**ELIGIBILITY:**
- ECOG 0-1
- Adequate renal and hepatic function
- Adequate hematological parameters (ANC greater than 1.5 x 10^9/L and platelets greater than 90 x 10^9/L)
- 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, BRAJFEDC, BRAJACT, etc) as decided by their treating physician.

**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, platelets, bilirubin, creatinine, liver enzymes (see Precaution #5 for guidelines regarding hepatic dysfunction and DOCEtaxel)
- Before each treatment (Day 1): CBC & diff, platelets
- If clinically indicated: creatinine, bilirubin, liver enzymes

**PREMEDICATIONS:**
- Antiemetic protocol for High/Moderate 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:
Administer cyclophosphamide first to reduce hypersensitivity response to DOCEtaxel

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>600 mg/m²</td>
<td>IV in 100 to 250 mL NS over 20 min to 1 hour</td>
</tr>
<tr>
<td>DOCEtaxel</td>
<td>75 mg/m²</td>
<td>IV in 250 mL* NS over 1 hour (use non-DEHP equipment)</td>
</tr>
</tbody>
</table>

* If 75 to 185 mg, use 250 mL bag. If greater than 185 mg, use 500 mL bag.

Repeat every 21 days x 4 cycles.
- If radiation therapy is required, it is given following completion of chemotherapy (see BCCA Cancer Management Manual).

DOSE MODIFICATIONS

1. Hematological

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Dose</th>
<th>Filgrastim (G-CSF) Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5</td>
<td>greater than 90</td>
<td>100%</td>
<td>100 % regimen with G-CSF 300 mcg SC daily on Days 5 to 12 (adjust as needed)</td>
</tr>
<tr>
<td>1 to 1.49</td>
<td>70 to 90</td>
<td>75%</td>
<td>Delay until ANC greater than 1.5 and platelets greater than 90 then give 75% of previous cycle doses</td>
</tr>
<tr>
<td>less than 1</td>
<td>less than 70</td>
<td>Delay until ANC greater than 1.5 and platelets greater than 90 then give 75% of previous cycle doses</td>
<td>Delay until ANC greater than 1.5 and platelets greater than 90 then give 100 % regimen with G-CSF 300 mcg SC daily on Days 5 to 12 (adjust as needed)</td>
</tr>
</tbody>
</table>

Febrile Neutropenia

<table>
<thead>
<tr>
<th>Event</th>
<th>Dose Reduction Option</th>
<th>Filgrastim (G-CSF) Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st episode</td>
<td>75% of previous cycle dose if Day 1 ANC greater than or equal to 1.5 and platelets greater than or equal to 100</td>
<td>100% regimen with G-CSF 300 mcg SC daily on Days 5 to 12 (adjust as needed)</td>
</tr>
<tr>
<td>2nd episode</td>
<td>50% of original cycle dose if Day 1 ANC greater than or equal to 1.5 and platelets greater than or equal to 100</td>
<td>75% regimen with G-CSF 300 mcg SC daily on Days 5 to 12 (adjust as needed)</td>
</tr>
<tr>
<td>3rd episode</td>
<td>Discontinue protocol or switch to Filgrastim (G-CSF) Option</td>
<td>50% regimen with G-CSF 300 mcg SC daily on Days 3 to 10 (adjust as needed)</td>
</tr>
<tr>
<td>4th episode</td>
<td>N/A</td>
<td>Discontinue protocol</td>
</tr>
</tbody>
</table>
2. **Hepatic**

<table>
<thead>
<tr>
<th>Alkaline Phosphatase</th>
<th>AST +/or ALT</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 2.5 x ULN</td>
<td>and</td>
<td>less than or equal to 1.5 x ULN</td>
</tr>
<tr>
<td>2.5 – 5 x ULN</td>
<td>and</td>
<td>1.6 – 5 x ULN</td>
</tr>
<tr>
<td>greater than 5 x ULN</td>
<td>or</td>
<td>greater than 5 ULN</td>
</tr>
</tbody>
</table>

ULN = upper limit of normal

**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 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:** DOCEtaxel causes pain and tissue necrosis if extravasated. Refer to BCCA 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 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 (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 BCCA Hypersensitivity Guidelines.

7. **Interstitial pneumonitis (DOCEtaxel)** may occur. Risk may be increased with radiation therapy.

**PATIENT EDUCATION:**

- For the Patient: cyclophosphamide, and DOCEtaxel.
Warning: The information contained in these documents is a statement of consensus of BC Cancer Agency professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer Agency's terms of use available at www.bccancer.bc.ca/legal.htm

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.

Date activated: 01 June 2007

Date revised: 01 Aug 2015 (Eligibility clarified)

References: