BC Cancer Protocol Summary for Therapy of Adjuvant Breast Cancer using Capecitabine

Protocol Code	*BRAJCAP*
Tumour Group	*Breast*
Contact Physician	*Dr. Stephen Chia*

ELIGIBILITY:

- Adjuvant breast cancer therapy in a patient (Pre or post-menopausal women/men treated) treated with a minimum of 6 cycles of anthracycline-taxane (either sequential or concurrent) in pre-operative setting
- HER-2 negative with stage I-IIIB breast cancer with residual invasive disease of greater than 2 cm AND node negative (T2-4 N0) or any T AND any nodal involvement (T0-4 N1-3)
- ECOG performance status 0-2
- patient must be able to report any severe toxicity such as diarrhea, hand/foot syndrome, severe nausea, stomatitis
- may use with tamoxifen or an aromatase inhibitor (at physician's discretion)
- concurrent radiation therapy with capecitabine is not permitted

EXCLUSIONS:

- severe renal impairment (calculated creatinine clearance less than 30 mL/min, see Cockcroft-Gault equation under **DOSE MODIFICATIONS**)
- suspected dihydropyrimidine dehydrogenase (DPD) deficiency (see **PRECAUTIONS**)

CAUTIONS:

- severe hepatic dysfunction (total bilirubin greater than 50 micromol/L)

TESTS:

- Baseline: CBC & diff, platelets, bilirubin, GGT, ALT, LDH, alk phos, and creatinine
- Prior to each cycle: CBC & diff, platelets, creatinine
- If clinically indicated: albumin, bilirubin, GGT, ALT, alk phos, LDH, BUN
- Consider weekly nursing assessment for capecitabine toxicity in first two cycles and when increasing capecitabine dose.

PREMEDICATIONS:

- not usually required

TREATMENT:

Drug	Dose*	BC Cancer Administration Guideline
capecitabine	1000 mg/m^2 BID x 14 days (d 1 to 14) (Total daily dose = 2000 mg/m^2/day)	PO

* Capecitabine is available as 150 mg and 500 mg tablets (refer to Capecitabine Suggested Tablet Combination Table for dose rounding).

Repeat every 21 days x 8 cycles.

DOSE MODIFICATIONS:

1. Hematological

ANC (x10^9/L)		Platelets (x10^9/L)	1st Event Dose	2nd Event Dose	3rd Event Dose	4th Event Dose
greater than or equal to 1.5	and	greater than or equal to 75	100%	100%	100%	100%
1.0 to less than 1.5	or	50 to less than 75	delay* then 100%	delay* then 75%	delay* then 50%	discontinue
0.5 to less than 1.0	or	25 to less than 50	delay* then 75%	delay* then 50%	discontinue	discontinue
less than 0.5	or	less than 25	discontinue or delay* then 50%	discontinue	discontinue	discontinue

*delay until ANC greater than or equal to 1.5 x 10^9/L and platelets greater than or equal to 75 x 10^9/L

2. Hand-Foot Skin Reaction

- if treatment is interrupted due to toxicity, retain the original stop and start dates (ie, do not make up for missed doses when treatment is resumed)

Grade	Hand-Foot Skin Reaction	1st Event Dose	2nd Event Dose	3rd Event Dose	4th Event Dose
1	Skin changes with discomfort (eg, numbness, dysesthesia, paresthesia, tingling, erythema) not disrupting normal activities	100%	100%	100%	100%
2	Skin changes with pain (eg, erythema, swelling) affecting activities of daily living	delay* then 100%	delay* then 75%	delay* then 50%	discontinue

Grade	Hand-Foot Skin Reaction	1st Event Dose	2nd Event Dose	3rd Event Dose	4th Event Dose
3	Severe skin changes with pain (eg, moist desquamation, ulceration, blistering) causing severe discomfort and inability to work or perform activities of daily living	delay* then 75%	discontinue or delay* then 50%	discontinue	discontinue

*stop treatment immediately and delay until resolved to grade 0-1

3. Other Non-Hematological Toxicity

- see next table for toxicity grading criteria for diarrhea, nausea and vomiting, and stomatitis
- if treatment is interrupted due to toxicity, retain the original stop and start dates (ie, do not make up for missed doses when treatment is resumed)

Toxicity Grade	1st Event Dose	2nd Event Dose	3rd Event Dose	4th Event Dose
0-1	100%	100%	100%	100%
2	delay* then 100%	delay* then 75%	delay* then 50%	discontinue
3	delay* then 75%	delay* then 50%	discontinue	discontinue
4	discontinue or delay* then 50%	discontinue	discontinue	discontinue

*stop treatment immediately and delay until toxicity resolved to grade 0-1

Toxicity Criteria

Grade	Diarrhea	Nausea and Vomiting	Stomatitis
0-1	Increase of 2 to 3 stools/day or nocturnal stools	1 vomit/day but can eat	Painless ulcers, erythema or mild soreness
2	Increase of 4 to 6 stools/day or nocturnal stools	2 to 5 vomits/day; intake decreased but can eat	Painful erythema, edema or ulcers but can eat
3	Increase of 7 to 9 stools/day or incontinence, malabsorption	6 to 10 vomits/day and cannot eat	Painful erythema, edema or ulcers and cannot eat
4	Increase of 10 or more stools/day or grossly bloody diarrhea; may require parenteral support; dehydration	10 vomits or more per day or requires parenteral support; dehydration	Mucosal necrosis, requires parenteral support

4. Hepatic dysfunction: Dose modification may be required. Capecitabine has not been studied in severe hepatic dysfunction.

5. Renal dysfunction:

Creatinine Clearance mL/min	Dose
greater than or equal to 50	100%
30 to less than 50	75%
less than 30	0%

Cockcroft-Gault Equation:

$$\text{Estimated creatinine clearance (mL/min)} = \frac{N\,(140 - \text{age})\,\text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

N = 1.23 male

N = 1.04 female

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Dihydropyrimidine dehydrogenase (DPD) deficiency** can result in severe toxicity secondary to reduced drug metabolism.
3. **Possible interactions with warfarin, phenytoin and fosphenytoin** have been reported and may occur at any time. Close monitoring is recommended (eg, for warfarin, monitor INR weekly during capecitabine therapy and for 1 month after stopping capecitabine).
4. **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. Stephen Chia or tumour group delegate at (604) 930-2098 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

Masuda N, Lee SJ, Ohtani S, et al. Adjuvant capecitabine for breast cancer after preoperative chemotherapy. N Engl J Med 2017;376:2147-59.