

BC Cancer Protocol Summary for Adjuvant Therapy for High-Risk Breast Cancer using Cyclophosphamide (oral), Methotrexate and Fluorouracil

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

ELIGIBILITY:

- adjuvant treatment for high risk breast cancer.

TESTS:

- Baseline: CBC & diff, platelets, bilirubin, ALT, creatinine
- Before each treatment: CBC & diff, platelets
- If clinically indicated: bilirubin, ALT, creatinine

PREMEDICATIONS:

- Antiemetic protocol for **moderately** emetogenic chemotherapy (see protocol SCNAUSEA)

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
cyclophosphamide	100 mg/m ² /day x 14 days (days 1-14)	oral
methotrexate	40 mg/m ² /day on days 1 and 8	IV push
fluorouracil (5-FU)	600 mg/m ² /day on days 1 and 8	IV push

- Repeat every 28 days x 6 cycles.
- Radiation therapy is given following 3rd cycle of chemotherapy (BC Cancer Management Manual).

DOSE MODIFICATIONS:

1. Hematological:

ANC (x10 ⁹ /L)	Platelets (x10 ⁹ /L)	Dose (all drugs)
greater than or equal to 1.5	greater than or equal to 90	100%
1.0 to less than 1.5	70 to less than 90	75%
less than 1.0	less than 70	delay

2. Renal dysfunction:

For Methotrexate

BC Cancer Drug Manual suggested dose modifications:

Creatinine clearance (mL/min)	Methotrexate dose
61 to 80	75%
51 to 60	70%
10 to 50	30 to 50%
less than 10	avoid

$$\text{Calculated creatinine clearance} = \frac{N \times (140 - \text{Age}) \times \text{weight (kg)}}{\text{Serum Creatinine in micromol/L}}$$

N for Males = 1.23,
Females = 1.04

For Cyclophosphamide:

BC Cancer Drug Manual suggested dose modifications:

Creatinine clearance (mL/min)	Cyclophosphamide dose
greater than or equal to 10	100%
less than 10	75%

3. Hepatic dysfunction:

For Methotrexate:

Bilirubin (micromol/L)		ALT (units/L)	Methotrexate Dose
less than 50		less than 180	100%
50 to 85	or	greater than 180	75%
greater than 85			Omit dose

For 5-Fluorouracil

Bilirubin (micromol/L)	Fluorouracil Dose
greater than 86	Omit dose

4. Third space fluids (ascites, pleural effusions): Omit methotrexate.

PRECAUTIONS:

- 1. Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- 2. 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).
- 3. 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 re-challenge 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 cardiologists 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.

Call 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.