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, BRAJFECED, 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>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclophoshamide</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 BC Cancer Management Manual).

DOSE MODIFICATIONS

1. Hematological

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>Dose</th>
<th>Filgrastim (G-CSF) Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5 and greater than or equal to 90</td>
<td>100%</td>
<td>100 % regimen with filgrastim 300 mcg SC daily on Days 5 to 12 (adjust as needed)</td>
<td></td>
</tr>
<tr>
<td>1.0 to less than 1.5 or 70 to less than 90</td>
<td>75%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>less than 1.0 or less than 70</td>
<td>Delay until ANC greater than 1.5 and plts greater than 90 then give 75% of previous cycle doses</td>
<td>Delay until ANC greater than 1.5 and plts greater than 90 then give 100 % regimen with filgrastim 300 mcg SC daily on Days 5 to 12 (adjust as needed)</td>
<td></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>1&lt;sup&gt;st&lt;/sup&gt; 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 filgrastim 300 mcg SC daily on Days 5 to 12 (adjust as needed)</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; 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 filgrastim 300 mcg SC daily on Days 5 to 12 (adjust as needed)</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; episode</td>
<td>Discontinue protocol or switch to Filgrastim (G-CSF) Option</td>
<td>50% regimen with filgrastim 300 mcg SC daily on Days 3 to 10 (adjust as needed)</td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt; 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 less than or equal to 1.5 x ULN</td>
<td>100%</td>
</tr>
<tr>
<td>2.5 – 5 x ULN</td>
<td>and 1.6 – 5 x ULN</td>
<td>75%</td>
</tr>
<tr>
<td>greater than 5 x ULN</td>
<td>or greater than 5 ULN</td>
<td>discuss with contact physician</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 filgrastim. Febrile neutropenia rates with prophylactic filgrastim 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 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 Hypersensitivity Guidelines.

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:
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.