum resistant ovarian, primary peritoneal or Fallopian tube carcinoma in cases where patient-specific concerns dissuade the clinician from selecting single-agent carboplatin
- Platinum sensitive ovarian, primary peritoneal or Fallopian tube carcinoma in cases where actual or potential toxicity precludes the use of carboplatin or cisplatin alone or in combination with a taxane or gemcitabine.
- Adequate hematologic, liver and cardiac function
- PS ECOG 3 or better

**EXCLUSIONS:**
- Peripheral neuropathy Grade 2 or higher (relative contraindication)
- Prior severe arthromyalgia unresponsive to treatment (relative contraindication)

**TESTS:**
- Baseline: CBC & diff, bilirubin, ALT, appropriate tumour marker(s)
- Before each treatment: CBC & diff; appropriate tumour marker(s); if clinically indicated: bilirubin, ALT
- Imaging for tumour assessment (at physician’s discretion)
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)
  - Additional antiemetics not usually required (see SCNAUSEA)

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>BC Cancer Administration Standard</th>
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<tbody>
<tr>
<td>PACLitaxel</td>
<td>175 mg/m²</td>
<td>IV in 250 to 500 mL NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
</tr>
</tbody>
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*For patients who have demonstrated an unusual degree of marrow toxicity with previous treatments or who are thought to be at risk of increased toxicity, a reduced initial dose of 155 mg/m² is suggested

Repeat every 21 days until disease progression (usual treatment 9 cycles).

DOSE MODIFICATIONS:

1. Hematological

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0 and greater than or equal to 100</td>
<td>175 mg/m²</td>
<td></td>
</tr>
<tr>
<td>less than 1.0 or less than 100</td>
<td>delay until recovery; resume at 175 mg/m²</td>
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2. Febrile Neutropenia: Reduce dose to 155 mg/m² after first occurrence of febrile neutropenia. In the case of a second occurrence, use filgrastim (G-CSF) together with the same dose of paclitaxel, or discontinue paclitaxel.

3. Hepatic Dysfunction

<table>
<thead>
<tr>
<th>ALT</th>
<th>Total bilirubin</th>
<th>Dose (mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 10 x ULN and less than or equal to 1.25 x ULN</td>
<td>175</td>
<td></td>
</tr>
<tr>
<td>less than 10 x ULN and 1.26-2 x ULN</td>
<td>135</td>
<td></td>
</tr>
<tr>
<td>less than 10 x ULN and 2.01-5 x ULN</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>greater than or equal to 10 x ULN or greater than 5 x ULN</td>
<td>not recommended</td>
<td></td>
</tr>
</tbody>
</table>

ULN = upper limit of normal
3. **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 persist, reduce subsequent PACLitaxel doses to 135 mg/m² or switch to Docetaxel (GOOVDOC).

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

**PRECAUTIONS:**

1. **Hypersensitivity**: Reactions 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 25-50 mg and Hydrocortisone IV 100 mg  
   | | 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.  
   | | if reaction recurs, discontinue PACLitaxel therapy. Consider use of docetaxel (GOOVDOC)  
   | | if no further reaction, and infusion is completed, in subsequent cycles, premedicate with dexamethasone 20 mg 12 and 6 hours prior to paclitaxel, and begin infusion at reduced rate with incremental increases as detailed above.  

   | **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. Consider use of docetaxel (GOOVDOC)  

2. **Extravasation**: PACLitaxel causes pain and 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. **Radiation recall reactions**: are occasionally seen.

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