Colon Cancer - Stage IV
GI Practice Guideline

Dr. Brian Dingle MSc, MD, FRCPC

Approval Date:
January 2007

This guideline is a statement of consensus of the GI Disease Site Team regarding their views of currently accepted approaches to treatment. It is not intended to replace the independent medical judgement of the physician in the context of individual clinical circumstances to determine any patient’s care or treatment.
# Table of Contents

Background/Incidence ................................................................. 3

Investigations .................................................................................. 4

Staging ............................................................................................. 5

Treatment .......................................................................................... 5
  Standard Treatment ........................................................................ 5
  Neoadjuvant Treatment ................................................................. 5
  Chemoradiotherapy ....................................................................... 6
  Adjuvant Chemotherapy ............................................................... 6

Treatment Benefits .......................................................................... 6

Palliative resection ........................................................................... 7

Metastasectomy ................................................................................ 7

Followup recommendations (following active treatment) .................... 7

Genetic Counselling ......................................................................... 8

References ...................................................................................... 9

NCCN Guideline Charts .................................................................. 10-12

Contact Information ......................................................................... 13
Colon Cancer - Stage IV
GI Practice Guideline

Background/Incidence
Approximately 30-40% of patients with colon or rectal cancer have metastatic disease at the time of diagnosis. Anywhere from 20 to 70 per cent of patients with resected disease who are candidates for adjuvant therapy will subsequently relapse. Only rare groups of patients with localized oligometastatic disease may ultimately be cured. This guideline outlines the current treatment offered at the London Regional Cancer Program, LHSC.

Investigations
A variety of investigations may identify recurrent disease, so there is no specific algorithm for investigation. Often a rising CEA may imply onset of disease, often followed by radiographic studies, and confirmed by biopsy. As a general rule, biopsy of the recurrent lesion is necessary to confirm the diagnosis, rule out a second malignancy, and should be omitted only when the totality of clinical evidence for recurrence is overwhelming (symptoms, radiographic studies, elevation of CEA, timing from previous presentation and initial stage).

Special presentations:

Rising CEA only
If after CT chest and abdomen, and colonoscopy, no evidence of recurrence is detected, consider a PET Scan (available under study).

Solitary (or few) nodules
Consider evaluation for either hepatic or pulmonary, metastatectomy in healthy patients with potential survival advantage

Staging
(See early stage guidelines)
Treatment

Generally, only palliative chemotherapy and best supportive care, with possible options for localized therapy in specific circumstances (resection of retained primary for obstructive symptoms) exist at this stage.

Timing

Although many physicians institute treatment at a time when patients are asymptomatic, there is little evidence supporting such therapy compared to ‘watchful waiting’. For those who wish to undertake this latter approach, it may be wise to ‘estimate’ when liver failure may ensue (if hepatic disease exists) in order to gain the benefit early of drugs, which cannot be used in the face of elevated bilirubin (i.e. Irinotecan).

Chemotherapy

The clinician needs to make a decision with the patient as to the aggressiveness of initial therapy, balancing toxicity, Quality of Life (QoL) objectives, and ease of delivery, comorbidities. Many physicians will approach initial therapy with ‘Mild therapies’, proceeding to ‘Aggressive therapies’ at a later date with progression of disease. Some patients may wish to start with ‘Aggressive therapies’ to begin with, possibly resorting to ‘Mild therapies’ when the disease is causing progressively worsening symptoms.

The following therapies are thought to be equivalent:

Note: modifications within OPIS protocols have been made when compared to original literature noted in italics

Mild (RR = 10-25%)

1. Capecitabine 2000-2500 mg/M$^2$ po in divided doses BID, 2 weeks out of 3
2. DeGramont-Modified (LV5FU2) Folinic Acid 400 mg/M$^2$ + 5FU 400 mg/M$^2$ bolus, then 2400 mg/M$^2$ CIV over 46 hours q2wk (Folinic Acid on day one, and 5FU doubled for infusion)
3. 5FU CIV 225-300 mg/M$^2$ continuous as tolerated
4. FUFA: 5FU 400 mg/M$^2$ + Folinic Acid 20 mg/M$^2$ IV OD x 5 q4wk
5. Roswell: 5FU 500 mg/M$^2$ + Folinic Acid 500 mg/M$^2$ IV q1wk
6. Tomudex 3 mg/M$^2$ IV q 3 weeks for patients who cannot tolerate 5FU

Of these therapies, FUFA is probably the most toxic, and should be avoided if possible.
For patients with metastatic colorectal cancer, several chemotherapy regimens are available.

**Aggressive (RR = 45-50%+)²**

1. **FOLFIRI:** Irinotecan 180 mg/M² IV, Folinic Acid 400 mg/M² + 5FU 400 mg/M² bolus, then 2400 mg/M² CIV over 46 hours q2wk, with atropine *(Folinic Acid on day one only)*

2. **FOLFOX4 - Modified:** Oxaliplatin 85mg/M² IV, Folinic Acid 400 mg/M² + 5FU 400 mg/M² bolus, then 2400 mg/M² CIV over 46 hours q2wk *(note: this is FOLFOX6 5FU dose with FOLFOX4 Oxaliplatin dose, and only one day of Folinic Acid: some literature refers to this as modified FOLFOX6)*

3. **XELOX:** Oxaliplatin 130 mg/M² IV, Capecitabine 2000 mg/M² po in divided doses BID, 2 weeks out of 3³

4. **TOMOX:** Tomudex 3 mg/M² IV and Oxaliplatin 100 mg/M² IV q 3 week

5. +/- Bevacizumab: See Bevacizumab guideline

6. Cetuximab with or without Irinotecan: See Cetuximab guideline

**Available Trials**

**Treatment Duration**

Optimox studies have suggested that in selected cases of patients with stable disease of a non-life threatening extent, breaks in chemotherapy of two months or so may occur without serious detrimental effect on life span and Q of L.

**Genetic Counselling**

*(See Rectal Cancer guideline)*

**References**


4. Additional reference from Michael s.
CHEMOTHERAPY FOR ADVANCED OR METASTATIC DISEASE:¹ (PAGE 1 of 6)

First-line therapy:  
- FOLFOX² + bevacizumab³  
  or  
- FOLFIRI⁴ + bevacizumab³

Second-line therapy:  
- FOLFIRI⁴,⁷ or Irinotecan⁴  
  → Irinotecan⁴ + cetuximab⁸

Third-line therapy:  
- FOLFOX or Irinotecan⁴ + cetuximab⁸  
  → FOLFOX  
  or  
- FOLFOX or Irinotecan⁴ + cetuximab⁸  
  → Irinotecan⁴,⁹ + cetuximab⁸

Fourth-line therapy:  
- Irinotecan⁴,⁹  
  → Irinotecan⁴,⁹ + cetuximab⁸

Patient can tolerate intensive therapy:

- 5-FU/leucovorin + bevacizumab³,⁶
  or  
- CAPOX + bevacizumab (category 2B)

  → Irinotecan⁴,⁹  
  or  
  → Irinotecan⁴,⁹ + cetuximab⁸
Author, Contact Information

Brian Dingle, MSc, MD, FRCPC
London Regional Cancer Program
London Health Sciences Centre
790 Commissioners Road East
London, Ontario, Canada  N6A 4L6

Telephone: 519.685.8600 Ext. 56184

This guideline is a statement of consensus of the GI Disease Site Team regarding their views of currently accepted approaches to treatment. It is not intended to replace the independent medical judgement of the physician in the context of individual clinical circumstances to determine any patient’s care or treatment.