

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

Protocol Code:

BRLACEF-G

Tumour Group:

Breast

Contact Physician:

Dr. Susan Ellard

ELIGIBILITY:

- women less than or equal to 60 years of age or fit women greater than 60 years of age with locally advanced breast cancer requiring filgrastim (G-CSF) support in order to complete protocol BRAJCEF

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 High/Moderate 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

Drug	Dose	BCCA Administration Guideline
Epirubicin	60 mg/m ² /day on Days 1 and 15	IV push
Fluorouracil	500 mg/m ² /day on Days 1 and 15	IV push
Cyclophosphamide	525 mg/m ² /day on days 1 and 15	IV in 100 to 250 mL NS or D5W over 20 min to 1 hour*
Filgrastim (G-CSF)	5 mcg/kg/day on Days 2-13 and Days 16-27 (or adjust as needed**)	SC
Cotrimoxazole***	2 tablets bid continuously	oral

Regimen at 75% Doses

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

Drug	Dose	BCCA Administration Guideline
Epirubicin	45 mg/m ² /day on Days 1 and 15	IV push
Fluorouracil	375 mg/m ² /day on Days 1 and 15	IV push
Cyclophosphamide	395 mg/m ² /day on Days 1 and 15	IV in 100 mL NS or D5W over 30 minutes
Filgrastim (G-CSF)	5 mcg/kg/day on Days 2-13 and Days 16-27 (or adjust as needed**)	SC
Cotrimoxazole***	2 tablets bid continuously	oral

*Use 250 mL for doses greater than 1000 mg

** reduce filgrastim treatment duration if ANC greater than 10 or intolerable bone pain.

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

- Repeat every 28 days x 6 cycles total, including BRAJCEF cycles
- 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:

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	% of Day 1 Current Cycle Dose (All Drugs)
greater than or equal to 1.5	and	greater than or equal to 100	100%
1 – 1.49	and	greater than or equal to 100	75%
less than 1	or	less than 100	Omit Day 15 for current cycle only

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).
- 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: 01 June 2011 (Infusion section 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.