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

***Protocol Code**:* *GOCISP*

***Tumour Group**:* *Gynecologic Oncology*

***Contact Physician**:* *Dr. Anna Tinker*

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
  - GOENDCAT, GOENDAJCAT, GOENDAVCAT

EXCLUSIONS:
Patient must not have:
- Creatinine clearance less than 45 mL/min at baseline

TESTS:
- Baseline: CBC & diff, platelets, creatinine, sodium, potassium, magnesium, tumour marker (CA 125, CA 15-3, CA 19-9), alkaline phosphatase, ALT, bilirubin, GGT (if indicated)
- Before each treatment: CBC & diff, platelets, creatinine, any initially elevated tumour marker
  - If clinically indicated: bilirubin, ALT, alkaline phosphatase, sodium, potassium, magnesium

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
(Administer PACLitaxel first)		
PACLitaxel	175 mg/m^2 * 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^2/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/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.

DOSE MODIFICATIONS:

1. **Hematology**

ANC (x 10^9/L)		**Platelets (x 10^9/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^2
45 to 59	35 mg/m^2
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 days (based on duration of arthromyalgia)

If arthralgia and/or myalgia persists, reduce subsequent PACLitaxel doses to 135 mg/m^2 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		**Bilirubin**	**Dose**
less than 10 x ULN	and	less than or equal to 1.25 x ULN	175 mg/m^2
less than 10 x ULN	and	1.26-2 x ULN	135 mg/m^2
less than 10 x ULN	and	2.01-5 x ULN	90 mg/m^2
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

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 to 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

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.

Call Dr. Anna Tinker or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.
Date activated:
Date revised:

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.