

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

Protocol Code:

BRAJCAFPO

Tumour Group:

Breast

Contact Physician:

Dr. Susan Ellard

ELIGIBILITY:

- Adjuvant treatment for high-risk node negative and node positive breast cancer age less than or equal to 60 years, extreme risk breast cancer age greater than or equal to 50 years, high risk node positive breast cancer age greater than 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)		and	Platelets (x 10 ⁹ /L)	Dose (all drugs)
greater than or equal to 1.5			greater than or equal to 100	100%
1.0-1.49			greater than or equal to 100	75%
less than 1.0		or	less than 100	ineligible for treatment

Table 1B. Cycles 2-6, Day 1

FIRST OCCURRENCE OF LOW COUNTS

when ANC less than 1.5 x10⁹/L and/or platelets less than 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
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	Delay until ANC greater than or equal to 1.5 and platelets greater than or equal to 100 then give 75%

Table 2. Cycles 2-6, Day 1

SECOND OCCURRENCE OF LOW COUNTS

when ANC less than $1.5 \times 10^9/L$ and/or platelets less than $100 \times 10^9/L$
after a one week delay and no febrile neutropenia in a previous cycle

ANC ($\times 10^9/L$)		Platelets ($\times 10^9/L$)	All Chemotherapy Drugs % of Previous Cycle Dose
greater than or equal to 1.5	and	greater than or equal to 100	75 % or convert to BRAJCAF-G
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% or convert to BRAJCAF-G
		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%

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 (x10⁹/L)		Platelets (x 10⁹/L)	All Chemotherapy Drugs % of Day 1 Dose of This Cycle	
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	and	greater than or equal to 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
		less than 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 greater than or equal to 1.5 and platelets greater than or equal to 100	Convert to BRAJCAF-G
2 nd 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	Convert to BRAJCAF-G
3 rd episode	No dose reduction option	Convert to BRAJCAF-G

5. Hepatic dysfunction: Dose modifications required for doxorubicin and fluorouracil (see BCCA Cancer Drug Manual).

6. **Renal dysfunction:** Dose modification may be required for cyclophosphamide (see BCCA Cancer Drug Manual).

PRECAUTIONS:

1. **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).
2. **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.
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).

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.

Date activated 1 Jan 2004

Date revised 01 June 2011 (Infusion section revised)

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).