

# BC Cancer Protocol Summary for Primary Treatment of Cancer of Unknown Primary Origin Using CARBOplatin and PACLitaxel

**Protocol Code:**

**Tumour Group:**

**Contact Physician:**

**Contact Pharmacist:**

*PUCAT*

*Primary Unknown*

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## ELIGIBILITY:

- metastatic carcinoma of unknown origin
- primary cancers with potential for cure or reliable palliation ruled out
- pathology: adenocarcinoma, squamous or undifferentiated tumours
- adequate renal, cardiac and bone marrow function
- measurable or evaluable index lesion (serum tumour marker useful)

## EXCLUSIONS:

- brain metastases

## RELATIVE CONTRAINDICATIONS:

- pre-existing motor or sensory neuropathy greater than grade 2

## TESTS:

- Baseline: CBC & diff, platelets, serum creatinine, [ALT](#), [Alk Phos](#), [bilirubin](#), [albumin](#), [GGT](#), [LDH](#), chest X-ray, camera nuclear renogram for GFR (if available).
- Before each treatment: CBC & diff, serum creatinine, any initially elevated tumor marker
- [If clinically indicated: bilirubin](#)

## 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)
- ondansetron 8 mg po 30 minutes pre-CARBOplatin

## ANTIEMETIC THERAPY POST-CHEMOTHERAPY:

- dexamethasone 4 mg po BID for 2 days and dimenhyDRINATE 50-100 mg prn after treatment is usually adequate

**TREATMENT** (give PACLitaxel first):

Drug	Starting Dose	BC Cancer Administration Standard
PACLitaxel	200 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

\* use AUC of 6

$$\text{GFR} = \frac{N \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}} \quad N = 1.04 \text{ (women) or } 1.23 \text{ (men)}$$

The estimated GFR 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.

Repeat every 21 days for 6-9 cycles.

**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

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 75	80%	100%
greater than 0.5	and	less than 75	100%	80%
febrile neutropenia at any time			80%	80%

2. **Arthralgia and/or myalgia:** If arthralgia and/or myalgia of grade 2 (moderate) or higher is not relieved by adequate doses of 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 7 to 10 days
 If arthralgia and/or myalgia persists, reduce subsequent PACLitaxel doses to 135 mg/m<sup>2</sup>.
3. **Neuropathy:** Dose modification or discontinuation may be required (see BC Cancer Drug Manual).
4. **Renal dysfunction:** If significant increase (greater than 20%) in creatinine, repeat nuclear renogram (if available) and recalculate CARBOplatin dose using new GFR.
5. **Hepatic dysfunction:** Dose reduction may be required for PACLitaxel (see BC Cancer Drug Manual)

**PRECAUTIONS:**

1. **Hypersensitivity:** Reactions 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 25-50 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.

**Call Dr. Anna Tinker at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

**Reference**

Briasoulis E, Kalofonos H, Bafaloukos D, et al. Carboplatin plus paclitaxel in unknown primary carcinoma: a phase II Hellenic Cooperative Oncology Group Study. *J Clin Oncol* 2000;18(17):3101-7.