

BCCA Protocol Summary for Adjuvant Therapy for Breast Cancer Using Fluorouracil, Epirubicin and Cyclophosphamide

Protocol Code
Tumour Group
Contact Physician

BRAJFEC
Breast
Dr. Susan Ellard

ELIGIBILITY:

- Women less than or equal to 60 years of age or fit women greater than 60 years of age with 1 or more axillary lymph node metastasis(es).
- High risk, lymph node-negative
- Adequate hematological parameters (ANC greater than $1.5 \times 10^9/L$ and platelets greater than $100 \times 10^9/L$)
- For other indications, an "Individual Use of Benefit Drug List Medication for an Undesignated Indication" form must be approved

EXCLUSIONS:

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

TESTS:

- Baseline: CBC & diff, platelets, bilirubin, creatinine
- Before each treatment (Day 1): 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 Standard
Epirubicin	100 mg/m ² on Day 1	IV push
Fluorouracil	500 mg/m ² on Day 1	IV push
Cyclophosphamide	500 mg/m ² on Day 1	IV in 100 to 250 mL NS over 20 min to 1 hour

- Repeat every 21 days x 6 cycles (including any BRAJCEF cycles given).
- Maximum cumulative epirubicin dose is 720 mg/m²
- 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 counts (Tables 1-2) and previous cycle febrile neutropenia (Table 3). No dose reduction for nadir counts.

1. Hematological

Table 1. FIRST OCCURRENCE OF LOW COUNTS

At the Beginning of a Cycle (Day 1):

IF ANC less than $1.5 \times 10^9/L$ and/or platelets less than $100 \times 10^9/L$, DELAY for one week

THEN after a one week delay and no febrile neutropenia in a previous cycle, treat as below:

ANC ($\times 10^9/L$)		Platelets ($\times 10^9/L$)	All Chemotherapy Drugs % Dose of Previous Cycle	Filgrastim (G-CSF) Option
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%*	100% regimen** with G-CSF 300 mcg sc daily on Days 4-11 (adjust as needed)
less than 1	or	less than 100	Delay until ANC greater than or equal to 1.5 and platelets greater than or equal to 100 then give 75%	Delay until ANC greater than or equal to 1.5 and platelets greater than or equal to 100 then give 100% regimen** with G-CSF 300 mcg sc daily on Days 4-11 (adjust as needed)

* if the ANC is greater than $1 \times 10^9/L$, 100% dose of previous cycle may be used at the discretion of the medical oncologist

**100% regimen refers to Cycle 1 doses ie. Epirubicin $100 \text{ mg}/\text{m}^2$, Fluorouracil $500 \text{ mg}/\text{m}^2$ and Cyclophosphamide $500 \text{ mg}/\text{m}^2$

Table 2. SECOND OCCURRENCE OF LOW COUNTS

At the Beginning of a Cycle (Day 1):

IF ANC less than $1.5 \times 10^9/L$ and/or platelets less than $100 \times 10^9/L$, **DELAY** for one week

THEN after a one week delay and no febrile neutropenia in a previous cycle, treat as below:

ANC (x10 ⁹ /L)		Platelets (x 10 ⁹ /L)	All Chemotherapy Drugs % of Previous Cycle Dose	Filgrastim (G-CSF) Option
greater than or equal to 1.5	and	greater than or equal to 100	75 % of previous cycle dose	100% regimen** with G-CSF 300 mcg sc daily on Days 4-11 (adjust as needed)
less than 1.5	and	greater than or equal to 100	Delay 1 week or until ANC greater than or equal to 1.5 - then give 75% of previous cycle dose	75% regimen*** with G-CSF 300 mcg sc daily on Days 4-11 (adjust as needed)
		less than 100	Delay 1 week or until ANC greater than or equal to 1.5 and platelets greater than or equal to 100 then give 75% of previous cycle dose	

**100% regimen refers to Cycle 1 doses ie. Epirubicin 100 mg/m², Fluorouracil 500 mg/m² and Cyclophosphamide 500 mg/m²

***75% regimen refers to 75% of Cycle 1 doses ie. Epirubicin 75 mg/m², Fluorouracil 375 mg/m² and Cyclophosphamide 375 mg/m²

Table 3. Febrile neutropenia

Event	Dose Reduction Option	Filgrastim (G-CSF) Option
1 st episode	75% of previous cycle dose if Day 1 ANC greater than or equal to 1.5 and platelets greater than or equal to 100	100% regimen** with G-CSF 300 mcg sc daily on Days 4-11 (adjust as needed)
2 nd episode	50% of previous cycle dose if Day 1 ANC greater than or equal to 1.5 and platelets greater than or equal to 100	75% regimen*** with G-CSF 300 mcg sc daily on Days 4-11 (adjust as needed)
3 rd episode	No dose reduction option	Use 75% regimen*** with G-CSF 300 mcg sc daily on Days 4-11 (adjust as needed)

**100% regimen refers to Cycle 1 doses ie. Epirubicin 100 mg/m², Fluorouracil 500 mg/m² and Cyclophosphamide 500 mg/m²

***75% regimen refers to 75% of Cycle 1 doses ie. Epirubicin 75 mg/m², Fluorouracil 375 mg/m² and Cyclophosphamide 375 mg/m²

2. **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.
3. **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).
4. **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).

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).

PATIENT EDUCATION:

- For the Patient: cyclophosphamide, epirubicin, and 5-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 Jan 2003

Date revised: 1 June 2011 (Infusion section revised)

References^{1, 2}:

1. French Adjuvant Study G. Benefit of a high-dose epirubicin regimen in adjuvant chemotherapy for node-positive breast cancer patients with poor prognostic factors: 5-year follow-up results of French Adjuvant Study Group 05 randomized trial. J Clin Oncol 2001;19(3):602-11.
2. Del Mastro L, Venturini M, Lionetto R, et al. Accelerated-intensified cyclophosphamide, epirubicin, and fluorouracil (CEF) compared with standard CEF in metastatic breast cancer patients: results of a multicenter, randomized phase III study of the Italian Gruppo Oncologico Nord-Ouest-Mammella Inter Gruppo Group. J Clin Oncol 2001;19(8):2213-21.