BCCA Protocol Summary for Treatment of Locally Advanced Breast Cancer using Doxorubicin and Cyclophosphamide followed by DOCEtaxel

Protocol Code *BRLAACD*

Tumour Group *Breast*

Contact Physician *Dr. Stephen Chia*

ELIGIBILITY:

- locally advanced and inflammatory breast cancer in patients less than or equal to 60 years of age or fit patients greater than 60 years of age.
- For other indications, a BCCA "Compassionate Access Program" request must be approved.

EXCLUSIONS:

- Pregnancy
- Severe cardiovascular disease with LVEF less than 55%

TESTS:

- Baseline: CBC & diff, platelets, liver enzymes (liver enzymes should be measured prior to first cycle of AC and first cycle of DOCEtaxel, see Precaution #5 for guidelines regarding hepatic dysfunction and DOCEtaxel)
- Before each treatment: CBC & diff, platelets
- If clinically indicated: creatinine, MUGA scan or echocardiogram, liver enzymes

PREMEDICATIONS:

- For the 4 cycles of doxorubicin and cyclophosphamide: Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)

- For the 4 cycles of 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.
- Additional antiemetics not usually required.
- 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:

- 4 consecutive cycles of DOXOrubicin and cyclophosphamide

Drug	Dose	BCCA Administration Guideline
DOXOrubicin	60 mg/m²	IV push
cyclophosphamide	600 mg/m²	IV in 100 to 250* mL NS over 20 min to 1 hour

*Use 250 mL for dose greater than 1000 mg

Repeat every 21 days x 4 cycles.

- Followed by 4 consecutive cycles of DOCEtaxel to start **21 days after** final cycle of DOXOrubicin and cyclophosphamide

Drug	Dose	BCCA Administration Guideline
DOCEtaxel	100 mg/m^2	IV in 250 to 500* mL NS or D5W over 1 hour (see precautions #2 & 6) (use non-DEHP equipment)

*Use 250 mL for doses 75 to185 mg, use 500 mL for doses greater than 185 mg

Repeat every 21 days x 4 cycles.

DOSE MODIFICATIONS:

1. **Hematological**

For cycles of DOXOrubicin and cyclophosphamide only:

ANC (x10^9/L)		Platelets (x10^9/L)	Dose (both drugs)
greater than or equal to 1.5	and	greater than 90	100%
1 to 1.4	or	70 to 90	75%
less than 1	or	less than 70	delay

For cycles of DOCEtaxel only:

ANC (x 10^9/L)		Platelets (x10^9/L)	Dose	Dose after Neutropenic Sepsis on DOCEtaxel
greater than or equal to 1.5	and	greater than 90	100%	75%
1 to 1.4	or	70 to 90	75%	delay
less than 1	or	less than 70	delay	delay

2. **Renal dysfunction**: Dose modification may be required for cyclophosphamide. Refer to BCCA Cancer Drug Manual.
3. **Hepatic dysfunction**: Dose modification required for doxorubicin and DOCEtaxel. Refer to BCCA Cancer Drug Manual for doxorubicin and BCCA chemotherapy protocol BRAVDOC for DOCEtaxel.

PRECAUTIONS:

1. **Febrile Neutropenia**. DOCEtaxel containing adjuvant chemotherapy for breast cancer is associated with an extreme risk of febrile neutropenia approaching 40% in real practice settings, as reported in two outcome studies from Ontario. Thus, strong consideration should be given to using prophylactic filgrastim (G-CSF). Febrile neutropenia rates with prophylactic G-CSF are lower (5-7%) making this the safer option. Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Extravasation (DOXOrubicin and DOCEtaxel)**: Doxorubicin and DOCEtaxel cause pain and tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.
3. **Cardiac Toxicity (DOXOrubicin)**: 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. **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 (eg, 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 judgement 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 BCCA Hypersensitivity Guidelines.
7. **Interstitial pneumonitis (DOCEtaxel)** may occur. Risk may be increased with radiation therapy.

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.

Date activated: 01 February 2003

Date last revised: 1 Jun 2015 (Eligibility clarified)

References:

1. Wolmark, N et al. The effect on primary tumor response of adding sequential Taxotere to Adriamycin and cyclophosphamide: preliminary results from NSABP Protocol B-27. [Abstract 5] Breast Cancer Res and Treat 2001;69(3):210.
2. 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 2010 April; 17(2):2-3.
3. Soong D et al. High rate of febrile neutropenia in patients with operable breast cancer receiving docetaxel and cyclophosphamide. JCO 2009, 27(26): 101-2.
4. 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.
5. 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. JCO 2009, 27(8):1177-83.