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

***Protocol Code**:*	*PUCAT*
***Tumour Group**:*	*Primary Unknown*
***Contact Physician**:*	*Dr. Anna Tinker*

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, creatinine, ALT, alkaline phosphatase, total bilirubin, albumin, GGT, LDH, chest X-ray, camera nuclear renogram for GFR (if available).
- Before each treatment: CBC & Diff, creatinine, any initially elevated tumor marker
- If clinically indicated: total 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)
- Antiemetic protocol for highly emetogenic chemotherapy protocols (see SCNAUSEA)

Activated: 1 Mar 2007 Revised: 1 Dec 2024 (Removed antiemetic therapy post-chemotherapy section, added emetogenic risk category, contact pharmacist removed)

TREATMENT (give PACLitaxel first):

Drug	Starting Dose	BC Cancer Administration Guideline
PACLitaxel	200 mg/m^2	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

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

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 10^9/L)		Platelets (x 10^9/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 10^9/L)		Platelets (x 10^9/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^2.

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

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 25-50 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 epinephhrine 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.

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.