BC Cancer Protocol Summary for Palliative Therapy for Metastatic Breast Cancer Using Metronomic Low-Dose Oral Cyclophosphamide and Methotrexate

Protocol Code	*BRAVCMPO*
Tumour Group	*Breast*
Contact Physician	*Dr. C. Lohrisch*

ELIGIBILITY:

- pretreated metastatic breast cancer with ECOG performance status 0, 1, or 2 and greater than 3 month life expectancy
- previously untreated metastatic breast cancer in patients unsuitable for other chemotherapy drugs due to excess toxicity risk

EXCLUSIONS:

- severe renal dysfunction, creatinine clearance less than 10 mL/min
- severe hepatic dysfunction, bilirubin greater than 85 or ALT greater than 3 x ULN

TESTS:

- Baseline: CBC and platelets, serum creatinine, bilirubin, liver enzymes
- Before each treatment: CBC and platelets, bilirubin, ALT
- If clinically indicated: creatinine, alkaline phosphatase

PREMEDICATIONS:

- Antiemetic protocol for low emetogenic chemotherapy protocols (see SCNAUSEA)

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
cyclophosphamide	50 mg orally once daily continuously	PO
methotrexate	2.5 mg orally BID on Days 1 and 2 each week	PO

1 cycle = 4 weeks

Repeat every 28 days x 6-8 cycles. Responding patient may be continued on treatment at the discretion of the treating physician. Discontinue if no response after 2 cycles or unacceptable toxicity.

DOSE MODIFICATIONS:

1. **Hematological**

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose (all drugs)
greater than or equal to 1.5	and	greater than or equal to 100	100%
1.0 to less than 1.5	or	75 to less than 100	proceed at 50%
less than 1.0	or	less than 75	delay, then dose at 50% after recovery

2. **Renal dysfunction**

For Methotrexate:

GFR (mL/min)	Dose
greater than 30	100%
15-30	50%
less than 15	omit

$$\text{GFR} = \frac{\text{N*} \times (140 - \text{Age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$$

* For males N = 1.23; for females N=1.04

For Cyclophosphamide: Renal failure may lead to reduced excretion of metabolites and increased toxicity. Significant falls in clearance with increased exposure have been documented in patients with renal impairment. Severe renally impaired patients (CrCl less than 10 mL/min) are at particular risk and should be treated at reduced dose and with caution. See BC Cancer Drug Manual.

3. **Hepatic dysfunction**: Dose modification required for methotrexate.

Bilirubin (micromol/L)	or	**ALT (units/L)**	**Methotrexate Dose**
50-85		3 x ULN	2.5 mg daily on Days 1 and 2
greater than 85		greater than 3 x ULN	omit

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.

Call Dr. Caroline Lohrisch or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

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7. Khan OA, Blann AD, Payne MJ, et al. Continuous low-dose cyclophosphamide and methotrexate combined with celecoxib for patients with advanced cancer. Br.J.Cancer 2011;104(12):1822-1827.
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10. Bocci G, et al. Cyclophosphamide-methotrexate 'metronomic' chemotherapy for the palliative treatment of metastatic breast cancer. A comparative pharmacoeconomic evaluation. Ann Oncol 2005;16:1243-52.