BCCA 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

Contact Pharmacist: Dr. Mário de Lemos

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 PACLitaxel first):

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>BCCA Administration Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>200 mg/m²</td>
<td>IV in 500 mL NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
</tr>
<tr>
<td>CARBOplatin</td>
<td>Dose = AUC* x (GFR +25)</td>
<td>IV in 250 mL NS over 30 minutes</td>
</tr>
</tbody>
</table>

* use AUC of 6

GFR = \[\frac{N \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}\]

N = 1.04 (women) or 1.23 (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:
   
<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Doses (both drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1 and greater than or equal to 100</td>
<td>treat as per nadir</td>
<td></td>
</tr>
<tr>
<td>less than 1 or less than 100</td>
<td>delay until recovery</td>
<td></td>
</tr>
</tbody>
</table>

   b) at nadir:
   
<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>PACLitaxel</th>
<th>CARBOplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than 1.5 and greater than 100</td>
<td>100%</td>
<td>120%*</td>
<td></td>
</tr>
<tr>
<td>0.5-1.4 and 75-99</td>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>less than 0.5 and less than 75</td>
<td>80%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>less than 0.5 and greater than 75</td>
<td>80%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>greater than 0.5 and less than 75</td>
<td>100%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>febrile neutropenia at any time</td>
<td>80%</td>
<td>80%</td>
<td></td>
</tr>
</tbody>
</table>

*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-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/m².

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 CARBOplatin dose using new GFR.
5. **Hepatic dysfunction**: Dose reduction may be required for PACLitaxel (see BCCA Cancer Drug Manual)

**PRECAUTIONS:**

1. **Hypersensitivity**: Reactions are common. See BCCA 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 epinephrine or bronchodilators if indicated  
   |▪ discontinue PACLitaxel therapy |

2. **Extravasation**: PACLitaxel 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 Aug 2016 (size of filter specified, TALLman lettering formatted)

Reference