

BCCA Protocol Summary for Palliative Therapy of Advanced Colorectal Cancer using Capecitabine

Protocol Code

GIAVCAP

Tumour Group

Gastrointestinal

Contact Physician

GI Systemic Therapy

ELIGIBILITY:

- First line metastatic or unresectable colorectal adenocarcinoma in a patient not suitable for infusional Fluorouracil, either alone (GIFUINF) or in combination with Irinotecan (GIFOLFIRI) or Oxaliplatin (UGIFOLFOX)
- ECOG performance status 0-2
- expected survival greater than 3 months
- patient must be able to report any severe toxicity such as diarrhea, hand/foot syndrome, severe nausea, stomatitis
- A BCCA “Class II Drug Registration Form” form must be submitted
 - * Note: this is for first line therapy only and all requests for other uses will still require an approval through the undesignated route

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 and differential, liver function tests and creatinine
- **Prior to each** cycle: CBC and differential, creatinine
- If clinically indicated: liver function tests, BUN and creatinine

PREMEDICATIONS:

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

TREATMENT:

Drug	Dose*	BCCA Administration Guideline
Capecitabine	1000-1250 mg/m ² BID x 14 days (d 1-14) (Total daily dose = 2000-2500 mg/m ² /day)	PO with food

*Starting dose of 1000 mg/m² bid recommended for elderly, poor performance status or extensively pretreated patients. Capecitabine is available as 150 mg and 500 mg tablets (see following table for dose calculations).

Repeat every 21 days for a maximum of 16 cycles. If there is continued evidence of response or stable disease by imaging or tumour markers, apply for additional cycles via the BCCA Compassionate Access Program. Discontinue if no response after 2 cycles.

Dose Calculation Table

Single Dose (mg)	Number of tablets per dose	
	150 mg	500 mg
1500	0	3
1650	1	3
1800	2	3
2000	0	4
2150	1	4
2300	2	4
2500	0	5
2650	1	5
2800	2	5

DOSE MODIFICATIONS:

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 – 1.49	or	50-74.9	delay* then 100%	delay* then 75%	delay* then 50%	discontinue
0.5-0.99	or	25-49.9	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 (ie, 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 (eg, numbness, dysesthesia, paresthesia, tingling, erythema) with discomfort not disrupting normal activities	100%	100%	100%	100%
2	Skin changes (eg, erythema, swelling) with pain affecting activities of daily living	delay* then 100%	delay* then 75%	delay* then 50%	discontinue
3	Severe skin changes (eg, moist desquamation, ulceration, blistering) with pain, 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	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 2-3 stools/day or nocturnal stools	1 vomit/day but can eat	Painless ulcers, erythema or mild soreness
2	Increase of 4-6 stools/day or nocturnal stools	2-5 vomits/day; intake decreased but can eat	Painful erythema, edema or ulcers but can eat
3	Increase of 7-9 stools/day or incontinence, malabsorption	6-10 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 50	100%
30-50	75%
less than 30	0%

Cockcroft-Gault Equation:

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

$$N = 1.23 \text{ male}$$

$$N = 1.04 \text{ female}$$

PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Dihydropyrimidine dehydrogenase (DPD) deficiency** may result in severe and unexpected toxicity – stomatitis, diarrhea, neutropenia, neurotoxicity – secondary to reduced drug metabolism. This deficiency is thought to be present in about 3% of the population.
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).

Call the GI Systemic Therapy physician at your regional cancer centre or Dr. Sanjay Rao at (250) 712-3900 or 1-888-563-7773 with any problems or questions regarding this treatment program.

Date activated: 01 March 2002 (as UGIAVCAP)

Date revised: 1 Apr 2011 (use of pyridoxine deleted)

References:

1. Hoff PM, Ansari R, Batist G, et al. Comparison of oral capecitabine versus intravenous fluorouracil plus leucovorin as first-line treatment in 605 patients with metastatic colorectal cancer: results of a randomized phase III study. *J Clin Oncol* 2001;19(8):2282-92.
2. Van Cutsem E, Twelves C, Cassidy J, et al. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: results of a large phase III study. *J Clin Oncol* 2001;19(21):4097-106.