BC Cancer Protocol Summary for Neoadjuvant or Adjuvant Therapy for Breast Cancer using DOCEtaxel and Cyclophosphamide

Protocol Code	*BRAJDC*
Tumour Group	*Breast*
Contact Physician	*Dr. Lee Ann Martin*

ELIGIBILITY:

Patient must have:

- High risk, node negative or node positive patients, not otherwise considered best treated with a longer standard 6 to 8 cycle anthracycline or anthracycline plus taxane regimen (e.g. BRAJFEC, BRAJFECD, BRAJACT, etc) as decided by their treating physician.

Patient should have:

- ECOG 0-1
- Adequate hematological, renal and hepatic function

EXCLUSIONS:

- ECOG 2-4
- pregnancy or lactation
- significant hepatic dysfunction
- greater than or equal to grade 2 sensory or motor neuropathy

TESTS:

- Baseline: CBC & Diff, total bilirubin, ALT, creatinine (see Precaution #5 for guidelines regarding hepatic dysfunction and DOCEtaxel).
- If clinically indicated: GGT, LDH, alkaline phosphatase
- Before each treatment (Day 1): CBC & Diff
- If clinically indicated: creatinine, total bilirubin, GGT, ALT, LDH, alkaline phosphatase

PREMEDICATIONS:

- Antiemetic protocol for moderately emetogenic chemotherapy (see protocol SCNAUSEA)
- For DOCEtaxel:
  - dexamethasone 8 mg PO bid for 3 days, starting one day prior to each DOCEtaxel administration; patient must receive minimum of 3 doses pre-treatment
- DOCEtaxel-induced onycholysis and cutaneous toxicity of the hands may be prevented by wearing frozen gloves starting 15 minutes before DOCEtaxel infusion until 15 minutes after end of DOCEtaxel infusion; gloves should be changed after 45 minutes of wearing to ensure they remain cold during the entire DOCEtaxel infusion.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
cyclophosphamide	600 mg/m^2	IV in 100 to 250 mL NS over 20 min to 1 hour
DOCEtaxel	75 mg/m^2	IV in 250 to 500 mL NS over 1 hour (use non-DEHP equipment)
filgrastim (G-CSF)	5 mcg/kg/day Starting on Day 3 for 5 to 7 doses (adjust as needed*)	subcutaneously

*reduce filgrastim treatment duration if ANC greater than 10 x 10^9/L or intolerable bone pain. Filgrastim should not be stopped before the time of predicted nadir from chemotherapy.

Repeat every 21 days x 4 cycles.

- If radiation therapy is required, it is given following completion of chemotherapy (see BC Cancer Management Manual).

DOSE MODIFICATIONS

1. Hematological

ANC (x 10^9/L)		Platelets (x 10^9/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 1.0 and platelets greater than or equal to 100. Increase the filgrastim treatment duration per provider discretion.
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 1.0 and platelets greater than or equal to 100
Less than 1.0	and	Less than 100	Delay for 1 week (or longer if needed), then give 75% if ANC greater than 1.0 and platelets greater than or equal to 100

Febrile Neutropenia

Event	Dose Reduction
1st episode	75% of previous cycle dose if Day 1 ANC greater than or equal to 1.0 and platelets greater than or equal to 100
2nd episode	50% of original cycle dose if Day 1 ANC greater than or equal to 1.0 and platelets greater than or equal to 100
3rd episode	Discontinue protocol

2. Hepatic

Alkaline Phosphatase		AST +/or ALT	Dose
Less than 2.5 x ULN	and	Less than or equal to 1.5 x ULN	100%
2.5 – 5 x ULN	and	1.6 – 5 x ULN	75%
Greater than 5 x ULN	or	Greater than 5 ULN	Discuss with contact physician

ULN = upper limit of normal

PRECAUTIONS:

1. **Febrile Neutropenia:** Risk of febrile neutropenia is greater than 20%. Febrile neutropenia can result in patient harm, treatment delays and hospitalization. Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Extravasation**: DOCEtaxel causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Renal Dysfunction**: Dose modification may be required for cyclophosphamide if creatinine clearance less than 0.3 mL/sec, i.e., less than 18 mL/minute (see BC Cancer Drug Manual).
4. **Fluid Retention (DOCEtaxel)**: Dexamethasone premedication must be given to reduce incidence and severity of fluid retention with DOCEtaxel.
5. **Hepatic Dysfunction (DOCEtaxel)**: DOCEtaxel undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST) may lead to increased toxicity and usually requires a dose reduction. Baseline liver enzymes are recommended before cycle 1 and then if clinically indicated (e.g., repeat liver enzymes prior to each treatment if liver enzymes are elevated or there is severe toxicity such as neutropenia). Note: this information is intended to provide guidance but physicians must use their clinical judgment when making decisions regarding monitoring and dose adjustments.

6. **Hypersensitivity:** reactions to DOCEtaxel are common but it is not necessary to routinely initiate the infusion slowly. If slow initiation of infusion is needed, start infusion at 30 mL/h x 5 minutes, then 60 mL/h x 5 minutes, then 120 mL/h x 5 minutes, then complete infusion at 250 mL/h (for 500 mL bag, continue 250 mL/h for 5 minutes and then complete infusion at 500 mL/h). Refer to BC Cancer SCDRUGRX protocol.
7. **Interstitial pneumonitis (DOCEtaxel)** may occur. Risk may be increased with radiation therapy.

Contact Dr. Lee Ann Martin or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Jones et al., Phase III Trial Comparing Doxorubicin plus cyclophosphamide with docetaxel plus cyclophosphamide as adjuvant therapy for operable breast cancer. J Clin Oncol 2006;24(34):5381-7.
2. Jones S, Holmes, F, O'Shaughnessy, J, et al. Extended follow-up and analysis by age of the US Oncology adjuvant trial 9735: docetaxel/cyclophosphamide is associated with an overall survival benefit compared to doxorubicin/cyclophosphamide and is well tolerated in women 65 or older. San Antonio Breast Cancer Symposium 2007, abstract 12.
3. Koch et al. Retrospective Analysis of the incidence of allergic reactions with the use of docetaxel in different combinations (TC vs TAC vs AC-T). ASCO 2009 Breast Cancer Symposium, abstract 309.
4. Vandenberg T, Younus J, and Al-Hkayyat S. Febrile neutropenia rates with adjuvant docetaxel and cyclophophamide chemotherapy in early breast cancer: discrepancy between published reports and community practice – a retrospective analysis. Curr Oncol 2010l;17(2):2-3.
5. Soong D et al. High rate of febrile neutropenia in patients with operable breast cancer receiving docetaxel and cyclophosphamide. J Clin Oncol 2009;27(26):101-2.
6. Chan A et al. Impact of colony-stimulating factors to reduce febrile neutropenic events in breast cancer patients receiving docetaxel plus cyclophosphamide chemotherapy. Supp Care Cancer 2011;19:497-504.
7. Jones S et al. Docetaxel with cyclophosphamide is associated with an overall survival benefit compared with doxorubicin and cyclophosphamide: 7-year follow-up of US Oncology Research Trial 9735. J Clin Oncol 2009;27(8):1177-83.