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

Protocol Code: GOOVТАΧ3
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., GOOVСATR, GOOVСАD, GOOVСAG, GOOVРLDC)
- 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., GOOVСΑRB)
- 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: GOOVТОР, GOОLDОX, GOОVGEM, GOОVETO, GOОVВIN, GOOVTAX3, GOOVDOC. If gemcitabine (GOOVGEM), 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 500 mL NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
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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 for 9 cycles or until disease progression or unacceptable toxicity occurs.

**DOSE MODIFICATIONS:**

1. **Hematological**
   - **ANC (x 10⁹/L)** and **Platelets (x 10⁹/L)**
   - **Dose**
     - greater than or equal to 1 and greater than or equal to 100: 175 mg/m²
     - less than 1 or less than 100: delay until recovery; resume at 175 mg/m²

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**
   - **ALT** less than 10 x ULN and **Total bilirubin** less than or equal to 1.25 x ULN: 175 mg/m²
   - less than 10 x ULN and 1.26-2 x ULN: 135 mg/m²
   - less than 10 x ULN and 2.01-5 x ULN: 90 mg/m²
   - greater than or equal to 10 x ULN or greater than 5 x ULN: not recommended

   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

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<tr>
<th>Symptom Level</th>
<th>Symptoms</th>
<th>Precautions</th>
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| Mild          | mild flushing, rash, pruritus | - complete PACLitaxel infusion.  
- Supervise at bedside  
- no treatment required |
| Moderate      | 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        | 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.