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

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| ***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 BC Cancer "Compassionate Access Program" request must be approved.

**EXCLUSIONS**:

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

**TESTS**:

- Baseline: CBC & diff, platelets, ALT, Alk Phos, Bilirubin, LDH, GGT
- Before each treatment: CBC & diff, platelets
- Prior to **cycle #5**: bilirubin, ALT, Alk Phos (see Precaution #5 for guidelines regarding hepatic dysfunction and DOCEtaxel)
- If clinically indicated: creatinine, protein level, albumin, bilirubin, ALT, Alk Phos, GGT, LDH, MUGA scan or echocardiogram

**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 | BC Cancer 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 | BC Cancer 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) |

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 or equal 90 | 100% |
| 1.0 to less than 1.5 | or | 70 to 90 | 75% |
| less than 1.0 | 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 or equal 90 | 100% | 75% |
| 1.0 to less than 1.5 | or | 70 to less than 90 | 75% | delay |
| less than 1.0 | or | less than 70 | delay | delay |

2. **Renal dysfunction**: Dose modification may be required for cyclophosphamide. Refer to BC Cancer Drug Manual.
3. **Hepatic dysfunction**: Dose modification required for doxorubicin and DOCEtaxel. Refer to BC Cancer Drug Manual for doxorubicin and BC Cancer 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 BC Cancer 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 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 or ALT) 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 BC Cancer 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.**

**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.