

BCCA Protocol Summary for Palliative Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan

Protocol Code
Tumour Group
Contact Physician

GIIR
Gastrointestinal
GI Systemic Therapy

ELIGIBILITY:

- Palliative treatment of metastatic colorectal cancer
- ECOG performance status 0-2 if age 18-65 years, or 0-1 if age greater than 65 years
- Class II form must be completed for first 6 cycles. For more than 6 cycles an "Individual use of Benefit Drug List Medication for an Undesignated Indication" form must be completed and approved.

EXCLUSIONS:

- Inadequate hepatic function (bilirubin greater than or equal to 35 micromol/L; AST/ Alkaline Phosphatase greater than or equal to 5 x ULN)
- Greater than 3 loose stools per day in patients without colostomy or ileostomy

TESTS:

Baseline: CBC, diff, platelets, LFTs (Bilirubin, AST, Alkaline Phosphatase), appropriate tumour markers and imaging study

Prior to each treatment: CBC, diff, platelets

If clinically indicated: LFTs (Bilirubin, AST, Alkaline Phosphatase), appropriate tumour markers

After 2 cycles, then every 2-3 cycles: imaging study

PREMEDICATIONS:

- Antiemetic protocol for high moderate emetogenic chemotherapy (see SCNAUSEA).
- prochlorperazine should be avoided on the same day as irinotecan treatment due to the increased incidence of akathisia.

TREATMENT:

A cycle equals -

Drug	Dose*	BCCA Administration Guideline
Irinotecan	350 mg/m ²	IV in 500 mL D5W over 1 hour 30 min

* Starting dose = 300 mg/m² for age 70 years and older, or PS=2
Maximum dose = 700 mg

Repeat every 21 days until disease progression, unacceptable toxicity or 6 cycles.
Discontinue if no clinical benefit after 2 cycles.

All patients should be advised to obtain an adequate supply of Loperamide (IMODIUM®) with explicit instructions for the management of diarrhea.

DOSE MODIFICATIONS:

1. If multiple toxicities are seen, the dose administered should be based on the most severe toxicity experienced. If not recovered after 2 weeks, consider discontinuing treatment.

2. Hematological

ANC ($\times 10^9/L$)		Platelets ($\times 10^9/L$)	Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
1.0-1.49	or	75-99	delay then 100%
less than 1.0	or	less than 75	delay then decrease 50 mg/m ²

3. **Neutropenic Fever:** Delay then decrease 50 mg/m² when resolved.

4. Diarrhea

Grade	Diarrhea	Dose
1-2	Increase of up to 6 stools, or nocturnal stools or moderate increase in loose watery colostomy output	100%
3-4	Increase of 7 or more stools/day or incontinence, malabsorption, severe increase in loose watery colostomy output, grossly bloody diarrhea, may require parenteral support	Delay until grade 2 or less then decrease 50 mg/m ²

PRECAUTIONS:

1. **Diarrhea** may be life-threatening and requires prompt, aggressive treatment.

- **Early diarrhea** or abdominal cramps occurring within the first 24 hours is treated with **atropine** 0.3 - 1.2 mg IV or SC. Prophylactic atropine may be required for subsequent treatments.
- **Late diarrhea** has a median onset of 5 days post-treatment with this regimen and must be treated with **loperamide** (eg, IMODIUM®). The loperamide dose is higher than recommended by the manufacturer. Instruct patient to have loperamide on hand and start treatment at the first poorly formed or loose stool, or earliest onset of more frequent stool than usual:
 - **4 mg stat**
 - **then 2 mg every 2 hours until diarrhea-free for 12 hours**
 - may take 4 mg every 4 hours at night

2. **Other cholinergic symptoms** may occur during or shortly after infusion of irinotecan, including rhinorrhea, increased salivation, lacrimation, diaphoresis and flushing. These should be treated with atropine 0.3 mg – 0.6 mg IV or SC. This dose may be repeated at the physician's discretion. Blood pressure and heart rate should be monitored. Prophylactic atropine may be required for subsequent treatments.

3. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.

4. **Gilbert's Syndrome** increases the risk of irinotecan-induced toxicity (Ann Oncol 1997;8:1049-51). A screen for Gilbert's Syndrome using direct/indirect serum bilirubin is recommended. If present, reduce the starting dose to 200 mg/m².

5. **Hepatic Dysfunction:** Irinotecan has not been studied in patients with bilirubin greater than 35 micromol/L or AST greater than 3x the upper limit of normal if no liver metastases, or AST greater than 5x the upper limit of normal with liver metastases.

6. **Pulmonary toxicity:** Severe pulmonary toxicity has been reported rarely. Supportive care is required.

7. **Prior pelvic radiotherapy or radiotherapy** to greater than 15% of the bone marrow bearing area may increase the degree of myelosuppression associated with this regimen, and caution is recommended in these cases. Close monitoring of the CBC is essential.

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 activate: N/A

Date revised: 01 June 2011 (Infusion section revised)

Reference:

1. Cunningham D, Pyrhonen S, James RD, et al. Randomised trial of irinotecan plus supportive care versus supportive care alone after fluorouracil failure for patients with metastatic colorectal cancer. *Lancet* 1998; 352: 1413-8.
2. Rougier P, Van Cutsem E, Bajetta E, et al. Randomised trial of irinotecan versus fluorouracil by continuous infusion after fluorouracil failure with metastatic colorectal cancer. *Lancet* 1998; 352: 1407-12.