**ELIGIBILITY:**
A number of studies suggest that the schedule of delivery of PACLitaxel is important in maximizing efficacy. The preferred delivery method of PACLitaxel before AC chemotherapy is either every two weeks with G-CSF (see protocol BRLATACG) or weekly for 12 weeks, as described in this protocol.

- Locally advanced and inflammatory breast cancer in patients less than or equal to 65 years of age or fit patients greater than 65 years of age.

**EXCLUSIONS:**
- Severe cardiovascular disease with LVEF less than 45%
- AST and/or ALT greater than 10 times the Upper Limit of Normal (ULN)
- total bilirubin greater than 128 micromol/L

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

**PREMEDICATIONS:**
- For the 4 cycles (=12 weeks) of PACLitaxel: 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 hypersensitivity reactions occur, no premedications may be needed for subsequent PACLitaxel doses and may be omitted at physician’s discretion.
  - If hypersensitivity 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, diphehydrAMINE 25 mg, and H2-antagonist (e.g., ranitidine 50 mg). If no hypersensitivity reactions occur, standard premedications (see above) will be used for subsequent PACLitaxel doses.
  - Additional antiemetics not usually required.
  - For the 4 cycles of DOXOrubicin and cyclophosphamide: Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)
TREATMENT:
- 4 consecutive cycles of PACLitaxel (Cycles 1 to 4)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>80 mg/m² weekly</td>
<td>IV in 250 mL* NS over 1 hour (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
</tr>
</tbody>
</table>

*Use 100 mL for dose less than 87 mg

- Cycle length = 3 weeks, repeat every 21 days for 4 cycles (= 12 weeks total), followed by
- 4 consecutive cycles of DOXOrubicin and cyclophosphamide (Cycles 5 to 8)
- Cycle 5 to start on week 13

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOXOrubicin</td>
<td>60 mg/m²</td>
<td>IV push</td>
</tr>
<tr>
<td>cyclophosphamide</td>
<td>600 mg/m²</td>
<td>IV in 100 to 250* mL NS over 20 min to 1 hour</td>
</tr>
</tbody>
</table>

*Use 250 mL for dose greater than 1000 mg

- Repeat every 21 days for 4 cycles

DOSE MODIFICATIONS:

1. Hematological
   For cycles of PACLitaxel only:

<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 1.5 and Greater than or equal to 90</td>
<td>80 mg/m²</td>
<td>65 mg/m²</td>
<td></td>
</tr>
<tr>
<td>1.0 to less than 1.5* or 70 to less than 90</td>
<td>65 mg/m²</td>
<td>50 mg/m²</td>
<td></td>
</tr>
<tr>
<td>Less than 1.0 or Less than 70</td>
<td>Delay and reduce next dose to 65mg/m² or add filgrastim</td>
<td>delay</td>
<td></td>
</tr>
</tbody>
</table>

* if ANC 1.0 to less than 1.5 and patient fit and well can consider full dose of 80 mg/m² at discretion of physician

BC Cancer Agency Protocol Summary BRALATWAC
Activated: 1 Nov 2014  Revised: 1 Aug 2016 (Institution name, Tests)
Warning: The information contained in these documents are a statement of consensus of BC Cancer Agency professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer Agency's terms of use available at [www.bccancer.bc.ca/legal.htm](http://www.bccancer.bc.ca/legal.htm)
For cycles of DOXOrubicin and cyclophosphamide only:

<table>
<thead>
<tr>
<th>ANC (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>Dose (both drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than or equal to 1.5 and Greater than 90</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>1 to 1.49 or 70 to 90</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>Less than 1 or Less than 70</td>
<td>Delay</td>
<td></td>
</tr>
</tbody>
</table>

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 of paclitaxel 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 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>

3. Hepatic dysfunction:

For Cycles 1 to 4: Reduce PACLitaxel dose:

<table>
<thead>
<tr>
<th>ALT or AST</th>
<th>Total bilirubin</th>
<th>Dose (mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 10 x ULN and less than or equal to 1.25 x ULN</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>less than 10 x ULN and 1.26 to 2 x ULN</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>less than 10 x ULN and 2.01 to 5 x ULN</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>greater than or equal to 10 x ULN and/or greater than 5 x ULN</td>
<td>not recommended</td>
<td></td>
</tr>
</tbody>
</table>

ULN = upper limit of normal

For Cycles 5 to 8: Dose modifications required for DOXOrubicin. Refer to BC Cancer Drug manual.

4. Renal dysfunction: Dose modification may be required for Cyclophosphamide. Refer to BC Cancer Drug Manual.

5. 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:
   - 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 persist, reduce subsequent PACLitaxel doses to 65mg/m².

6. Neuropathy: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).
PRECAUTIONS:
1. **Hypersensitivity:** Reactions to PACLitaxel 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 to 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:** DOXOrubicin and 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  