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Colon Cancer

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Note: Consider Clinical Trials as treatment options for eligible patients. Initial evaluation should include assessment of family history for HNPCC, FAP, or other less common germline mutations associated with colorectal cancer.

PRESENTATION

1. Advanced adenoma with high grade dysplasia and/or intramucosal adenocarcinoma, villous architecture > 25% or ≥ 10 mm in size

2. Repeat colonoscopy within 12 months

3. Pathology’ and colonoscopy review

4. Completely removed

5. Transected or residual adenoma

6. Observation, see Page 10

7. Single specimen, completely removed, no unfavorable histology

8. Endoscopic polyectomy

9. Endoscopically removable?

10. Endoscopic polyectomy

PRIMARY TREATMENT

1. Adenoma with invasive carcinoma

2. Pedunculated

3. Adenocarcinoma of the colon

4. Observation, see Page 10

5. Single endoscopic resection specimen, completely removed, no unfavorable histology

6. Diverting colostomy

7. Is primary tumor resectable?

8. Yes

9. Consider systemic chemotherapy

10. Yes

11. Colon resection, see Principles of Surgery

12. No

13. Yes

14. Consider clinical trial

15. No

16. Individualized management

CEA = carcinoembryonic antigen colorectal cancer MMR/dMMR = mismatch repair/deficient mismatch repair FAP = familial adenomatous polyposis MSI = microsatellite instability HNPCC = hereditary nonpolyposis colorectal cancer

1. See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

2. Refer to Principles of Endoscopic Therapy

3. Consider MD Anderson approved GI biomarkers including immunohistochemistry for MMR protein expression or MSI analysis by PCR

4. In the absence of unfavorable characteristics, CT of chest with or without contrast and enhanced CT or MRI of abdomen and pelvis is optional

5. There is controversy regarding endoscopic management of malignant polyps. The depth of penetration into the submucosa has been shown to be associated with the risk of metastasis or recurrence. Those with minimal penetration into the submucosa and no adverse histologic features may be a candidate for endoscopic resection followed by observation. Careful histopathologic review is prerequisite for this approach. See Page 11 for Principles of Endoscopic Therapy.

6. High-risk features for Stage II colon cancer: Poor differentiation, Obstruction, Inadequate nodal sampling (< 12 nodes), Lympathic, vascular or perineural invasion, T4 disease (invasion of serosa or other organ)

7. Low-risk defined by absence of high-risk features (see footnote 8) or dMMR

8. High-risk features for Stage II colon cancer: Poor differentiation, Obstruction, Inadequate nodal sampling (< 12 nodes), Lympathic, vascular or perineural invasion, T4 disease (invasion of serosa or other organ)

9. Refer to Page 14 for Principles of Adjuvant Systemic Therapy

10. Endoscopic stent decompression may be considered in selected circumstances without adjacent angulation. Stents should not be deployed in the rectum.

CEA = carcinoembryonic antigen colorectal cancer

Malignant polyps

MMR/dMMR = mismatch repair/deficient mismatch repair

FAP = familial adenomatous polyposis

MSI = microsatellite instability

HNPCC = hereditary nonpolyposis colorectal cancer

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Colon Cancer

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PRESENTATION1 AND EVALUATION

Stage IV with metastatic confirmation2

- CEA
- Pathology review3
- CT of chest with or without contrast
- Contrast-enhanced CT or MRI of abdomen/pelvis
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Surrogate Decision-Maker (SDM)4

Surgically resectable metastasis

Recommend multidisciplinary management

Choice and timing of systemic chemotherapy, surgery and radiation (if appropriate) are to be individualized based on multidisciplinary management discussion between the medical, surgical, and radiation oncologists

Refer to Principles of Colon Surgery5, Principles of Systemic Therapy6, and consider radiation therapy (if appropriate)

Conversion to surgically resectable metastatic disease?

Yes

Individualized treatment considering response

No

Surgically unresectable metastasis

Primary tumor asymptomatic

- Endoscopic evaluation of luminal patency
- First line systemic therapy6,7

First line systemic therapy6,7

Primary tumor symptomatic, including obstructing

- Colon resection8
- Fecal diversion (bypass, ostomy)
- Endoscopic palliation9 (stent or ablation) when possible

Individualized treatment considering response

Yes

Refractoriness to first line therapy

No

Primary tumor as symptomatic

Endoscopic palliation9 (stent or ablation) when possible

Secondary line systemic therapy6,7

Endoscopic palliation9

Note: Consider Clinical Trials as treatment options for eligible patients. Initial evaluation should include assessment of family history for HNPCC, FAP, or other less common germline mutations associated with colorectal cancer.

1 See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

2 See Page 4 for Stage IV with carcinomatosis

3 Confirm biomarker studies include expanded RAS, BRAF V600E, HER2 amplification, MSI status, and NTRK gene fusion (if positive for MSI-H). Refer to MD Anderson approved GI biomarkers.

4 GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients or if clinically indicated the SDM should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

5 See Page 12 for Principles of Colon Surgery

6 See Page 14 for Principles of Systemic Therapy

7 See Page 6 or 7 for Systemic Therapy for Advanced or Metastatic Disease as indicated

8 If the potential for resectability of metastases remains, extent of resection should be curative, rather than palliative

9 Refer to Page 11 for Principles of Endoscopic Therapy

ECOG = Eastern Cooperative Oncology Group
CEA = carcinoembryonic antigen colorectal cancer
MSI = microsatellite instability

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Approved by the Executive Committee of the Medical Staff on 11/15/2022
Colon Cancer

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PRESENTATION\(^1\) AND EVALUATION

Stage IV with carcinomatosis

- CEA
- Pathology review\(^2\)
- CT of chest with or without contrast
- Contrast-enhanced CT or MRI of abdomen/pelvis
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Surrogate Decision-Maker (SDM)\(^3\)

Widespread/ unresectable metastasis or poor surgical candidate?

- Evaluation of symptomatic primary or metastatic disease (e.g., obstruction). See Page 3.
- Consider diagnostic laparoscopy with washings and biopsies as indicated
- Calculate Peritoneal Cancer Index (PCI)\(^6\)

Is peritoneal metastasis site resectable?\(^7\)

- Continue current chemotherapy regimen until progression of disease followed by second line chemotherapy\(^4,5\) if tolerating therapy and ECOG performance status \(\leq 2\)
- Best supportive care
- Consideration and discussion of clinical trials when available

Disease progression?

Yes

- Consider 3-6 months of systemic therapy\(^4,5\)
- Consider immunotherapy for MSI-High tumors\(^4,5\)

Diagnostic laparoscopy with washings and biopsies as indicated

No

ECOG = Eastern Cooperative Oncology Group
CEA = carcinoembryonic antigen colorectal cancer
MSI = microsatellite instability
HIPEC = heated intraperitoneal chemotherapy

Treatment and Evaluation

- Surveillance with imaging and tumor markers as indicated
- Consider evaluation for minimal residual disease and further systemic therapy\(^4,5\)

Complete cytoreduction

Incomplete cytoreduction

\(^1\) See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
\(^2\) Confirm biomarker studies include expanded RAS, BRAF V600E, HER2 amplification, MSI status, and NTRK gene fusion (if positive for MSI-H).
\(^3\) Refer to MD Anderson approved GI biomarkers.
\(^4\) GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist.
\(^5\) Patients or if clinically indicated the SDM should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated.
\(^6\) The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).
\(^7\) PCI < 20 without prohibitive solid organ involvement (e.g., major hepatectomy required, head of pancreas involved, retroperitoneal lymphadenopathy, prohibitive small bowel or abdominal wall resection)

ECOG = Eastern Cooperative Oncology Group
CEA = carcinoembryonic antigen colorectal cancer
MSI = microsatellite instability
HIPEC = heated intraperitoneal chemotherapy
EVALUATION AND MANAGEMENT OF SUSPECTED OR DOCUMENTED RECURRENT COLON CANCER

Elevated CEA, positive monitoring exam

- CT of chest with or without contrast
- Contrast-enhanced CT or MRI of abdomen/pelvis
- Colonoscopy with biopsy if endoluminal recurrence suspected

Consider PET/CT scan and if positive consider biopsy

Recurrence not confirmed

- Negative
  - Biopsy
  - Pathology review

- Positive
  - Biopsy
  - Pathology review

Recurrence confirmed

- Is recurrence site resectable?
  - Yes
    - Multidisciplinary management including medical, surgical and radiation oncologists (if appropriate)
  - No
    - First line chemotherapy
    - Palliative care

Individualized treatment considering response

- Yes
  - Continue current chemotherapy regimen until progression of disease followed by second line chemotherapy if tolerating therapy and ECOG performance status ≤ 2
  - Discuss GCC with patient or if clinically indicated, with SDM
- No

Individualized surveillance

- Metastatic
  - Conversion to surgically resectable disease?
    - Yes
      - Multidisciplinary management including medical, surgical and radiation oncologists (if appropriate)
    - No
      - First line chemotherapy
      - Palliative care

ECOG = Eastern Cooperative Oncology Group
CEA = carcinoembryonic antigen colorectal cancer

1 Consider MD Anderson approved GI biomarkers
2 Multidisciplinary evaluation to determine resectability, treatment options, and plans
3 See Page 12 for Principles of Colon Surgery
4 See Page 14 for Principles of Systemic Therapy
5 GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients or if clinically indicated the SDM should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).
6 See Page 6 or 7 for Systemic Therapy for Advanced or Metastatic Disease as indicated

Note: Consider Clinical Trials as treatment options for eligible patients. Initial evaluation should include assessment of family history for HNPCC, FAP, or other less common germline mutations associated with colorectal cancer.

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**SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE**

### First-line Therapy
- **FOLFOX with or without bevacizumab**
- **FOLFOX with or without anti-epidermal growth factor receptor (EGFR) therapy**
- **CapeOx with or without bevacizumab**
- **CapeOx with or without panitumumab**
- **FOLFIRI with or without bevacizumab**
- **FOLFIRI with or without anti-EGFR therapy**
- **FOLFOXIRI with or without bevacizumab**
- **FOLFOXIRI with anti-EGFR therapy**
- **Nivolumab with or without ipilimumab (if dMMR/MSI-H)**
- **Pembrolizumab (if dMMR/MSI-H)**
- **Screen for NTRK gene fusion, especially if dMMR/MSI-H. If positive, may use larotrectinib or entrectinib.**

### Second-line Therapy
- Consider the following second-line therapy if received any of the first line therapy options:
  - Encorafenib (if BRAFT600E) with anti-EGFR therapy
  - Single agent nivolumab or pembrolizumab (if dMMR/MSI-H) and did not receive immunotherapy in first line setting
  - Consider nivolumab with ipilimumab for those who previously received single agent pembrolizumab (if dMMR/MSI-H)
  - Fam-trastuzumab deruxtecan-nxki (for HER2-amplified)
  - Trastuzumab with either pertuzumab or lapatinib or tucatinib (for HER2-amplified and RAS and BRAFT WT)
  - Screen for NTRK gene fusion, especially if dMMR/MSI-H. If positive, may use larotrectinib or entrectinib.
  - Clinical trial

- Consider the following additional second-line therapy options if received nivolumab, pembrolizumab, or FOLFIRI as the first line therapy option:
  - FOLFOX with or without bevacizumab
  - FOLFOX with anti-EGFR therapy, if did not receive anti-EGFR therapy in first-line setting
  - CapeOx with or without bevacizumab
  - CapeOx with or without panitumumab, if did not receive anti-EGFR therapy in first-line setting

- Consider the following additional second-line therapy options if received pembrolizumab, FOLFOX, or CapeOx as the first line therapy option:
  - Single agent nivolumab or pembrolizumab (if dMMR/MSI-H)
  - Consider nivolumab with ipilimumab for those who previously received single agent pembrolizumab and did not receive anti-EGFR therapy in first-line setting

- If no suitable second-line therapy options, consider third-line therapy options:

### Third-line (plus) Therapy
- Consider one of the following:
  - Clinical trial
  - Trifluridine/tipiracil with or without bevacizumab
  - Regorafenib
  - Anti-EGFR therapy with or without irinotecan, if not previously given or if stable disease from prior anti-EGFR therapy
  - Re-challenge with FOLFOX or CapeOx, if no prior progression on oxaliplatin
  - Reconsider second line therapy options as indicated and not previously given

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**Note:** Consider Clinical Trials as treatment options for eligible patients. Initial evaluation should include assessment of family history for HNPCC, FAP, or other less common germline mutations associated with colorectal cancer.

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Note: Consider Clinical Trials as treatment options for eligible patients. Initial evaluation should include assessment of family history for HNPCC, FAP, or other less common germline mutations associated with colorectal cancer.

SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE

First-line Therapy

- Capecitabine\(^1\,\,^2\) with or without bevacizumab\(^3\) or
- Infusional 5-fluorouracil with leucovorin and bevacizumab\(^7\) or
- Anti-EGFR therapy\(^4,\,^5\) (for RAS WT/BRAF WT and left sided tumors only) or
- Single agent nivolumab or pembrolizumab (if dMMR/MSI-H) or
- Trastuzumab with either pertuzumab or lapatinib or tucatinib (for HER2-amplified, RAS and BRAF WT) or
- Encorafenib (if BRAF V600E) with anti-EGFR therapy\(^4,\,^5\)

Second-line Therapy

- Consider first-line therapy for patients able to tolerate intensive therapy on Page 6
- Yes
- No
- Best supportive care

Improvement in functional status?

Patient not able to tolerate intensive therapy

anti-EGFR = cetuximab or panitumumab

dMMR = deficient mismatch repair

MSI = microsatellite instability

1. Patients with diminished creatinine clearance (CrCl) 30-50 mL/minute will require dose reduction. Patients with CrCl < 30 mL/minute will not be eligible to receive capecitabine.

2. Patients on warfarin or phenytoin should switch to appropriate alternative agents prior to starting capecitabine due to potential drug-drug interactions.

3. Elderly patients with a prior arterial thrombotic event are at increased risk of stroke, myocardial infarct and other arterial events. The incidence of venous thrombosis is statistically significant in colorectal cancer patients.

4. A RAS mutation indicates resistance to cetuximab and panitumumab.

5. Consider anti-EGFR therapy only if primary tumor is left sided/rectal cancer.
### CapeOx (XELOX)
- Oxaliplatin 100-130 mg/m² IV on Day 1
- Capecitabine<sup>a,b</sup> 850-1,000 mg/m² PO twice daily on Days 1-14
- With or without bevacizumab 7.5 mg/kg IV on Day 1 or with panitumumab<sup>c</sup> 9 mg/kg IV on Day 1
- Repeat every 3 weeks

### mFOLFOX 6
- Oxaliplatin 85 mg/m² IV over 2 hours on Day 1
- Leucovorin 400 mg/m² IV over 2 hours on Day 1
- 5-fluorouracil 400 mg/m² IV bolus on Day 1, then 5-fluorouracil 2,400 mg/m² over 46 hours IV continuous infusion
- With or without bevacizumab 5 mg/kg IV on Day 1 or with cetuximab<sup>c</sup> 500 mg/m² IV or panitumumab<sup>c</sup> 6 mg/kg IV on Day 1
- Repeat every 2 weeks

### mFOLFIRI
- Irinotecan 180 mg/m² IV over 90 minutes on Day 1
- Leucovorin 400 mg/m² IV over 2 hours during irinotecan infusion on Day 1
- 5-fluorouracil 400 mg/m² IV bolus, then 5-fluorouracil 2,400 mg/m² over 46 hours IV continuous infusion
- With or without bevacizumab 5 mg/kg IV on Day 1 or with cetuximab<sup>c</sup> 500 mg/m² IV or panitumumab<sup>c</sup> 6 mg/kg IV on Day 1
- Repeat every 2 weeks

### 5-Fluorouracil, leucovorin or capecitabine
- Capecitabine<sup>a,b</sup> 1,000 mg/m² PO twice daily on Days 1-14
- With or without bevacizumab 7.5 mg/kg IV on Day 1
- Repeat every 3 weeks
  or
- Leucovorin 400 mg/m² IV over 2 hours on Day 1
- 5-fluorouracil 400 mg/m² IV bolus on Day 1, then 5-fluorouracil 2,400 mg/m² over 46 hours IV continuous infusion
- With or without bevacizumab 5 mg/kg IV on Day 1
- Repeat every 2 weeks

### Regorafenib
- Regorafenib 160 mg PO daily for 21 days then 1 week off; one cycle is every 28 days (recommend to start at 80-120 mg PO daily for 21 days then 1 week off for the first 1-2 months, then dose escalate as appropriate)

### Trifluridine-tipiracil
- Trifluridine-tipiracil 35 mg/m² of trifluridine component (maximum 80 mg) PO twice per day on Days 1-5 and 8-12 of a 28 day cycle
- With or without bevacizumab 5 mg/kg IV on Day 1 and 15

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<sup>a</sup> Patients with diminished creatinine clearance (CrCl) 30-50 mL/minute will require dose reduction. Patients with CrCl < 30 mL/minute will not be eligible to receive capecitabine.

<sup>b</sup> Patients on warfarin or phenytoin should switch to appropriate alternative agents prior to starting capecitabine due to potential drug-drug interactions.

<sup>c</sup> A RAS mutation indicates resistance to cetuximab and panitumumab (refer to Principles of Systemic Therapy on Page 14).
## Colon Cancer

**SYSTEMIC THERAPY REGIMENS FOR ADVANCED OR METASTATIC DISEASE - continued**

### Anti-EGFR therapy
- Panitumumab\(^a\) 6 mg/kg IV on Day 1 every 2 weeks or Cetuximab\(^a\) 500 mg/m\(^2\) IV every 2 weeks
- Panitumumab\(^a\) 9 mg/kg IV on Day 1 every 3 weeks or Cetuximab\(^a\) 6 mg/kg IV every 2 weeks

### Irinotecan
- Irinotecan 180 mg/m\(^2\) IV over 90 minutes on Day 1
- Repeat every 2 weeks or Irinotecan 300-350 mg/m\(^2\) IV over 90 minutes on Day 1
- Repeat every 3 weeks

### Anti-EGFR therapy\(^a\) plus Irinotecan
- Cetuximab\(^a\) 500 mg/m\(^2\) IV every 2 weeks or panitumumab\(^a\) 6 mg/kg IV on Day 1
- With or without irinotecan 180 mg/m\(^2\) IV on Day 1
- Repeat every 2 weeks

### FOLFOXIRI\(^b\)
- Consider dosing as FOLFIRINOX for toxicity
- Oxaliplatin 85 mg/m\(^2\) IV over 2 hours on Day 1
- Irinotecan 180 mg/m\(^2\) IV over 90 minutes on Day 1
- 5-fluorouracil 2,400 mg/m\(^2\) IV continuous infusion over 46 hours on Day 1
- Repeat every 2 weeks

### BRAF V600E Mutation
- Encorafenib 300 mg PO once daily in combination with cetuximab\(^a\) 400 mg/m\(^2\) IV on Day 1, then 250 mg/m\(^2\) IV weekly or panitumumab\(^a\) 6 mg/kg IV every 2 weeks

### Microsatellite instability (MSI-H)/deficient mismatch repair (dMMR)
- Nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks
- Ipilimumab 1 mg/kg IV with nivolumab 3 mg/kg IV every 3 weeks for 4 doses, then nivolumab monotherapy at 240 mg IV every 2 weeks or 480 mg IV every 4 weeks
- Pembrolizumab 200 mg IV every 3 weeks or 400 mg IV every 6 weeks

### HER2-amplification (RAS and BRAF V600E WT)
- Trastuzumab 8 mg/kg (loading dose) IV on Day 1, then 6 mg/kg IV every 21 days with pertuzumab 840 mg (loading dose) IV on Day 1, then 420 mg IV every 21 days
- Trastuzumab 4 mg/kg (loading dose) IV on Day 1, then 2 mg/kg IV weekly with lapatinib 1,000 mg PO daily
- Trastuzumab 8 mg/kg (loading dose) IV on Day 1, then 6 mg/kg IV every 21 days with tucatinib 300 mg twice daily
- Fam-trastuzumab deruxtecan-nxki 6.4 mg/kg IV on Day 1 every 21 days

### NTRK gene fusion positive
- Larotrectinib 100 mg PO twice daily
- Entrectinib 600 mg PO once daily

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\(^a\) A RAS mutation indicates resistance to cetuximab and panitumumab (refer to Principles of Systemic Therapy on Page 14)

\(^b\) Consider regimen only in patients with adequate Eastern Cooperative Oncology Group (ECOG). Check blood counts regularly. May be best used for neoadjuvant therapy.
### Observation/Surveillance

**Stage I (low risk), managed with endoscopic resection alone**
- Colonoscopy: at 6-12 months, then (if normal) after 3 years, and then once every five years or sooner if indicated based on findings of prior colonoscopy

**Stage I**<sup>2,3</sup>
- Physical exam: every 6-12 months for 3 years
- CEA: every 6-12 months for 3 years
- CT scan of chest and contrast-enhanced CT of abdomen/pelvis or MRI: every 12 months for 3 years<sup>2</sup>
- Colonoscopy: at one year, then (if normal) after 3 years, and then once every 5 years or sooner if indicated based on findings of prior colonoscopy

**Stage II (low risk)<sup>4</sup>**
- Physical exam: every 6 months for up to 5 years
- CEA: every 6 months for up to 5 years
- CT scan of chest and contrast-enhanced CT or MRI of abdomen/pelvis: every 12 months for 3 to 5 years<sup>2</sup>
- Colonoscopy: at one year, then (if normal) after 3 years, and then once every 5 years or sooner if indicated based on findings of prior colonoscopy

**Stage II (high risk)<sup>4</sup> and Stage III**
- Physical exam: every 3-6 months for 2-3 years, then every 6 months through year 5
- CEA: every 3-6 months for 2-3 years, then every 6 months up to year 5
- Consider circulating tumor DNA testing every 3 months for 2-3 years
- CT of chest and contrast-enhanced CT or MRI of abdomen/pelvis: every 12 months for 5 years<sup>2</sup>
- Colonoscopy: at one year, then after 3 years (if normal), and then once every 5 years or sooner if indicated based on findings of prior colonoscopy

**Stage IV - NED**
- Individualized if on therapy
- Physical exam: every 3-4 months for 2 years, then every 6 months for 3 years
- Refer to GI endoscopy to evaluate patency of lumen every 4-6 months if primary tumor is intact (or sooner if clinically indicated)
- CEA: every 3-4 months for 2 years, then every 6 months for 3 years, then annually
- Consider circulating tumor DNA testing every 3 months for 2-3 years
- CT of chest and contrast-enhanced CT or MRI of abdomen/pelvis: every 3-4 months<sup>2</sup>

Upon becoming NED, 3-4 months for 2 years, then every 6 months for 3 years, then annually as dictated by primary site, response and site of metastasis if clinically appropriate.

**CEA** = carcinoembryonic antigen colorectal cancer  
**NED** = no evidence of disease

<sup>1</sup>Surveillance should be individualized based on the patient’s underlying risk for recurrence and preferences. It should include evaluation on lifestyle risks, treatment associated toxicity, and psychosocial needs with each visit.

<sup>2</sup>Surveillance imaging with PET/CT alone is not recommended as primary imaging modality, unless patient has a contrast allergy or renal dysfunction precluding intravenous contrast

<sup>3</sup>Evidence regarding the role of routine surveillance for patients with stage I colon cancer is controversial. Surveillance should be considered for patients with stage I colon cancer who have an increased risk for recurrence (e.g., poor differentiation, presence of lymphatic, vascular, or perineural invasion, T2 disease).

<sup>4</sup>Surveillance for patients with low risk stage II colon cancer should be a minimum of 3 years, and up to the clinicians’ discretion for years 4 and 5. For high risk stage II colon cancer, 5 years of surveillance is recommended (e.g., poor differentiation, inadequate nodal sampling (<12 nodes), lymphatic/vascular/perineural invasion, or T4 disease (invasion of serosa or other organ)).
Endoscopy has become an important tool in the diagnosis and treatment of patients with colorectal polyps and early colorectal cancer. The following principles of endoscopic therapy are adapted from the United States Multi-Society Task Force on Colorectal Cancer recommendations on the endoscopic management of malignant polyps and from the Japan Gastroenterology Endoscopy Society guidelines.

- A malignant polyp is defined as the presence of submucosally invasive adenocarcinoma, (e.g., T1) within a polyp.
- Where local expertise exists, endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) are suitable and complementary techniques in the endoscopic management of colorectal adenomas, superficial/early colorectal carcinomas, and neuroendocrine tumors.
- En bloc endoscopic resection is desirable where there is suspicion for early colorectal carcinoma (e.g., submucosal invasion).
- Deep submucosal invasion can be suspected based on the following endoscopic features: narrow-band imaging international colorectal endoscopic (NICE) classification type 3, or Kudo pit pattern classification type V. Nonpedunculated lesions with these features should be biopsied (in the area of surface feature disruption), tattooed (unless in or near the cecum), and referred for surgical resection. Pedunculated polyps with these features should undergo endoscopic polypectomy, as overall histological features may still be favorable.
- Superficial submucosal invasion can be suspected based on the following endoscopic features: nongranular lateral spreading tumors (LST-NG) morphology with suspicious surface features, or granular lateral spreading tumors (LST-G) morphology with a dominant nodule. When technically feasible, nonpedunculated lesions with these features should be considered for en bloc endoscopic resection. In the case of LST-G morphology with a dominant nodule, at least the nodular area should be considered for en bloc resection.
- All other nonpedunculated polyps without features suspicious for submucosal invasion can be resected with either EMR or ESD, based on technical feasibility and local expertise.
- All pedunculated polyps should be resected en bloc with the stalk, when technically feasible.
- Unfavorable pathology characteristics for nonpedunculated polyps include the following features: poor tumor differentiation, lymphovascular invasion, submucosal invasion depth > 1 mm, tumor involvement of the cautery margin, or tumor budding.
- Unfavorable pathology characteristics for pedunculated polyps include the following features: poor tumor differentiation, lymphovascular invasion, and tumor within 1 mm of the resection margin.
- College of American Pathologists (CAP) synoptic reporting should be performed for all malignant polyps. Pathology reports should include the following information: (1) histologic type, (2) grade of differentiation, (3) tumor extension/invasion, (4) stalk and mucosal margin status, and (5) presence or absence of lymphovascular invasion. Other aspects such as specimen integrity, polyp size, polyp morphology, tumor budding, and depth of submucosal invasion should also be included, as these are all factors which may contribute to the risk of lymph node metastasis and whether additional surgery is recommended.
PRINCIPLES OF COLON SURGERY

Extent of Bowel Resection
- A minimum of 5-10 cm of normal bowel should be resected on either side of the primary colon tumor. However, the length of bowel to be removed will be dictated by the blood supply of the colon which parallels the lymphatic drainage.
- Synchronous tumors may be resected as separate resections if workup for hereditary cancer is negative or may undergo subtotal colectomy

Mesocolic Excision and Lymphadenectomy
- A complete lymphadenectomy is essential for the treatment and prognosis of colon cancer. Lymphadenectomy should be complete, radical and en bloc.
- Lymph nodes are contained within the mesocolon which should be resected completely and en bloc
- Lymph nodes at the origin of feeding vessels, if suspected to be involved with cancer, should be resected and marked for pathologic examination
- Lymph nodes outside the field of resection considered suspicious should be biopsied or removed
- A minimum of 12 lymph nodes need to be examined to clearly establish stage II (T3 - T4, N0) colon cancer

Minimally Invasive Colectomy
- Oncologic principles for surgical resection including exploration are the same for minimally invasive colectomy as for open colectomy
- Tumors should be preoperatively localized by cross-sectional imaging or endoscopic localization with tattoo or endo-clip marking and abdominal x-ray

Management of Patients with Hereditary Colorectal Cancer Syndromes
- Hereditary Non-polyposis Colorectal Cancer (HNPCC) associated carcinoma
  - Individualized treatment may include tumor directed segmental resection or subtotal colectomy with ileo-rectal anastomosis. In selected cases, restorative proctocolectomy with ileal J-pouch anal anastomosis may be performed.
- Familial Adenomatous Polyposis Syndrome (FAP) associated carcinoma
  - Restorative total proctocolectomy with ileal J-pouch anal anastomosis or subtotal colectomy with ileo-rectal anastomosis (if rectal sparing or if patient is a candidate for endoscopic management of rectal polyp burden)

Resection Needs to be Complete to be Considered Curative – Not Palliative
- The completeness of resection should be assessed. The resected mesentery should be en bloc and intact, without defects.
- Involved adjacent organs should be resected en bloc
- The closest distance from the tumor to the non-peritonealized margin should be assessed during pathological evaluation [circumferential resection margin (CRM)]. To be considered margin negative, the CRM should be > 1 mm.
- The completeness of resection should be evaluated and noted in a synoptic operative report

Note: Consider Clinical Trials as treatment options for eligible patients. Initial evaluation should include assessment of family history for HNPCC, FAP, or other less common germline mutations associated with colorectal cancer.
PRINCIPLES OF COLON SURGERY - METASTASES

Liver
- Complete resection must be feasible based on anatomic grounds and the extent of disease; maintenance of normal hepatic function is required
- Resectable extrahepatic metastases do not preclude curative hepatic resection
- Re-evaluation for resection can be considered in otherwise unresectable patients after neoadjuvant therapy. All original sites of disease must be resectable.
- Hepatic resection is the treatment of choice for resectable liver metastases from colorectal cancer
- Ablative techniques may be considered in conjunction with resection in unresectable patients
- Primary tumor should be resected with curative intent (R0). Consider completion colectomy with radical lymphadenectomy if synchronous metastasis at presentation and only a palliative resection of the primary was performed.
- **Prior resection does not preclude re-resection in selected patients**

Lung
- Complete resection must be feasible based on anatomic grounds and the extent of disease; maintenance of adequate pulmonary function is required
- Resectable extrapulmonary metastases do not preclude resection
- Primary tumor should be resected with curative intent (R0)
- Prior resection does not preclude re-resection in selected patients

Other Sites (Other than Liver or Lung)
- Resection of isolated metastasis outside of the liver or lung may be considered if complete resection can be performed, but treatment should be individualized and based on a multidisciplinary treatment plan
- Peritoneal carcinomatosis
  - Cytoreductive surgery without intra-peritoneal chemotherapy may improve survival for patients with limited volume disease and where complete cytoreductive clearance can be achieved. The role of intraperitoneal chemotherapy has not been established.
PRINCIPLES OF SYSTEMIC THERAPY

- Identify the primary site of tumor when treatment naïve
- Anti-EGFR therapy is contraindicated in the setting of right sided primary tumors in treatment naïve patients
- The presence of microsatellite instability (MSI-H) status regardless if due to somatic or germline mutation may benefit from immune checkpoint inhibition
- Capecitabine was shown to be at least equivalent to adjuvant 5-fluorouracil/leucovorin
- Beware of the unique treatment related toxicities with these agents and engage in active management and prevention of these treatment related toxicities
  - Consider dihydropyrimidine dehydrogenase (DPD) screening for those with severe adverse drug reactions (ADRs) (e.g., diarrhea, neutropenia, mucositis) after initial exposure to 5-fluorouracil-based regimens
  - Consider UGT1A*28 screening for severe ADRs after initial exposure to irinotecan
- Metastatic colorectal cancer should be evaluated and managed by multidisciplinary team to define the goal of the therapy: curative or palliative
- Metastatic frontline treatment standard consists of combination chemotherapy with infusional 5-fluorouracil/leucovorin (or capecitabine) with either irinotecan and/or oxaliplatin based chemotherapy with or without bevacizumab. Alternatively, cetuximab or panitumumab may be considered rather than bevacizumab if inappropriate candidate for bevacizumab and/or RAS wild-type.
- Any RAS mutation indicates resistance to cetuximab and panitumumab
- The presence of the BRAF mutation indicates anti-EGFR resistance
- Maximize the duration of the effective therapy and timely switching to non-cross resistant chemotherapy agents at the time of tumor progression to allow the maximal exposure of all the active agents for survival
- Early recognition and prevention of treatment related toxicities and timely discontinuation of ineffective or toxic agents to improve the patient’s quality of life

PRINCIPLES OF ADJUVANT SYSTEMIC THERAPY

- Few data are available for the benefit of adjuvant therapy in deficient mismatch repair (dMMR) stage II patients with high-risk features and a thorough discussion is required, especially in those with T4b tumors
  - All patients with dMMR undergoing adjuvant therapy should receive a fluoropyrimidine in combination with oxaliplatin
- In patients with standard risk proficient mismatch repair (pMMR) stage II colon cancer, a thorough discussion is recommended and patients are advised that any 5-year survival benefit is likely to be less than 5%. After such a discussion, if wishing to proceed with adjuvant therapy, they are offered single agent fluoropyrimidine for 3-6 months.
- Patients with pMMR and high-risk stage II colon cancer may be offered adjuvant chemotherapy for 3-6 months and the inclusion of oxaliplatin will need to be individualized based on the observed risk factors, patient preferences and comorbidities
- Stage III patients are offered combination chemotherapy with fluoropyrimidine and oxaliplatin irrespective of (mismatch repair) MMR status
  - Patients with low risk disease (T1-3 and N1) are offered 3 months of CapeOx or 3-6 months of FOLFOX. Patients with high-risk disease are offered 3-6 months of CapeOx or 6 months of FOLFOX
- Adjuvant therapy should begin within 4 to 8 weeks after surgery, unless postoperative complications warrant a delay
SUGGESTED READINGS


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SUGGESTED READINGS - continued


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SUGGESTED READINGS - continued


SUGGESTED READINGS - continued


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Colon Cancer

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

SUGGESTED READINGS - continued


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SUGGESTED READINGS - continued


Colon Cancer

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