BC Cancer Protocol Summary for Induction Treatment of Locally Advanced Cervical Cancer using Weekly CARBOplatin and PACLitaxel

Protocol Code	*GOCXLACATW*
Tumour Group	*Gynecology*
Contact Physician	*GO Systemic Therapy*

ELIGIBILITY:
Patient must have:
- Newly diagnosed locally advanced cervical cancer, meeting one of the following staging criteria, per FIGO 2018:
  - IB1-3 disease with pelvic nodal involvement
  - IIA or IIB, with or without pelvic nodal involvement
  - IIIB or IVA with or without pelvic nodal involvement
- Plan for treatment with concurrent CISplatin and radiation therapy (GOCXCRT) following GOCXLACATW completion

Patient should have:
- Good performance status

Note: Chemoradiation planning should be initiated early to allow treatment to commence 7 days after completion of the last GOCXLACATW dose. Every effort should be made to minimize delays in chemoradiation initiation.

EXCLUSIONS:
Patient must not have:
- Para-aortic lymph node involvement

TESTS:
- Baseline: CBC & Diff, creatinine, ALT, total bilirubin
- Baseline, if clinically indicated: alkaline phosphatase, LDH, GGT, sodium, potassium, magnesium, calcium, CA 125, CA 15-3, CA 19-9, CEA, SCC
- Before each treatment: CBC & Diff, creatinine, total bilirubin, ALT
- If clinically indicated, before each treatment: alkaline phosphatase, LDH, GGT, sodium, potassium, magnesium, calcium, 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 10 mg IV in 50 mL NS over 15 minutes

30 minutes prior to PACLitaxel:

- diphenhydrAMINE 25 mg IV in 50 mL NS over 15 minutes and famotidine 20 mg IV in 100 mL NS over 15 minutes (Y-site compatible)
- **NOTE:** If no PACLitaxel hypersensitivity reactions occur in Cycle 1, no hypersensitivity premedications may be needed for subsequent doses and may be omitted at physician's discretion (dexamethasone 8 to 12 mg PO may be given in place of the regimen in the first bullet point above).
- Antiemetic protocol for moderately emetogenic chemotherapy protocols (see SCNAUSEA).

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	80 mg/m^2	IV in 100 to 500 mL NS over 60 minutes (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)
CARBOplatin	Dose = AUC 2 x (GFR* + 25)	IV in 100 to 250 mL NS over 30 minutes

- Repeat weekly for 6 weeks. Chemoradiation with GOCXCRT should be initiated in week 7 (i.e. 7 days after the last induction treatment).

**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

$$\text{CrCl} = \frac{\text{N (140-age) x weight (kg)}}{\text{serum creatinine (micromol/L)}}$$

Where N = 1.04 for females, and 1.23 for males

Note: The *same* method of estimation should be used throughout the treatment course (i.e. if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft-Gault estimate).

NOTE: If creatinine increases by greater than 20% or rises above the upper limit of normal, recalculate GFR and recalculate CARBOplatin dose using new GFR.

DOSE MODIFICATIONS:

1. **Hematology:**

On treatment days:

ANC (X 10^9/L)		**Platelets (x 10^9/L)**	**PACLitaxel Management**	**CARBOplatin Management**
Greater than or equal to 1.0	and	Greater than or equal to 75	100%	100%
Greater than or equal to 1.0	and	Greater than 50 to 74	100%	Omit from this week's treatment, then reduce to 80% for all future doses

Less than 1.0	or	Less than or equal to 50	• **If first occurrence:**
			  • Omit this week's treatment.
			  • Once ANC recovers to greater than or equal to 1.0 and platelets greater than or equal to 75, resume treatment at 80% for all future doses.
			• **If second occurrence:**
			  • Discontinue treatment	

Febrile neutropenia			• **If first occurrence:**
			  • Omit this week's treatment.
			  • Once ANC recovers to greater than or equal to 1.0 and platelets greater than or equal to 75, resume treatment at 80% for all future doses.
			• **If second occurrence:**
			  • Discontinue treatment	

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-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)

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

3. **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**:

ALT		Total Bilirubin	PACLitaxel Dose
Less than 10 x ULN	and	Less than or equal to 1.25 x ULN	100%
Less than 10 x ULN	and	Greater than 1.25 x ULN to 2 x ULN	75% If ALT and total bilirubin continue to rise despite dose reduction, discontinue treatment
Greater than or equal to 10 x ULN	and/or	Greater than 2 x ULN to 5 x ULN	Omit If recovery to ALT to less than 10 x ULN and total bilirubin to less than 1.25 x ULN occurs within 7 days, resume treatment at 75% dose.
Greater than or equal to 10 x ULN	and/or	Greater than 5 x ULN	Not recommended

ULN = upper limit of normal

PRECAUTIONS:

1. **Hypersensitivity**: Reactions are common. See BC Cancer Protocol Summary for Management of Infusion-Related Reactions to Chemotherapeutic Agents – SCDRUGRX

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, generalized 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.

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

REFERENCES:

1. McCormack M, Eminowicz G, Gallardo D et al. Induction Chemotherapy Followed by Standard Chemoradiotherapy versus Standard Chemoradiotherapy Alone in Patients with Locally Advanced Cervical Cancer (GCIG INTERLACE): an International, Multicentre, Randomised Phase 3 Trial.Lancet 2024; 404: 1525–35