BC Cancer Protocol Summary for Neoadjuvant or Adjuvant Therapy for Breast Cancer using Dose Dense Therapy: DOXOrubicin and Cyclophosphamide followed by PACLitaxel

**Protocol Code**
BRAJACTG

**Tumour Group**
Breast

**Contact Physician**
Dr. Susan Ellard

**ELIGIBILITY:**
- Patients with 1 or more axillary lymph node metastasis(es), or node negative but with high risk of recurrence (see Cancer Management Guidelines for categories of risk)
- Filgrastim (G-CSF) is not covered as a benefit at the BC Cancer

**EXCLUSIONS:**
- Pregnancy
- Congestive heart failure (LVEF less than 45%) or other significant heart disease
- Known hypersensitivity to E. coli derived products

**TESTS:**
- Baseline: CBC & diff, platelets, bilirubin, ALT (ALT and bilirubin should be measured prior to first cycle of AC and first cycle of PACLitaxel)
- Before each treatment: CBC & diff, platelets
- If clinically indicated: creatinine; MUGA scan or echocardiogram, bilirubin, ALT

**PREMEDICATIONS:**
- For the 4 cycles of DOXOrubicin and cyclophosphamide: Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)
- For the 4 cycles of PACLitaxel: **PACLitaxel must not be started unless the following drugs have been given:**
  - 45 minutes prior to PACLitaxel give dexamethasone 20 mg IV in NS 50 mL over 15 minutes
  - 30 minutes prior to PACLitaxel give diphenhydrAMINE 50 mg IV and ranitidine 50 mg IV in 50 mL over 20 minutes (compatible up to 3 hours when mixed in bag)
  - additional anti-emetics are not usually required
TREATMENT:
Four consecutive cycles of DOXOrubicin and cyclophosphamide

<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 NS 100 to 250* mL over 20 mins to 1 hour</td>
</tr>
<tr>
<td>filgrastim (G-CSF)</td>
<td>5 mcg/kg/day</td>
<td>SC</td>
</tr>
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</table>

*Use 250 mL for dose greater than 1000 mg
**reduce filgrastim treatment duration if ANC greater than 10 or intolerable bone pain. Filgrastim should not be stopped before the time of the predicted nadir from chemotherapy.

- Repeat every 14 days x 4 cycles.

Four consecutive cycles of PACLitaxel to start **14 days after** final cycle of DOXOrubicin and cyclophosphamide

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<th>Drug</th>
<th>Dose</th>
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<tr>
<td>PACLitaxel</td>
<td>175 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>filgrastim (G-CSF)</td>
<td>5 mcg/kg/day</td>
<td>SC</td>
</tr>
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Days 3 to 10 (or adjust as needed**)

- Repeat cycle every 14 days x 4 cycles
**reduce filgrastim treatment duration if ANC greater than 10 or intolerable bone pain. Filgrastim should not be stopped before the time of the predicted nadir from chemotherapy
DOSE MODIFICATIONS:
1. Hematological (for Day 1 counts)

Table 1.

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Dose (all drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than or equal to 1.0 and Greater than or equal to 100</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Less than 1.0 and Greater than or equal to 100</td>
<td>delay for 1 week (or longer if needed), then give 100% dose if ANC greater than 1 and platelets greater than or equal to 100. Give filgrastim days 3 to 13 for remaining cycles.</td>
<td></td>
</tr>
<tr>
<td>Greater than or equal to 1.0 and Less than 100</td>
<td>delay for 1 week (or longer if needed), then give 75% if ANC greater than 1 and platelets greater than or equal to 100</td>
<td></td>
</tr>
<tr>
<td>Less than or equal to 1.0 and Less than 100</td>
<td>delay for 1 week (or longer if needed), then give 75% if ANC greater than 1 and platelets greater than or equal to 100</td>
<td></td>
</tr>
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2. Febrile neutropenia: 75% of dose for current and subsequent cycles.
3. 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 from PACLitaxel of grade 2 (moderate) or higher is not relieved by adequate doses of NSAIDS or acetaminophen with codeine (TYLENOL #3®) a limited number of studies report a possible therapeutic benefit from the following:
   - prednisone 10 mg PO BID x 5 days starting 24 hours post PACLitaxel
   - gabapentin 300 mg PO on day prior to PACLitaxel, 300 mg PO BID on treatment day and then 300 mg PO TID x 7 to 10 days
6. Neuropathy: Dose modification or discontinuation for PACLitaxel may be required. Refer to BC Cancer Drug Manual.

PRECAUTIONS:
1. Neutropenia: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. Extravasation: DOXOrubicin and PACLitaxel may cause pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. Cardiac Toxicity: DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction. Cardiac assessment
recommended if lifelong dose of 450 mg/m² to be exceeded. Refer to BC Cancer Drug Manual.

4. **Hypersensitivity**: Reactions are common with PACLitaxel. Refer to BC Cancer Hypersensitivity Guidelines.

<table>
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<tr>
<th>Symptoms</th>
<th>Action</th>
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| **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 |

Call Dr. Susan Ellard or tumour group delegate at (250) 712-3900 or 1-888-563-7773 with any problems or questions regarding this treatment program.

References: