

# BC Cancer Protocol Summary for Treatment of Primary Advanced or Recurrent Endometrial Cancer using CARBOplatin and PACLitaxel

**Tumour Group:** *Gynecology*

**Protocol Code:** *GOENDCAT*

**Contact Physician:** *Dr. Yvette Drew*

**Note:** new patients should be started on GOENDAJCAT and GOENDAVCAT instead of this protocol. Only use GOENDCAT to complete treatment with existing patients.

## ELIGIBILITY:

- advanced endometrial cancer, including malignant mixed Mullarian tumour (MMMT) or carcinosarcoma
  - Stage I papillary serous or MMTT or clear cell, with myometrial invasion
  - Stage 1a, Grade 3 endometrioid with myometrial invasion or other risk feature
  - Stage 1b, Grade 3 endometrioid
  - Stage II, Grade 3
  - Stage III or IV (any grade\*\*)
- recurrent disease

\* any component if mixed histology

\*\* though if Grade 1, consider hormonal therapy

## EXCLUSIONS:

- uterine sarcomas, small cell histology
- 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

## TESTS:

- Baseline: CBC & diff, platelets, creatinine
- If clinically indicated at baseline: tumour marker (CA 125, CA 15-3, CA 19-9, CEA), ALT, alkaline phosphatase, bilirubin, camera nuclear renogram for GFR
- 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
- If clinically indicated before each treatment: any initially elevated tumour marker, ALT, alkaline phosphatase, bilirubin, GGT, LDH, protein level, 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:

- 3 cycles if to be followed by radical radiation therapy (i.e. patients with disease that is radio-encompassable)
- up to 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.

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.

**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 G-CSF or dose reduction.

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.

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)
 If arthralgia and/or myalgia persists, reduce subsequent PACLitaxel doses to 135 mg/m<sup>2</sup> or switch PACLitaxel to DOCEtaxel (GOENDCAD).
3. **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.

4. **Hepatic dysfunction:** reduce PACLitaxel dose:

ALT		Total bilirubin	Dose (mg/m <sup>2</sup> )
less than 10 x ULN	and	less than or equal to 1.25 x ULN	175
less than 10 x ULN	and	1.26-2 x ULN	135
less than 10 x ULN	and	2.01-5 x ULN	90
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 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/hr for 5 minutes, 30 mL/hr for 5 minutes, 40 mL/hr for 5 minutes, then 60 mL/hr 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. Yvette Drew or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.**