

BCCA Protocol Summary for Adjuvant Therapy for Breast Cancer using Oral Cyclophosphamide, Doxorubicin and Fluorouracil

Protocol Code:

BRAJCAFPO

Tumour Group:

Breast

Contact Physician:

Dr. Brian Norris

ELIGIBILITY:

- Adjuvant treatment for high-risk node negative and node positive breast cancer age ≤ 60 years, extreme risk breast cancer age ≥ 50 years, high risk node positive breast cancer age >60 years.

TESTS:

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

PREMEDICATIONS:

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

TREATMENT:

Drug	Dose	BCCA Administration Guideline
doxorubicin (ADRIAMYCIN®)	30 mg/m ² Days 1 and 8	IV push
fluorouracil (5-FU)	500 mg/m ² Days 1 and 8	IV push
cyclophosphamide	100 mg/m ² /day x 14 days Days 1-14 (round to nearest 25 mg)	PO

- Repeat every 28 days x 6 cycles.
- Regular antiemetics may be required on days 1-14.
- If radiation therapy is required, it is given following completion of chemotherapy (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 BRAJCAF-G
< 1.5	and ≥ 100	Delay 1 week or until ANC ≥ 1.5 - then give 75% or convert to BRAJCAF-G
	< 100	Delay 1 week or until ANC ≥ 1.5 and platelets ≥ 100 then give 75%

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 BRAJCAF-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 – 1.49	and ≥ 100	75%	
< 1	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 BRAJCAF-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 BRAJCAF-G
2 nd episode	75% of previous cycle dose if Day 1 ANC ≥ 1.5 and platelets ≥ 100	Convert to BRAJCAF-G
3 rd episode	No dose reduction option	Convert to BRAJCAF-G

- Hepatic dysfunction:** Dose modifications required for doxorubicin and fluorouracil (see BCCA Cancer Drug Manual).
- Renal dysfunction:** Dose modification may be required for cyclophosphamide (see BCCA Cancer Drug Manual).

PRECAUTIONS:

- Cardiac Toxicity:** Doxorubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction. Cardiac assessment recommended if lifelong dose of 400 mg/m² to be exceeded (see BCCA Cancer Drug Manual).
- Extravasation:** Doxorubicin causes pain and tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.

3. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.

Call 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 1 Jan 2004

Date revised **1 May 2004 (dose modifications tables clarified)**

References

1. Hutchins L, Green S, Ravdin P, et al. CMF versus CAF with and without tamoxifen in high-risk node-negative breast cancer patients and a natural history follow-up study in low-risk node-negative patients: first results of intergroup trial INT 0102. *Proc Am Soc Clin Oncol* 1998;17:1a (abstr 2).
2. Albain K, Green S, Osborne K, et al. Tamoxifen (T) versus cyclophosphamide, Adriamycin® and 5-FU plus either concurrent or sequential T in postmenopausal, receptor(+), node(+) breast cancer: a Southwest Oncology Group phase III intergroup trial (SWOG-8814, INT-0100). *Proc Am Soc Clin Oncol* 1997;16:128a (abstr 450).
3. Albain K, Green S, Ravdin P, et al. Overall survival after cyclophosphamide, Adriamycin, 5-FU, and tamoxifen (CAFT) is superior to T alone in postmenopausal, receptor(+), node(+) breast cancer: new findings from phase III Southwest Oncology Group intergroup trial S8814 (INT-0100). *Proc Am Soc Clin Oncol* 2001;20:24a (abstr 94).