

BCCA Protocol Summary of Therapy for Locally Advanced Breast Cancer Using Cyclophosphamide, Epirubicin and Fluorouracil

Protocol Code:

BRLACEF

Tumour Group:

Breast

Contact Physician:

Dr. Brian Norris

ELIGIBILITY:

- locally advanced* breast cancer in women ≤ 60 years of age or fit women > 60 years of age ***see BCCA Cancer Management Manual

EXCLUSIONS:

- Congestive heart failure (LVEF $< 45\%$) or other significant heart disease

TESTS:

- Baseline: CBC & diff, platelets, bilirubin, creatinine
- Before each treatment (Day 1 and 8): CBC & diff, platelets
- If clinically indicated: bilirubin, creatinine, MUGA scan or echocardiogram

PREMEDICATIONS:

- Antiemetic protocol for High/Moderate emetogenic chemotherapy (see protocol [SCNAUSEA](#))

TREATMENT:

| Drug | Dose | BCCA Administration Guideline |
|----------------------------------|---|-------------------------------|
| Epirubicin | 60 mg/m ² /day on days 1 and 8 | IV push |
| Fluorouracil | 500 mg/m ² /day on days 1 and 8 | IV push |
| Cyclophosphamide | 75 mg/m ² /day x 14 days (d1-14) (round to nearest 25 mg) | oral |
| Cotrimoxazole* | 2 tablets bid continuously | oral |

*If allergic, substitute ciprofloxacin 500 mg po bid or norfloxacin 400 mg po bid.

- Regular antiemetics may be required on days 1-14.
- Repeat every 28 days x 6 cycles.
- If radiation therapy is required, it is given following completion of chemotherapy (see BCCA Cancer Management Manual).

DOSE MODIFICATIONS

Doses are adjusted based on Day 1 and Day 8 counts (Tables 1-3) and previous cycle febrile neutropenia (Table 4). No dose reduction for nadir counts.

DAY 1

Table 1A. Cycle 1, Day 1

| ANC (x 10 ⁹ /L) | | Platelets (x 10 ⁹ /L) | Dose (all drugs) |
|----------------------------|-----|----------------------------------|--------------------------|
| ≥ 1.5 | and | ≥ 100 | 100% |
| 1.0-1.49 | and | ≥ 100 | 75% |
| < 1.0 | or | < 100 | ineligible for treatment |

Table 1B. Cycles 2-6, Day 1

FIRST OCCURRENCE OF LOW COUNTS

when ANC < 1.5 x10⁹/L and/or platelets < 100 x 10⁹/L

after a one week delay and no febrile neutropenia in a previous cycle

| ANC (x 10 ⁹ /L) | Platelets (x 10 ⁹ /L) | All Chemotherapy Drugs % Dose of Previous Cycle |
|----------------------------|----------------------------------|---|
| ≥ 1.5 | and ≥ 100 | 100% |
| 1 - 1.49 | and ≥ 100 | 75% |
| < 1 | or < 100 | Delay until ANC ≥ 1.5 and platelets ≥ 100 then give 75% |

Table 2. Cycles 2-6, Day 1

SECOND OCCURRENCE OF LOW COUNTS

when ANC < 1.5 x10⁹/L and/or platelets < 100 x 10⁹/L

after a one week delay and no febrile neutropenia in a previous cycle

| ANC (x10 ⁹ /L) | Platelets (x 10 ⁹ /L) | All Chemotherapy Drugs % of Previous Cycle Dose |
|---------------------------|----------------------------------|---|
| ≥ 1.5 | and ≥ 100 | 75 % or convert to BRAJCEF-G |
| < 1.5 | and ≥ 100 | Delay 1 week or until ANC ≥ 1.5 then convert to BRAJCEF-G |
| | < 100 | Delay 1 week or until ANC ≥ 1.5 and platelets ≥ 100 then give 50% |

Note: Following a dose reduction for Day 1 of the current cycle due to low ANC, do not attempt dose re-escalation in subsequent cycles without converting to BRAJCEF-G.

DAY 8**Table 3. Cycles 1-6, Day 8**

| ANC (x10 ⁹ /L) | Platelets (x 10 ⁹ /L) | All Chemotherapy Drugs % of Day 1 Dose of This Cycle | |
|------------------------------|-------------------------------------|--|--|
| ≥ 1.5 | and ≥ 100 | 100 % | |
| 1.0 – 1.49 | and ≥ 100 | 75% | |
| < 1.0 | and ≥ 100 | Tell patient to STOP oral cyclophosphamide. Omit IV treatment. | |
| | | 1st dose reduction or delay Start next cycle on Day 22 if counts permit using 75% | 2nd dose reduction or delay Start next cycle on Day 22 if counts permit using BRAJCEF-G |
| < 100 | | Tell patient to STOP oral cyclophosphamide. Omit IV treatment. | |
| | | 1st dose reduction or delay Start next cycle on Day 22 if counts permit using 75% | 2nd dose reduction or delay Start next cycle on Day 22 if counts permit using 75% |

Note: Doses modified on Day 8 due to hematological toxicity are re-escalated on Day 1 of subsequent cycles if Day 1 counts are adequate.

Table 4. Febrile neutropenia

| Event | Dose Reduction Option | Filgrastim (G-CSF) Option |
|-------------------------|---|---|
| 1 st episode | 75% of previous cycle dose if Day 1 ANC ≥ 1.5 and platelets ≥ 100 | Convert to BRAJCEF-G using 100% regimen |
| 2 nd episode | 50% of previous cycle dose if Day 1 ANC ≥ 1.5 and platelets ≥ 100 | Convert to BRAJCEF-G using 75% regimen |
| 3 rd episode | No dose reduction option | Convert to BRAJCEF-G using 75% regimen |

5. Stomatitis: For Grade 3 or 4 stomatitis (painful erythema, edema or ulcers and cannot eat; mucosal necrosis and/or requires enteral support; dehydration), delay until recovered then give 75% dose of Day 1 of previous cycle. Maintain dose reduction for all subsequent cycles.

6. Hepatic Dysfunction: Dose modification required for epirubicin if total bilirubin ≥ 25 μmol/L and for fluorouracil if > 85 μmol/L (see BCCA [Cancer Drug Manual](#)).

7. Renal Dysfunction: Dose modification may be required for cyclophosphamide if creatinine clearance < 0.3 mL/sec, i.e., < 18 mL/minute (see BCCA Cancer Drug Manual) and for antibiotic if < 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).

PATIENT EDUCATION:

- For the Patient: [CEF](#)

Contact Dr. Brian Norris or tumour group delegate @ (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 01 September 1998

Date revised: 01 Jun 2005 (age limit eligibility revised)

REFERENCES:

1. Levine MN, Bramwell VH, Pritchard KI et al. Randomized trial of intensive cyclophosphamide, epirubicin, and fluorouracil chemotherapy compared with cyclophosphamide, methotrexate, and fluorouracil in premenopausal women with node-positive breast cancer. *J Clin Oncol* 1998;16(8):2651-8.
2. Califaretti N, Davidson M, Goss, P et al. Is there a role for G-CSF with adjuvant CEF chemotherapy for breast cancer (BC)? (abstract) *Proc Am Soc Clin Oncol* 1999;18:90a.
3. National Cancer Institute of Canada. Clinical Trials Group. Protocol MA.21: A phase III adjuvant trial of sequenced EC + filgrastim + epoetin alfa followed by paclitaxel versus sequenced AC followed by 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. Kingston, 02 Oct 2000.