

# BC Cancer Protocol Summary for Primary Treatment of Visible Residual (Extreme Risk) Invasive Epithelial Ovarian, Fallopian Tube or Peritoneal Cancer using CARBOplatin and PACLitaxel

**Protocol Code:**

GOOVCATX

**Tumour Group:**

Gynecologic Oncology

**Contact Physicians:**

Dr. Anna Tinker

## ELIGIBILITY:

- visible residual, invasive epithelial ovarian, fallopian tube or peritoneal cancer, or borderline with invasive implants
- Stage III or IV disease (patients may have upfront or interval debulking surgery – see below)

## EXCLUSIONS:

- no visible residual disease (use protocol GOOVCA~~TM~~ or GOOVCA~~DM~~)
- borderline (low malignant potential) tumours with non-invasive implant – contact BC Cancer
- prior chemotherapy or radiotherapy for this malignancy (use relapse protocols)
- uncontrolled brain metastases
- AST and/or ALT greater than 10 times the upper limit of normal
- 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

## INCOMPLETE PRIMARY SURGERY:

Responders with "incomplete" primary surgery i.e., debulking to less than 2 cm not carried out, should be discussed for consideration of re-laparotomy after 3-4 cycles. Survival benefits may be realised with "interval debulking" after several cycles of chemotherapy.

## NO PRIMARY SURGERY:

If no primary surgery was carried out, these patients are candidates for interval debulking after three or four cycles.

## TESTS:

- Baseline: CBC & diff, platelets, creatinine, tumour markers as indicated (CA 125, CA 15-3, CA 19-9, CEA), bilirubin, ALT, alkaline phosphatase, camera nuclear renogram for GFR (optional)
- Day 14 (and Day 21 if using a 4 week cycle 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
  - If clinically indicated: bilirubin, alkaline phosphatase, GGT, ALT, LDH, total protein, albumin

## 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 in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)
- Antiemetic protocol for highly emetogenic chemotherapy protocols (see [SCNAUSEA](#))

**TREATMENT** (give PACLitaxel first):

Drug	Starting Dose	BC Cancer Administration Guideline
PACLitaxel	175 mg/m <sup>2</sup> *	IV in 250 to 500 mL NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)
CARBOplatin	Dose = AUC** x (GFR +25)	IV in 100 to 250 mL NS over 30 minutes

\* Conservative dosing (i.e., 155 mg/m<sup>2</sup> or 135 mg/m<sup>2</sup>) 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/m<sup>2</sup> is recommended in patients greater than 75 years of age, with escalation to 155 mg/m<sup>2</sup> and then 175 mg/m<sup>2</sup> if tolerated.

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

Repeat every 21-28 days for 6 cycles. May continue to treat until disease progression if the patient has not achieved a complete response but is continuing to respond.

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

$$\text{GFR} = \frac{1.04 \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

Recalculate GFR if, at a point of (optional) checking, creatinine increases by greater than 20% or rises above the upper limit of normal.

If PACLitaxel toxicity is a concern or becomes problematic, consider use of single agent CARBOplatin (GOOVCARB at AUC = 5) or protocols GOOVCAD or GOOVCAg.

## DOSE MODIFICATIONS:

### 1. Hematology:

a) on treatment day:

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	Doses (both drugs)
greater than or equal to 1.0	and	greater than or equal to 100	treat as per nadir (if applicable); otherwise, proceed at same doses
less than 1.0*	or	less than 100	Delay until recovery. If using 21-day interval, switch to 28-day interval. If 2 <sup>nd</sup> delay, use filgrastim (G-CSF) or dose reduction.

\* 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):

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	PACLitaxel*	CARBOplatin*
greater than or equal to 0.5	and	greater than or equal to 75	100%	100%
less than 0.5	and	less than 75	80%	80%
less than 0.5	and	greater than or equal to 75	80%	100%
greater than or equal to 0.5	and	less than 75	100%	80%
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.

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

- 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-PACLitaxel
  - 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 PACLitaxel doses to 135 mg/m<sup>2</sup> or switch taxane to DOCEtaxel (GOOVCA DX)
- Neuropathy:** Dose modification or discontinuation may be required (see BC Cancer Drug Manual).
- 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 PACLitaxel

ALT		Bilirubin	Dose
less than 10 x ULN	and	less than or equal to 1.25 x ULN	175 mg/m <sup>2</sup>
less than 10 x ULN	and	1.26 to 2 x ULN	135 mg/m <sup>2</sup>
less than 10 x ULN	and	2.01 to 5 x ULN	90 mg/m <sup>2</sup>
greater than or equal to 10 x ULN	and/or	greater than 5 x ULN	not recommended

**PRECAUTIONS:**

1. **Hypersensitivity:** Reactions are common. See BC Cancer Hypersensitivity Guidelines

<u>Mild</u> symptoms (e.g., mild flushing, rash, pruritus)	<ul style="list-style-type: none"> <li>▪ complete PACLitaxel infusion. Supervise at bedside</li> <li>▪ no treatment required</li> </ul>
<u>Moderate</u> symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension)	<ul style="list-style-type: none"> <li>▪ stop PACLitaxel infusion</li> <li>▪ give IV diphenhydrAMINE 25 to 50 mg and hydrocortisone IV 100 mg</li> <li>▪ 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.</li> <li>▪ if reaction recurs, discontinue PACLitaxel therapy</li> </ul>
<u>Severe</u> symptoms (i.e. <u>one</u> or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)	<ul style="list-style-type: none"> <li>▪ stop PACLitaxel infusion</li> <li>▪ give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated</li> <li>▪ discontinue PACLitaxel therapy</li> </ul>

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.**