BCCA Protocol Summary for Primary Treatment of Stage III less than or equal to 1 cm Visible Residual Invasive Epithelial Ovarian Cancer or Stage I Grade 3 or Stage II Grade 3 Papillary Serous Ovarian Cancer Using Intravenous and Intraperitoneal PACLitaxel and Intraperitoneal CARBOplatin

**Protocol Code:** GOOVIPPC

**Tumour Group:** Gynecology

**Contact Physician:** Paul Hoskins

**Contact Pharmacist:** James Conklin

**ELIGIBILITY:**
- First-line treatment of stage III invasive epithelial ovarian cancer, (epithelial ovarian, primary peritoneal, or fallopian tube carcinoma) residual less than or equal to 1 cm
- First-line treatment of Stage I Grade 3 and Stage II Grade 3 papillary serous ovarian cancer, residual less than or equal to 1 cm, including no visible residual disease
- First-line treatment of low stage clear cell ovarian cancer (i.e., Stage 1c based upon positive washings or surface positivity, or any Stage II): eligible for 3 cycles
- Post-primary debulking surgery
- Placement of intraperitoneal catheter should be performed at the primary laparotomy by individual skilled in its placement* (*see [www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Gynecology/OvaryEpithelial/Management](www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Gynecology/OvaryEpithelial/Management))

**EXCLUSIONS:**
- Age greater than 80
- ECOG performance status greater than 2
- Borderline (low malignant potential) tumours
- Gynecologic tumours of origin or histology other than listed above, in Eligibility
- Prior chemotherapy or radiotherapy for this malignancy
- Bowel obstruction
- Brain metastases
- Stage IV disease
- Relapse or recurrence
- Bilirubin greater than or equal to 5xULN or ALT greater than or equal to 10xULN
- Residual greater than 1 cm

**RELATIVE CONTRAINDICATIONS:**
- Pre-existing motor or sensory neuropathy greater than grade 2
TESTS:
- Baseline: CBC & diff, platelets, creatinine, best tumour marker (CA 125, CA 15-3, CA 19-9), LFT’s, camera nuclear renogram for GFR (if available)
- Day 14 after first cycle (and in subsequent cycle if dose modification made): CBC & diff
- Before each treatment (Day 1): CBC & diff, creatinine (if indicated), any initially elevated tumour marker
- Before each treatment (Day 8): CBC & diff [NB – results not needed prior to treatment as no dosage adjustment to be made on Day 8]

PREMEDICATIONS:

On Day 1 (IV PACLtxel + intraperitoneal CARBOplatin):
- **PACLtxel must not be started unless the following drugs have been given:**
  - 45 minutes prior to PACLtxel:
    - dexamethasone 20 mg IV in 50 mL NS over 15 minutes (unless oral dexamethasone 20mg 12 and 6 hours before PACLtxel has been given)
  - 30 minutes prior to PACLtxel:
    - diphenhydrAMINEe 50 mg IV and ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in same bag)
    - ondansetron 8 mg po 30 minutes pre-CARBOplatin

On Day 8 (intraperitoneal PACLtxel):
- **PACLtxel must not be started unless the following drugs have been given:**
  - 45 minutes prior to PACLtxel:
    - dexamethasone 10 mg IV in 50 mL NS over 15 minutes (unless oral dexamethasone 20 mg 12-hours and 6-hours before PACLtxel has been given)
  - 30 minutes prior to PACLtxel:
    - diphenhydrAMINE 25 mg IV and ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in same bag)

ANTIEMETIC THERAPY POST-CHEMOTHERAPY:
- dexamethasone 4 mg PO q12h for 4 doses, beginning in the evening of treatment day (following Day 1 only)
- dimenhyDRINATE 50-100 mg PO q6h prn nausea/vomiting
- prochlorperazine 10 mg PO q6h prn nausea/vomiting
- if delayed emesis occurs, consider adding ondansetron to regimen
TREATMENT:

q3week cycle (x6 cycles if surgery has occurred; x 3 cycles if clear cell (see Eligibility section); or to complete 6 cycles of chemotherapy treatment if chemotherapy began prior to surgery)

Nurses should use BCCA Nursing Practice Reference C-252 for guidance on delivery of IP chemotherapy.

If IP access device fails, patients will complete treatment according to GOOVCATX protocol, modified to a q3week treatment interval.

If debulking surgery has included bowel resection, IP portion of chemotherapy should be omitted from the treatment cycle that follows the surgery.

DAY ONE (give PACLitaxel first)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Route</th>
<th>BCCA Administration Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>175 mg/m²</td>
<td>IV</td>
<td>in 500 mL NS over 3 hours</td>
</tr>
<tr>
<td></td>
<td>(or conservative dosing of 155 mg/ m² or 135 mg/ m²)*</td>
<td></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>[refer to CDM monograph for dose adjustments if bilirubin greater than 1.25xULN]</td>
<td></td>
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</tr>
<tr>
<td>CARBOplatin</td>
<td>AUC = 6</td>
<td>IP</td>
<td>in 1000 mL NS, infused as rapidly as possible, by gravity</td>
</tr>
<tr>
<td></td>
<td>Dose = 6 x (GFR +25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NS solution for injection</td>
<td>1000 mL</td>
<td>IP</td>
<td>Immediately following infusion of IP CARBOplatin, infused as rapidly as possible, by gravity. Rotate positioning of patient x1 hour, according to Nursing Practice Reference C-252.</td>
</tr>
</tbody>
</table>

* Conservative dosing may be considered in the following cases: existing or potential myelosuppression; reduced bone marrow capacity; elderly i.e. physiologically 75 or greater.

**Measured GFR** (e.g. nuclear renogram) is preferred in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, age greater than 70, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR; the estimated GFR reported by the lab or calculated using the Cockcroft-Gault equation should be capped at 125 mL/min when it is used to calculate the initial CARBOplatin dose. When a nuclear renogram is available, this clearance would take precedence.

Cockcroft-Gault Formula

\[
GFR = \frac{1.04 \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}
\]
Recalculate GFR if, at a point of (optional) checking, creatinine increases by greater than 20% or rises above the upper limit of normal.

DAY EIGHT

[refer to Premedications section of this protocol for Day 8 recommendations]

<table>
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<th>Starting Dose</th>
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<th>BCCA Administration Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>60 mg/m²</td>
<td>IP</td>
<td>in 1000 mL NS, infused as rapidly as possible, by gravity (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
</tr>
<tr>
<td>NS solution for injection</td>
<td>1000 mL</td>
<td>IP</td>
<td>Immediately following infusion of IP PACLitaxel, infused as rapidly as possible, by gravity. Rotate positioning of patient for one hour, according to Nursing Practice Reference C-252</td>
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</table>

DOSE MODIFICATIONS:

1. **Hematology:**
   a) on Day 1:
      
      | ANC (x 10⁹/L) | Platelets (x 10⁹/L) | Doses (all drugs) |
      |---------------|---------------------|-------------------|
      | greater than or equal to 1.5 | and | greater than or equal to 100 | treat as per nadir |
      | less than 1.5 | or | less than 100 | Delay until recovery. Check counts in one week. |

   b) at nadir:
      
      - If platelet nadir is less than 50, subsequent IP CARBOplatin dose should be reduced to 90% of preceding cycle
      - If neutrophil nadir is less than 0.5, subsequent IV PACLitaxel dose should be reduced by 20 mg/m² from dose of preceding cycle (e.g. 175 mg/m² reduce to 155 mg/m²; 155mg/m² reduce to 135 mg/m²)
      - No adjustments need be made to IP PACLitaxel dose based on nadir counts

NB – No dosage adjustments to be made for hematologic counts on Day 8.

2. **Febrile neutropenia:** Once resolved, reduce subsequent cycle IP CARBOplatin to 90% and IV PACLitaxel by 20 mg/m². Maintain IP PACLitaxel dose at 100%.

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 5 to 10 days, based on duration of arthromyalgias. If disabling arthralgia and/or myalgia persists, reduce subsequent PACLitaxel doses to 135 mg/m^2.

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

5. **Renal dysfunction:** If significant increase (greater than 20%) in creatinine, repeat nuclear renogram (if available) and recalculate CARBOplatin dose using new GFR.

6. **Hepatic dysfunction:** Dose reduction may be required for PACLitaxel (see BCCA Cancer Drug Manual)

7. **Bacterial Peritonitis:** Remove IP access device. After resolution of infection, switch to GOOVCATX protocol, modified to q3week treatment interval, to complete a total of 6 treatment cycles (GOOVIPPC + GOOVCATX combined)

8. **Abdominal Pain:** If Grade 3, i.e. requiring narcotic analgesics or hospital admission, remove IP access device. Switch to GOOVCATX protocol, modified to q3week treatment interval, to complete a total of 6 treatment cycles (GOOVIPPC + GOOVCATX combined)

**PRECAUTIONS:**

1. **Hypersensitivity:** Reactions are common. See BCCA 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/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 |

Refer to BCCA Hypersensitivity Guidelines for appropriate premedications in subsequent cycles.

**NB:** If a patient experiences a hypersensitivity reaction to PACLitaxel or CARBOplatin given intravenously, then that same drug should NOT be given intraperitonealy in that cycle or subsequent cycles. Any rechallenge considered for future treatments should be for the intravenous route only; intraperitoneal treatment with that drug should not be re-instituted.

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

Date activated: 25 Jan 2007 (initial activation was for Vancouver Centre Use only)

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