

# 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 in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)
  - additional anti-emetics are not usually required

**TREATMENT:**

Four consecutive cycles of DOXOrubicin and cyclophosphamide

Drug	Dose	BC Cancer Administration Guideline
DOXOrubicin	60 mg/m <sup>2</sup>	IV push
cyclophosphamide	600 mg/m <sup>2</sup>	IV in NS 100 to 250* mL over 20 mins to 1 hour
filgrastim (G-CSF)	5 mcg/kg/day Days 3 to 10 (or adjust as needed**)	SC

\*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

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	175 mg/m <sup>2</sup>	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)
filgrastim (G-CSF)	5 mcg/kg/day Days 3 to 10 (or adjust as needed**)	SC

- 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.

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	Dose (all drugs)
Greater than or equal to 1.0	and	Greater than or equal to 100	100%
Less than 1.0	and	Greater than or equal to 100	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.
Greater than or equal to 1.0	and	Less than 100	delay for 1 week (or longer if needed), then give 75% if ANC greater than 1 and platelets greater than or equal to 100
Less than or equal to 1.0		Less than 100	delay for 1 week (or longer if needed), then give 75% if ANC greater than 1 and platelets greater than or equal to 100

- Febrile neutropenia:** 75% of dose for current and subsequent cycles.
- Renal dysfunction:** Dose modification may be required for cyclophosphamide. Refer to BC Cancer Drug Manual.
- Hepatic dysfunction:** Dose modification required for DOXOrubicin and for PACLitaxel. Refer to BC Cancer Drug Manual.
- 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
- Neuropathy:** Dose modification or discontinuation for PACLitaxel may be required. Refer to BC Cancer Drug Manual.

## PRECAUTIONS:

- Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- Extravasation:** DOXOrubicin and PACLitaxel may cause pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
- 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/m<sup>2</sup> to be exceeded. Refer to BC Cancer Drug Manual.

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

<u>Mild</u> symptoms (e.g. mild flushing, rash, pruritus)	<ul style="list-style-type: none"> <li>▪ complete PACLitaxel infusion. Supervise at bedside</li> <li>▪ no treatment required</li> </ul>
<u>moderate</u> symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension)	<ul style="list-style-type: none"> <li>▪ stop PACLitaxel infusion</li> <li>▪ give IV diphenhydrAMINE 25 to 50 mg and hydrocortisone IV 100 mg</li> <li>▪ 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.</li> <li>▪ if reaction recurs, discontinue PACLitaxel therapy</li> </ul>
<u>severe</u> symptoms (i.e. <u>one</u> or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)	<ul style="list-style-type: none"> <li>▪ stop PACLitaxel infusion</li> <li>▪ give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated</li> <li>▪ discontinue PACLitaxel therapy</li> </ul>

**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:**

1. Citron ML, Berry DA, Cirrincione C, et al. Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of nod-positive primary breast cancer: first report of intergroup trial C9741/cancer and leukemia group b trial 9741. J Clin Oncol 2003; 21:1431-1439.