# BC Cancer Protocol Summary for Palliative Chemotherapy of Metastatic Colorectal Cancer using Irinotecan

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| ***Protocol Code*** | *GIIR* |
| ***Tumour Group*** | *Gastrointestinal* |
| ***Contact Physician*** | *GI Systemic Therapy* |

**ELIGIBILITY**:

Patients must have:

- Metastatic colorectal cancer, requiring palliative treatment

Patients should have:

- ECOG performance status 0 to 2 if age 18 to 75 years, or 0 to 1 if age greater than 75 years

**EXCLUSIONS:**

Patients must not have:

- Inadequate hepatic function (total bilirubin greater than or equal to 35 micromol/L; AST or 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, creatinine, ALT, alkaline phosphatase, total bilirubin, albumin, sodium, potassium
- Baseline if clinically indicated: CEA, CA19-9, GGT, ECG
- Prior to each treatment: CBC & Diff, creatinine, total bilirubin, ALT
- If clinically indicated: CEA, CA 19-9, alkaline phosphatase, albumin, GGT, sodium, potassium, ECG

**PREMEDICATIONS:**

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

**TREATMENT:**

| Drug | Dose* | BC Cancer Administration Guideline |
|---|---|---|
| irinotecan | 350 mg/m$^2$ | IV in 500 mL D5W over 1 hour 30 min |

* Starting dose = 300 mg/m$^2$ for age 70 years and older, or ECOG = 2

Repeat every 21 days until disease progression or unacceptable toxicity.

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 ($x10^9$/L) | | Platelets ($x10^9$/L) | Dose |
|---|---|---|---|
| Greater than or equal to 1.5 | and | Greater than or equal to 100 | 100% |
| 1.0 to less than 1.5 | or | 75 to less than 100 | 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/m$^2$ when resolved.

4. **Diarrhea**

| Grade | Diarrhea | Dose |
|---|---|---|
| 1 to 2 | Increase of up to 6 stools, or nocturnal stools or moderate increase in loose watery colostomy output | 100% |
| 3 to 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 mg subcutaneously. Dose may be repeated every 30 minutes as needed to a maximum of 1.2 mg. 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 subcutaneously. Dose may be repeated every 30 minutes as needed to a maximum of 1.2 mg. 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. A screen for Gilbert's Syndrome using direct/indirect serum bilirubin is recommended. If present, reduce the starting dose to 200 mg/m$^2$.

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 the GI Systemic Therapy Chair Dr. Theresa Chan at (604) 930-2098 with any problems or questions regarding this treatment program.**

**References:**


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 fluororuracil failure with metastatic colorectal cancer. Lancet 1998; 352: 1407-12.
3. Wasserman E, Myara A, Lokiec F, et al. Severe CPT-11 toxicity in patients with Gilbert's syndrome: two case reports. Ann Oncol 1997;8(10):1049-51.