

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

Protocol Code

BRAJCAP

Tumour Group

Breast

Contact Physician

BR Systemic Therapy

ELIGIBILITY:

Patients must have:

- HER-2 negative resected Stage I to IIIB breast cancer,
- Received prior neoadjuvant chemotherapy with a minimum of 6 cycles of anthracycline-taxane (either sequential or concurrent), and
- Residual invasive disease of greater than 2 cm AND node negative (T2-4 N0), or
- Residual disease in the lymph nodes (N1-3, regardless of T stage)

Patients should have:

- ECOG performance status 0 to 2
- Ability to report any severe toxicity such as diarrhea, hand/foot syndrome, severe nausea, stomatitis

Notes:

- May use with tamoxifen or an aromatase inhibitor (at physician's discretion)
- Concurrent radiation therapy with capecitabine is not permitted
- Use of capecitabine (BRAJCAP) before one of the following is funded if patients meet eligibility criteria:
 - olaparib (UBRAJOLA),
or
 - abemaciclib (UBRAJABEAI/UBRAJABET)Use of BRAJCAP after these protocols will not be funded
- **BRAJCAP is not funded for use with concurrent or sequential pembrolizumab in the adjuvant setting. Switching for toxicity is allowed, provided all other BRAJCAP eligibility criteria are met.**

EXCLUSIONS:

Patients must not have:

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

CAUTIONS:

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

TESTS:

- Baseline: CBC & Diff, total bilirubin, GGT, ALT, LDH, alkaline phosphatase, creatinine, DPYD test (not required if previously tested, or tolerated fluorouracil or capecitabine)
- Prior to each cycle: CBC & Diff, creatinine
- If clinically indicated: albumin, total bilirubin, GGT, ALT, alkaline phosphatase, LDH, urea
- 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 (Days 1 to 14) (Total daily dose = 2000 mg/m ² /day)	PO

*select dose per Dose Banding Table (appendix).

Repeat every 21 days x 8 cycles.

DOSE MODIFICATIONS:**Capecitabine Dosing Based on DPYD Activity Score (DPYD-AS)**

Refer to “Fluorouracil and Capecitabine Dosing Based on DPYD Activity Score (DPYD-AS)” [in the BC Cancer Drug Manual appendix](#).

1. Hematological

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	1 st Event Dose	2 nd Event Dose	3 rd Event Dose	4 th 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 10⁹/L and platelets greater than or equal to 75 x 10⁹/L

2. Hand-Foot Skin Reaction

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

Grade	Hand-Foot Skin Reaction	1 st Event Dose	2 nd Event Dose	3 rd Event Dose	4 th Event Dose
1	Skin changes with discomfort (e.g., numbness, dysesthesia, paresthesia, tingling, erythema) not disrupting normal activities	100%	100%	100%	100%
2	Skin changes with pain (e.g., erythema, swelling) affecting activities of daily living	Delay* then 100%	Delay* then 75%	Delay* then 50%	Discontinue
3	Severe skin changes with pain (e.g., 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 (i.e., do not make up for missed doses when treatment is resumed)

Toxicity Grade	1 st Event Dose	2 nd Event Dose	3 rd Event Dose	4 th 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 (e.g., 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.

Contact the BR Systemic Therapy physician at your regional cancer centre or the BR Systemic Therapy Chair 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.

Appendix. Dose Bands

CAPECITABINE BANDING TABLE

Ordered Dose (mg)		Rounded dose (mg)	Number of Tablets Per Dose	
From:	To:		150 mg	500 mg
226	375	300	2	
376	475	450	3	
476	575	500		1
576	725	650	1	1
726	900	800	2	1
901	1075	1000		2
1076	1225	1150	1	2
1226	1400	1300	2	2
1401	1575	1500		3
1576	1725	1650	1	3
1726	1900	1800	2	3
1901	2075	2000		4
2076	2225	2150	1	4
2226	2400	2300	2	4
2401	2575	2500		5
2576	2725	2650	1	5
2726	2900	2800	2	5
2901	3075	3000		6
3076	3225	3150	1	6
3226	3400	3300	2	6
3401	3575	3500		7
3576	3725	3650	1	7
3726	3900	3800	2	7