BCCA Protocol Summary for Adjuvant Therapy for Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF)

Protocol Code: BRAJCEFG
Tumour Group: Breast
Contact Physician: Dr. Susan Ellard

ELIGIBILITY:
- patients less than or equal to 60 years of age or fit patients greater than 60 years of age with 1 or more axillary lymph node metastasis(es) requiring filgrastim (G-CSF) support in order to complete the CEF chemotherapy

EXCLUSIONS:
- Congestive heart failure (LVEF less than 45%) or other significant heart disease

TESTS:
- Before each treatment (Day 1 and 15): CBC & diff, platelets
- If clinically indicated: bilirubin, creatinine, MUGA scan or echocardiogram

PREMEDICATIONS:
- Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)

TREATMENT:

Regimen at 100% doses
- second or more occurrence of ANC less than 1.5 and no previous dose reduction or
- first occurrence of febrile neutropenia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>epirubicin</td>
<td>60 mg/m²/day on Days 1 and 15</td>
<td>IV push</td>
</tr>
<tr>
<td>fluorouracil</td>
<td>500 mg/m²/day on Days 1 and 15</td>
<td>IV push</td>
</tr>
<tr>
<td>cyclophosphamide</td>
<td>525 mg/m²/day on days 1 and 15</td>
<td>IV in 100 to 250 mL NS or D5W over 20 min to 1 hour*</td>
</tr>
<tr>
<td>filgrastim (G-CSF)</td>
<td>5 mcg/kg/day on Days 2-13 and Days 16-27 or adjust as needed**</td>
<td>SC</td>
</tr>
</tbody>
</table>
Regimen at 75% Doses

- previous 25% dose reduction or
- 2nd or more episode of febrile neutropenia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>epirubicin</td>
<td>45 mg/m²/day on Days 1 and 15</td>
<td>IV push</td>
</tr>
<tr>
<td>fluorouracil</td>
<td>375 mg/m²/day on Days 1 and 15</td>
<td>IV push</td>
</tr>
<tr>
<td>cyclophosphamide</td>
<td>395 mg/m²/day on Days 1 and 15</td>
<td>IV in 100 mL NS or D5W over 30 minutes</td>
</tr>
<tr>
<td>filgrastim (G-CSF)</td>
<td>5 mcg/kg/day on Days 2-13 and Days 16-27 (or adjust as needed**)</td>
<td>SC</td>
</tr>
</tbody>
</table>

*Use 250 mL for doses greater than 1000 mg
** reduce filgrastim treatment duration if ANC greater than 10 or intolerable bone pain.

- Repeat every 28 days x 6 cycles total
- If radiation therapy is required, it is given following completion of chemotherapy (BCCA Cancer Management Manual).

DOSE MODIFICATIONS

1. Hematological (100% and 75% Regimens)

**Day 1:**
- Delay until ANC greater than or equal to 1.5 and platelets greater than or equal to 100.

**Day 15:**

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>% of Day 1 Current Cycle Dose (All Drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5 and greater than or equal to 100</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>1 to 1.49 and greater than or equal to 100</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>less than 1 or less than 100</td>
<td>Omit Day 15 for current cycle only</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** If there is full hematological recovery (ANC greater than or equal to 1.5, platelets greater than or equal to 100) on Day 1 in subsequent cycles, re-escalation to 100% on Day 15 with filgrastim (G-CSF) support may be attempted at the physician’s discretion.
2. **Hepatic Dysfunction**: Dose modification required for epirubicin if total bilirubin greater than or equal to 25 micromol/L and for fluorouracil if greater than 85 micromol/L (see BCCA Cancer Drug Manual).

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) and for antibiotic if less than 50 mL/minute (see product monograph).

**PRECAUTIONS:**

1. **Extravasation**: Epirubicin causes pain and tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.

2. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.

3. **Cardiac Toxicity**: Clinical cardiac assessment is required prior to CEF if cardiac function is equivocal and recommended at any time if clinically indicated with a formal evaluation of LVEF (MUGA scan or ECHO). **Myocardial ischemia and angina occurs rarely in patients receiving fluorouracil or capecitabine.** Development of cardiac symptoms including signs suggestive of ischemia or of cardiac arrhythmia is an indication to discontinue treatment. If there is development of cardiac symptoms patients should have urgent cardiac assessment. Generally rechallenge with either fluorouracil or capecitabine is not recommended as symptoms potentially have a high likelihood of recurrence which can be severe or even fatal. Seeking opinion from cardiology and oncologists with expert knowledge about fluorouracil or capecitabine toxicity is strongly advised under these circumstances. The toxicity should also be noted in the patient’s allergy profile.

4. **Possible drug interactions with fluorouracil and warfarin, phenytoin and fosphenytoin** have been reported and may occur at any time. Close monitoring is recommended (eg, for warfarin, monitor INR weekly during fluorouracil therapy and for 1 month after stopping fluorouracil).

Contact Dr. Susan Ellard or tumour group delegate at (250) 712-3900 or 1-888-563-7773 with any problems or questions regarding this treatment program.

Date activated: 01 Oct 2002

Date revised: 1 Aug 2015 (Eligibility and number of treatment cycles clarified)

**REFERENCES:**


paclitaxel versus CEF as therapy for premenopausal women and early postmenopausal women who have had potentially curative surgery for node positive or high risk node negative breast cancer.