BC Cancer Protocol Summary for Second Line Treatment of Invasive Epithelial Ovarian, Fallopian Tube or Peritoneal Cancer Relapsing after Primary Treatment Using PACLitaxel and CARBOplatin

Protocol Code: GOOVCATR
Tumour Group: Gynecology
Contact Physician: Dr. Anna Tinker

ELIGIBILITY:
- epithelial ovarian, Fallopian tube or peritoneal cancer relapsing after remission of at least four months’ duration after completion of primary treatment with PACLitaxel and CARBOplatin

EXCLUSIONS:
- isolated brain metastases (use radiation therapy and/or surgery)
- uncontrolled brain metastases in the presence of systemic disease
- AST and/or ALT greater than 10 times the Upper Limit of Normal (ULN)
- total bilirubin greater than 128 micromol/L

RELATIVE CONTRAINDICATIONS:
- pre-existing motor or sensory neuropathy greater than grade 2
- performance status greater than ECOG 3
- intolerable side effects during first line treatment with PACLitaxel and CARBOplatin. Consider using GOOVCARB, GOOVCADR, or GOOVCAG instead.

TESTS:
- Baseline: CBC & diff, platelets, creatinine, tumour marker (CA 125, CA 15-3, CA 19-9), LFT’s (if abnormal liver function is a potential concern), camera nuclear renogram for GFR (optional)
- Day 14 (and Day 21 if using 4 week interval) of first cycle (and in subsequent cycle(s) if a dose modification has been made): CBC & diff, platelets. No need for interim count check once safe nadir pattern has been established.
- Before each treatment: CBC & diff, creatinine, any initially elevated tumour marker, LFT’s (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)
  - ondansetron 8 mg po 30 minutes pre-CARBOplatin

ANTIEMETIC THERAPY POST-CHEMOTHERAPY:
- Antiemetic protocol for moderate emetogenic chemotherapy protocols (see SCNAUSEA)
- dexamethasone 4 mg PO bid for 2 days and dimenhyDRINATE 50 to 100 mg prn after treatment is usually adequate
TREATMENT (give PACLitaxel first):

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>BC Cancer 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>
<tr>
<td>CARBOplatin</td>
<td>Dose = AUC** x (GFR +25)</td>
<td>IV in 250 mL NS over 30 minutes</td>
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</table>

* Conservative dosing (i.e., 155 mg/m² or 135 mg/m²) may be considered in the following cases: ECOG greater than 2, existing or potential myelosuppression; existing or potential arthralgia and myalgia; prior radiotherapy, particularly to the pelvic region; reduced bone marrow capacity. An initial dose of 135 mg/m² is recommended in patients greater than 75 years of age, with escalation to 155 mg/m² and then 175 mg/m² if tolerated.

** use AUC of 6; if extensive prior radiation therapy, use AUC of 5

Repeat every 21-28 days up to a maximum of 6 cycles. May extend to 9 cycles if the patient has not achieved a complete response but is continuing to respond. BC Cancer CAP application must be made to continue beyond 9 cycles. Single agent CARBOplatin at AUC=5 is an alternative (see GOOVCARB).

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.

DOSE MODIFICATIONS:

1. Hematology:

   a) on treatment day:

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Doses (both drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1 and greater than or equal to 100</td>
<td>treat as per nadir (if applicable); otherwise, proceed at same doses</td>
<td></td>
</tr>
<tr>
<td>less than 1* or less than 100</td>
<td>Delay until recovery. If using 21-day interval, switch to 28-day interval. If 2nd delay, use G-CSF or dose reduction.</td>
<td></td>
</tr>
</tbody>
</table>

   * If ANC greater than 0.8 and monocytes greater than or equal to 20%, neutrophil count recovery is likely imminent. Continuation without delay may occur at physician’s discretion.
b) at nadir (until nadir pattern established):

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>PACLtaxel</th>
<th>CARBOplatin*</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5</td>
<td>greater than or equal to 100</td>
<td>100%</td>
<td>120%**</td>
</tr>
<tr>
<td>0.5-1.4</td>
<td>and</td>
<td>greater than or equal to 75</td>
<td>100%</td>
</tr>
<tr>
<td>less than 0.5</td>
<td>and</td>
<td>less than 75</td>
<td>80%</td>
</tr>
<tr>
<td>less than 0.5</td>
<td>and</td>
<td>greater than or equal to 75</td>
<td>80%</td>
</tr>
<tr>
<td>greater than or equal to 0.5</td>
<td>and</td>
<td>less than 75</td>
<td>100%</td>
</tr>
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</table>

febrile neutropenia at any time 80% 80%

* % of previous cycle’s dose, at physician’s discretion. If dose is changed, subsequent nadir counts must be checked.

** If dose has been reduced, dose increase/re-escalation for good nadir counts is not recommended.

2. **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-PACLtaxel**
- **gabapentin 300 mg PO on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 5 to 15 days (based on duration of arthromyalgia)**

If arthralgia and/or myalgia persists, reduce subsequent PACLtaxel doses to 135 mg/m² or switch taxane to DOCEtaxel (GOOVCADX) or gemcitabine (GOOVCAG)

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

4. **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.

5. **Hepatic dysfunction**: Dose reduction may be required for PACLtaxel

<table>
<thead>
<tr>
<th>ALT</th>
<th>Bilirubin</th>
<th>Dose</th>
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<tbody>
<tr>
<td>less than 10 x ULN</td>
<td>and</td>
<td>less than or equal to 1.25 x ULN</td>
</tr>
<tr>
<td>less than 10 x ULN</td>
<td>and</td>
<td>1.26-2 x ULN</td>
</tr>
<tr>
<td>less than 10 x ULN</td>
<td>and</td>
<td>2.01-5 x ULN</td>
</tr>
<tr>
<td>greater than or equal to 10 x ULN</td>
<td>and/or</td>
<td>greater than 5 x ULN</td>
</tr>
</tbody>
</table>
**PRECAUTIONS:**

1. **Hypersensitivity:** Reactions are common. See [BC Cancer Hypersensitivity Guidelines](#).

<table>
<thead>
<tr>
<th>Symptom Level</th>
<th>Instructions</th>
</tr>
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</table>
| **Mild** symptoms (e.g., mild flushing, rash, pruritus) | - complete PACLitaxel infusion. Supervise at bedside  
- no treatment required |

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| **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 |

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| **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. **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) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.