BCCA Protocol Summary for 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 BCCA

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, AST (AST 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, AST

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

Drug	Dose	BCCA Administration Guideline
DOXOrubicin	60 mg/m²	IV push
cyclophosphamide	600 mg/m²	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	BCCA Administration Guideline
PACLitaxel	175 mg/m²	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)
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 10^9/L)		Platelets (x 10^9/L)	Dose (all drugs)
Greater than or equal to 1	and	Greater than or equal to 100	100%
Less than 1	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	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		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

2. **Febrile neutropenia**: 75% of dose for current and subsequent cycles.
3. **Renal dysfunction**: Dose modification may be required for cyclophosphamide. Refer to BCCA Cancer Drug Manual.
4. **Hepatic dysfunction**: Dose modification required for DOXOrubicin and for PACLitaxel. Refer to BCCA 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 BCCA 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 BCCA 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/m^2 to be exceeded. Refer to BCCA Cancer Drug Manual.

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

Date activated: 01 Jul 2004

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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.