

# BCCA Protocol Summary for Primary Treatment of Cancer of Unknown Primary Origin Using CARBOplatin and PACLItaxel

<b>Protocol Code:</b>	<i>PUCAT</i>
<b>Tumour Group:</b>	<i>Primary Unknown</i>
<b>Contact Physician:</b>	<i>Dr. Anna Tinker</i>
<b>Contact Pharmacist:</b>	<i>Dr. Mário de Lemos</i>

## 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, LFT's, chest X-ray, camera nuclear renogram for GFR (if available).
- Before each treatment: CBC & diff, serum creatinine, any initially elevated tumor marker, LFT's (if clinically indicated)

## 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 and Ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in bag)
- 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 **PACLI**taxel first):

Drug	Starting Dose	BCCA Administration Standard
<b>PACLI</b> taxel	200 mg/m <sup>2</sup>	IV in 500 mL NS over 3 hours (use non-PVC equipment, in-line filter)
<b>CARBO</b> platin	Dose = AUC* x (GFR +25)	IV in 250 mL D5W 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 up to a maximum of 6 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
less than 1.0	or	less than 100	delay until recovery

b) at nadir:

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	<b>PACLI</b> taxel	<b>CARBO</b> platin
greater than 1.5	and	greater than 100	100%	120%*
0.5-1.4	and	75-99	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%

\*no escalation above 120% of cycle 1 dose

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-**PACLI**taxel
  - Gabapentin 300 mg po on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 7-10 days
 If arthralgia and/or myalgia persists, reduce subsequent **PACLI**taxel doses to 135 mg/m<sup>2</sup>.
3. **Neuropathy:** Dose modification or discontinuation may be required (see BCCA Cancer Drug Manual).
4. **Renal dysfunction:** If significant increase (greater than 20%) in creatinine, repeat nuclear renogram (if available) and recalculate **CARBO**platin dose using new GFR.
5. **Hepatic dysfunction:** Dose reduction may be required for **PACLI**taxel (see BCCA Cancer Drug Manual)

**PRECAUTIONS:**

1. **Hypersensitivity:** Reactions are common. See BCCA Hypersensitivity Guidelines

<i>Mild</i> symptoms (e.g., mild flushing, rash, pruritus)	<ul style="list-style-type: none"> <li>▪ complete <b>PACLI</b>taxel 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 <b>PACLI</b>taxel infusion</li> <li>▪ give IV Diphenhydr<b>AMINE</b> 25-50 mg and Hydrocortisone IV 100 mg</li> <li>▪ after recovery of symptoms resume <b>PACLI</b>taxel 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 <b>PACLI</b>taxel therapy</li> </ul>
<i>Severe</i> 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 <b>PACLI</b>taxel infusion</li> <li>▪ give IV antihistamine and steroid as above. Add Epinephrine or bronchodilators if indicated</li> <li>▪ discontinue <b>PACLI</b>taxel therapy</li> </ul>

2. **Extravasation:** **PACLI**taxel causes pain and may, rarely, cause tissue necrosis if extravasated. Refer to BCCA 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.**

Date activated: 1 March 2007

Date revised: 1 Apr 2011 (estimated GFR capped, reformatted with TALLman lettering)

### **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.