

# BC Cancer Protocol Summary for Alternative Treatment of Gynecological Malignancies using CISplatin and PACLitaxel

**Protocol Code:** GOCISP  
**Tumour Group:** Gynecologic Oncology  
**Contact Physician:** GO Systemic Therapy

## ELIGIBILITY:

Patients must have:

- Previous non-life threatening infusion-related reactions to CARBOplatin, and
- Been treated with and eligible for the following protocols:
  - GOOVCATM, GOOVCATR, GOOVCATX, GOOVDDCAT
  - GOCXCAT, GOCXCATP
  - GOENDAJCAT, GOENDAVCAT

## EXCLUSIONS:

Patient must not have:

- Creatinine clearance less than 45 mL/min at baseline

## TESTS:

- Baseline: CBC & Diff, creatinine, ALT, total bilirubin
- Baseline, if clinically indicated: CA 125, CA 15-3, CA 19-9, CEA, SCC, sodium, potassium, magnesium, calcium, LDH, GGT, alkaline phosphatase
- Before each treatment: CBC & Diff, creatinine, total bilirubin, ALT
- If clinically indicated: sodium, potassium, magnesium, calcium, LDH, GGT, alkaline phosphatase, CA 125, CA 15-3, CA 19-9, CEA, SCC

## 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:

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	175 mg/m <sup>2</sup> * on day 1	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)
CISplatin	75 mg/m <sup>2</sup> /day on day 1	Prehydrate with 1000 mL NS over 1 hour, then CISplatin IV in 500 mL NS with potassium chloride 20 mEq, magnesium sulfate 1 g, mannitol 30 g over 1 hour

- Repeat every 21 days to complete total number of cycles in original CARBOplatin/PACLitaxel protocol.

\* 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.

## DOSE MODIFICATIONS:

### 1. Hematology

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	100%
Less than 1.0	or	Less than 100	Delay

### 2. Renal Dysfunction

Creatinine Clearance (mL/min)	CISplatin dose
Greater than or equal to 60	75 mg/m <sup>2</sup>
45 to 59	35 mg/m <sup>2</sup>
Less than 45	Delay

**3. 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 switching to an alternate taxane may be considered

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

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

ALT		Total 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	1.26-2 x ULN	135 mg/m <sup>2</sup>
Less than 10 x ULN	and	2.01-5 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 to PACLitaxel are common. See BC Cancer Hypersensitivity Guidelines

<i>Mild</i> 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>
<i>moderate</i> 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>
<i>severe</i> symptoms (i.e. <i>one</i> 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. **Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Use caution with pre-existing renal dysfunction.
5. **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.

**Contact the GO Systemic Therapy physician at your regional cancer centre or GO Systemic Therapy Chair with any problems or questions regarding this treatment program.**

**References:**

Ozols RF, Bundy BN, Greer BE, et al. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group Study. *J Clin Oncol* 2003;21:3194-200.