BC Cancer Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using Weekly PACLitaxel (3 Weeks out of 4 Weeks Schedule)

**Protocol Code:** BRAVTW

**Tumour Group:** Breast

**Contact Physician:** Dr. Stephen Chia

**ELIGIBILITY:**
- First, second, or third line treatment of metastatic breast cancer patients with ECOG performance status 0, 1, or 2, and greater than 3 month life expectancy
- Patients unable to tolerate BRAVTAX, such as those with limited marrow reserve, or who are frail and / or elderly

**TESTS:**
- Baseline: CBC & diff, platelets, bilirubin, ALT
- Baseline if clinically indicated: alk phos, LDH, GGT, CA15-3
- Prior to each treatment: CBC & diff, platelets
- If clinically indicated: bilirubin, ALT

**PREMEDICATIONS:**
- PACLitaxel must not be started unless the following drugs have been given:
  - 45 minutes prior to PACLitaxel:
    - dexamethasone 10 mg IV in 50 mL NS over 15 minutes
    - diphenhydramINE 25 mg IV and ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in bag)

  - If no PACLitaxel infusion reactions occur, no premedications may be needed for subsequent PACLitaxel doses and may be omitted at physician’s discretion.
  - If infusion reactions occur, premedications for re-challenge include dexamethasone 20 mg PO given 12 hours and 6 hours prior to treatment, plus IV premedications given 30 minutes prior to PACLitaxel: dexamethasone 10 mg, diphenhydramINE 25 mg, and H2-antagonist (e.g., ranitidine 50 mg). If no infusion reactions occur, standard premedications (see above) will be used for subsequent PACLitaxel doses.

  - Additional antiemetics not usually required.
**TREATMENT:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>90 mg/m² once weekly x 3 weeks, then 1 week rest</td>
<td>IV in <strong>100 to 250 mL NS</strong> over 1 hour (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
</tr>
</tbody>
</table>

- Cycle length = 4 weeks, repeat every 28 days until disease progression
- **Discontinue** if progression or lack of clinical benefit after 3 cycles.

**DOSE MODIFICATIONS:**

1. **Hematological**

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Dose</th>
<th>Dose after Neutropenic Sepsis on PACLitaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0 and greater than or equal to 100</td>
<td>90 mg/m²</td>
<td>65 mg/m²</td>
<td></td>
</tr>
<tr>
<td>less than 1.0 or less than 100</td>
<td><strong>Contact Physician:</strong> Delay treatment. Reduce next dose to 65 mg/m²</td>
<td>delay</td>
<td></td>
</tr>
</tbody>
</table>

Note: patients who cannot tolerate treatment after a dose reduction or require a treatment delay of greater than 2 weeks, should discontinue treatment.
2. Non-Hematological Toxicity

<table>
<thead>
<tr>
<th>Grade</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2 motor or sensory neuropathy</td>
<td>Decrease dose by 10 mg/m²</td>
</tr>
<tr>
<td>All other grade 2 non-hematological toxicity</td>
<td>Hold treatment until toxicity resolved to less than or equal to grade 1 Decrease subsequent doses by 10 mg/m²</td>
</tr>
<tr>
<td>greater than or equal to Grade 3</td>
<td>Discontinue treatment</td>
</tr>
</tbody>
</table>

Note: patients who cannot tolerate treatment after 2 dose reductions or require a treatment delay of greater than 2 weeks, should discontinue treatment

3. Hepatic Dysfunction

<table>
<thead>
<tr>
<th>Bilirubin (micromol/L)</th>
<th>ALT</th>
<th>Dose (mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than or equal to 25 and less than 2 x ULN</td>
<td>90 mg/m²</td>
<td></td>
</tr>
<tr>
<td>less than or equal to 25 and greater than or equal to 2 x ULN with no liver metastases or greater than or equal to 5 x ULN with liver metastases</td>
<td>65 mg/m²</td>
<td></td>
</tr>
<tr>
<td>26-50</td>
<td></td>
<td>40 mg/m²</td>
</tr>
<tr>
<td>greater than 50</td>
<td></td>
<td>25 mg/m²</td>
</tr>
</tbody>
</table>

ULN = upper limit of normal

4. 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 7-10 days
If arthralgia and/or myalgia persist, reduce subsequent PACLitaxel doses to 65 mg/m².

4. **Neuropathy**: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

**PRECAUTIONS:**

1. **Infusion-related reactions**: Reactions to paclitaxel are common. See BC Cancer Infusion-Related Reactions 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 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. Stephen Chia or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

**References:**

2. Rugo HS, et al. Randomized phase III trial of weekly paclitaxel compared to weekly nanoparticle albumin bound nab-paclitaxel or ixabepilone with or without bevacizumab as first line therapy for locally recurrent or metastatic breast cancer. J Clin Oncol 2012;30(18)suppl:CRA1002