BC Cancer 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 BC Cancer “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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOXOrubicin</td>
<td>60 mg/m²</td>
<td>IV push</td>
</tr>
<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>
</tbody>
</table>

*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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOCEtaxel</td>
<td>100 mg/m²</td>
<td>IV in 250 to 500* mL NS or D5W over 1 hour (see precautions #2 &amp; 6) (use non-DEHP equipment)</td>
</tr>
</tbody>
</table>

*Use 250 mL for doses 75 to 185 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:

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose (both drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5</td>
<td>greater than or equal 90</td>
<td>100%</td>
</tr>
<tr>
<td>1.0 to less than 1.5</td>
<td>70 to 90</td>
<td>75%</td>
</tr>
<tr>
<td>less than 1.0</td>
<td>less than 70</td>
<td>delay</td>
</tr>
</tbody>
</table>

For cycles of DOCEtaxel only:

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose after Neutropenic Sepsis on DOCEtaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5</td>
<td>greater than or equal 90</td>
<td>75%</td>
</tr>
<tr>
<td>1.0 to less than 1.5</td>
<td>70 to less than 90</td>
<td>delay</td>
</tr>
<tr>
<td>less than 1.0</td>
<td>less than 70</td>
<td>delay</td>
</tr>
</tbody>
</table>
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/m² 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:**