

# BCCA Protocol Summary for the Chemotherapy of Pseudomyxoma Peritonei Using Intraperitoneal Mitomycin and Fluorouracil

**Protocol Code**

*GIFUIP*

**Tumour Group**

*Gastrointestinal*

**Contact Physicians**

*GI Systemic Therapy*

The surgery and the early postoperative intraperitoneal chemotherapy (cycle #1) are to be carried out only at the Vancouver General Hospital with the participation of medical oncologists from the BCCA Vancouver Center. Cycles # 2, 3, 4 can be given in a hospital with a renal dialysis unit under the supervision of a medical or regional oncologist.

## **ELIGIBILITY:**

- Pathologic diagnosis of pseudomyxoma peritonei
- Patient is grossly disease free after cytoreductive surgery

## **EXCLUSIONS:**

- Invasive adenocarcinoma of GI or ovarian origin
- Gross residual disease

## **TESTS:**

Before each treatment:

- CBC & diff, platelets, liver enzymes, electrolytes, creatinine, appropriate tumour markers
- CT abdomen/pelvis with IP contrast to ensure even distribution
- For patients on warfarin, weekly INR during fluorouracil therapy until stable warfarin dose established, then INR prior to each cycle.

## **PREMEDICATIONS:**

- For most patients this regimen has low/moderate emetogenicity. Some patients may require pre treatment antiemetics.
- See SCNAUSEA protocol

## **TREATMENT:**

### **Cycle # 1**

#### Early Postoperative Intraperitoneal Chemotherapy

Day 1 Postoperative cytoreductive surgery – to be started on the surgical unit

1. Add mitomycin 10 mg/m<sup>2</sup> (to a maximum of 20 mg) to 1000 mL 1.5% dextrose dialysis solution. Drain all fluid from the abdominal cavity prior to instillation, then close suction drains.
2. Run the chemotherapy solution into the abdominal cavity as rapidly as possible. Dwell for 23 hours with all abdominal drains clamped.

Days 2 - 5

1. Add fluorouracil 15 mg/kg and sodium bicarbonate 50 mEq to 1000 mL 1.5% dextrose dialysis solution.
2. Drain all fluid from the abdominal cavity prior to instillation, then clamp closed suction drains.

- Run the chemotherapy solution into the abdominal cavity as rapidly as possible. Dwell for 23 hours then drain for one hour. Repeat chemotherapy instillation each day.
- Drain the abdominal cavity after final 24-hour dwell and cap the TENCKHOFF™ catheter for removal later.

### **Cycles # 2, 3, 4**

#### Delayed Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis

##### Days 1 - 5

- Add fluorouracil 20 mg/kg and sodium bicarbonate 50 meq to 1000 mL 1.5% dextrose dialysis solution. Instill as rapidly as possible. Dwell for 23 hours, then drain for 1 hour.
- Drain all fluid from abdominal cavity prior to next instillation. If fluid fails to drain, proceed with next instillation.

##### Day 3 only

- Give mitomycin 10 mg/m<sup>2</sup> (to a maximum of 20 mg) IV push.

Repeat chemotherapy every four weeks for a total of three cycles.

### **DOSE MODIFICATIONS:**

#### **1. Hematological**

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Dose Fluorouracil and Mitomycin
greater than 1.5	and	greater than 100	100%
1 to 1.49	or	75 to 100	50%
less than 1.0	or	less than 75	0

#### **2. Non – Hematologic Toxicities**

Grade	Stomatitis	Diarrhea	Dose Fluorouracil only
1	Painless ulcers, erythema or mild soreness	Increase of 2-3 stools/day or mild increase in loose watery colostomy output	100%
2	Painful erythema, edema, or ulcers but can eat	Increase of 4-6 stools, or nocturnal stools or mild increase in loose watery colostomy output	80%
3	Painful erythema, edema, or ulcers and cannot eat	Increase of 7-9 stools/day or incontinence, malabsorption; or severe increase in loose watery colostomy output	70%
4	Mucosal necrosis, requires parenteral support	Increase of 10 or more stools/day or grossly bloody diarrhea, or grossly bloody colostomy output or loose watery colostomy output requiring parenteral I support; dehydration	70%

- Renal dysfunction:** If GFR is less than 0.2 mL/sec (12 mL/min), reduce dose of Mitomycin only to 75%.

Cockcroft/Gault formula:

$$CrCl (mL/min) = \frac{N (140-age) \times weight (kg)}{\text{serum creatinine (micromol/L)}}$$

Where  $N = 1.04$  for females, and  $1.23$  for males

- Hepatic dysfunction:** Omit Fluorouracil if bilirubin is greater than 85 micromol/L, unless secondary to biliary obstruction (BCCA Cancer Drug Manual)

#### PRECAUTIONS:

- Pulmonary toxicity:** Mitomycin is associated with pulmonary toxicity consisting of dyspnea and non-productive cough, with an incidence of 3-12%. Threshold dose for pulmonary toxicity is 50-60 mg/m<sup>2</sup>.
- Renal toxicity:** Mitomycin is associated with a syndrome of renal failure and **microangiopathic hemolytic anemia**, with an incidence of 10%. Threshold dose for syndrome is 50-60 mg/m<sup>2</sup>, usually appearing after 6 months of therapy.
- 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 / capecitabine toxicity is strongly advised under these circumstances. The toxicity should also be noted in the patient's allergy profile.
- Diarrhea:** Patients should report mild diarrhea that persists over 24 hours or moderate diarrhea (4 stools or more per day above normal, or a moderate increase in ostomy output). Mild diarrhea can be treated with loperamide (eg. IMODIUM®) following the manufacturer's directions or per the [BCCA Guidelines for Management of Chemotherapy-Induced Diarrhea](#). Note that diarrhea may result in increased INR and the risk of bleeding in patients on warfarin.
- 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.
- Possible drug interaction with fluorouracil and warfarin** has been reported and may occur at any time. For patients on warfarin, weekly INR during fluorouracil therapy is recommended until a stable warfarin dose is established. Thereafter, INR prior to each cycle. Consultation to cardiology/internal medicine should be considered if difficulty in establishing a stable warfarin dose is encountered. Upon discontinuation of fluorouracil, repeat INR weekly for one month.
- Possible drug interaction with fluorouracil and phenytoin and fosphenytoin** has been reported and may occur at any time. Close monitoring is recommended. Fluorouracil may increase the serum concentration of these two agents.

**Call Dr. JP McGhie at (250) 519-5500 or 1-800-670-3322 with any problems or questions regarding this treatment program.**

Date activated: 08 Mar 1999

Date revised: 1 Nov 2015 (addition of Diarrhea Precaution)

**References:**

Sugarbaker PH, Chang D. Results of treatment of 385 patients with peritoneal surface spread of appendiceal malignancy. Ann Surg Oncol 1999;6(8):727-31.