

# BCCA Protocol Summary for Adjuvant Therapy Of Colon Cancer using Fluorouracil Injection and Infusion and Folinic Acid (Leucovorin) Infusion

**Protocol Code:** GIAJFL

**Tumour Group:** Gastrointestinal

**Contact Physician:** GI Systemic Therapy

## ELIGIBILITY:

- Resected Stage III or high risk Stage II colon cancer
- ECOG performance status 0-2
- Patient must be able to report any severe toxicity such as diarrhea, hand/foot syndrome, severe nausea, stomatitis

## TESTS AND MONITORING:

- **Baseline** CBC and differential, Creatinine, LFTs (Bilirubin, AST, Alkaline Phosphatase) appropriate imaging study and tumor markers.
- CBC **prior to each cycle**.
- For patients on warfarin, weekly INR until stable warfarin dose established, then INR prior to each cycle.
- Quantitative evaluation of disease response status every eight to twelve weeks; discontinue therapy if any progression of disease.

## PREMEDICATIONS:

- Antiemetics are not usually required (see SCNAUSEA)

## TREATMENT:

A cycle equals -

Drug	Dose	BCCA Administration Guidelines
Folinic Acid (Leucovorin)	400 mg/m <sup>2</sup>	IV in 250 ml D5W over 2 hours
Fluorouracil	400 mg/m <sup>2</sup>	IV bolus, after Folinic Acid, THEN
Fluorouracil	2400 mg/m <sup>2</sup>	IV over 46 h in D5W to a total volume of 92 mL by continuous infusion at 2 mL/h via appropriate infusor device**

Repeat every 14 days for 12 cycles.

**\*\*for total dose greater than 4400 mg, to a total volume of 230 mL by continuous infusion at 5 mL/h via Baxter LV5 infusor**

*(Inpatients: 1200 mg/m<sup>2</sup>/day in 1000 mL D5W by continuous infusion daily over 23 h for 2 days)*

Patients with PICC lines should have a weekly assessment of the PICC site for evidence of infection or thrombosis.

## DOSAGE MODIFICATIONS

Agent	Dose Level 0 (Starting Dose)	Dose Level -1	Dose Level - 2	Dose Level -3
<b>Folinic Acid* (Leucovorin)</b>	400 mg/m <sup>2</sup>	400 mg/m <sup>2</sup>	400 mg/m <sup>2</sup>	Discontinue Therapy
<b>FLUOROURACIL BOLUS</b>	400 mg/m <sup>2</sup>	320 mg/m <sup>2</sup>	240 mg/m <sup>2</sup>	Discontinue Therapy
<b>FLUOROURACIL INFUSION</b>	2400 mg/m <sup>2</sup>	2000 mg/m <sup>2</sup>	1600 mg/m <sup>2</sup>	Discontinue Therapy

*\*Folinic Acid (Leucovorin) dose does not require dose adjustment; Folinic Acid (leucovorin) is delayed or omitted if Fluorouracil is delayed or omitted*

### A. Dose Modifications for HEMATOLOGIC Toxicity

Prior to a Cycle (Day 1)	Toxicity		Dose Level For Subsequent Cycles
	Grade	ANC (x10 <sup>9</sup> /L)	Fluorouracil
<ul style="list-style-type: none"> <li>▪ If ANC less than 1.0 on Day 1 of cycle, hold treatment. Perform weekly CBC, maximum of 2 times.</li> <li>▪ If ANC is greater than or equal to 1.0 within 2 weeks of initial treatment delay, proceed with treatment at the dose level noted across from the <b>lowest ANC</b> result of the delayed week(s).</li> <li>▪ If ANC remains less than 1.0 after 2 weeks, discontinue treatment.</li> </ul>	1	greater than or equal to 1.0	Maintain dose level
	2	1.0 – 1.49	Maintain dose level
	3	0.5 – 0.99	↓ 1 dose level
	4	less than 0.5	↓ 1 dose level
	<b>Grade 4 neutropenia &amp; greater than or equal to Grade 2 fever</b>		↓ 1 dose level
	Grade	Platelets (x10 <sup>9</sup> /L)	Fluorouracil
<ul style="list-style-type: none"> <li>▪ If platelets less than 75 on Day 1 of cycle, hold treatment. Perform weekly CBC, maximum of 2 times.</li> <li>▪ If platelets greater than or equal to 75 within 2 weeks of initial treatment delay, proceed with treatment at the dose level noted across from the <b>lowest platelets</b> result of the delayed week(s).</li> <li>▪ If platelets remain less than 75 after 2 weeks, discontinue treatment.</li> </ul>	1	greater than or equal to 75	Maintain dose level
	2	50 – 74.9	Maintain dose level
	3	10 – 49.9	Maintain dose level
	4	less than 10.0	Maintain dose level

## B. Dose Modifications for NON-HEMATOLOGIC Toxicity

Prior to a Cycle (Day 1)	Toxicity		Dose Level For Subsequent Cycles
	Grade	Diarrhea	Fluorouracil
<ul style="list-style-type: none"> <li>▪ If diarrhea greater than or equal to Grade 2 on Day 1 of cycle, hold treatment. Perform weekly checks, maximum 2 times.</li> <li>▪ If diarrhea is less than Grade 2 within 2 weeks of treatment delay, proceed with treatment at the dose level noted across from the <b>highest</b> Grade experienced.</li> <li>▪ If diarrhea remains greater than or equal to Grade 2 after 2 weeks, discontinue treatment.</li> </ul>	1	Increase of 2-3 stools/day, or mild increase in loose watery colostomy output	Maintain dose level
	2	Increase of 4-6 stools, or nocturnal stools or mild increase in loose watery colostomy output	Maintain dose level
	3	Increase of 7-9 stools/day or incontinence, malabsorption; or severe increase in loose watery colostomy output	↓ 1 dose level of
	4	Increase of 10 or more stools/day or grossly bloody colostomy output or loose watery colostomy output requiring parenteral support; dehydration	↓ 1 dose level
	Grade	Stomatitis	
<ul style="list-style-type: none"> <li>▪ If stomatitis greater than or equal to Grade 2 on Day 1 of cycle, hold treatment. Perform weekly checks, maximum 2 times.</li> <li>▪ If stomatitis is less than Grade 2 within 2 weeks of initial treatment delay, proceed with treatment at the dose level noted across from the <b>highest</b> Grade experienced.</li> <li>▪ If stomatitis remains greater than or equal to Grade 2 after 2 weeks, discontinue treatment.</li> </ul>	1	Painless ulcers, erythema or mild soreness	Maintain dose level
	2	Painful erythema, edema, or ulcers but can eat	Maintain dose level
	3	Painful erythema, edema, ulcers, and cannot eat	↓ 1 dose level
	4	As above but mucosal necrosis and/or requires enteral support, dehydration	↓ 2 dose levels

## PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Myocardial** ischemia and angina occurs rarely in patients receiving Fluorouracil. Development of cardiac symptoms including signs suggestive of ischemia or of cardiac arrhythmia is an indication to discontinue treatment.
3. **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.
4. **Stomatitis:** Sucking ice chips may be considered for patients experiencing stomatitis. Remove dentures and place ice chips in mouth five minutes before chemotherapy. Continuously swish in mouth for 30 minutes, replenishing as ice melts. This may cause numbness or headaches, which subside quickly.
5. **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 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: 1 Jan 2007

Date revised: 01 June 2011 (Infusion section revised)

## REFERENCES: