PREFACE:

- In platinum sensitive disease: patients will ideally receive doublet therapy consisting of carboplatin plus either a taxane or gemcitabine (e.g., GOOVCATR, GOOVODR, GOOVGAG).
- 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., GOOVCRB).
- 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, GOOVDX, GOOVGEM, GOOVETO, GOOVVIN, GOOVCRB, GOOVDO. If gemcitabine (GOOVGEM), topotecan (GOOVTOP) or pegylated liposomal doxorubicin (GOOVLO) 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 BCCA 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>BCCA Administration Standard</th>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>

*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 6 cycles or until disease progression or unacceptable toxicity occurs.

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</td>
<td>greater than or equal to 100</td>
<td>175 mg/m²</td>
</tr>
<tr>
<td>less than 1</td>
<td>less than 100</td>
<td>delay until recovery; resume at 175 mg/m²</td>
</tr>
</tbody>
</table>

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</td>
<td>less than or equal to 1.25 x ULN</td>
<td>175</td>
</tr>
<tr>
<td>less than 10 x ULN</td>
<td>1.26-2 x ULN</td>
<td>135</td>
</tr>
<tr>
<td>less than 10 x ULN</td>
<td>2.01-5 x ULN</td>
<td>90</td>
</tr>
<tr>
<td>greater than or equal to 10 x ULN</td>
<td>greater than 5 x ULN</td>
<td>not recommended</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 BCCA Cancer Drug Manual).

**PRECAUTIONS:**

1. **Hypersensitivity**: Reactions are common. See BCCA Hypersensitivity Guidelines

<table>
<thead>
<tr>
<th><strong>mild</strong> symptoms (e.g. mild flushing, rash, pruritus)</th>
<th>• complete PACLitaxel infusion. Supervise at bedside • no treatment required</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>moderate</strong> symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension)</td>
<td>• 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.</td>
</tr>
<tr>
<td><strong>severe</strong> symptoms (i.e. one or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)</td>
<td>• stop PACLitaxel infusion • give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated • discontinue PACLitaxel therapy. Consider use of docetaxel (GOOVDOC)</td>
</tr>
</tbody>
</table>

2. **Extravasation**: PACLitaxel causes pain and tissue necrosis if extravasated. Refer to BCCA 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.

Date activated: N/A

Dated revised: 1 Aug 2016 (Size of filter specified, TALLman lettering formatted)