Rectal 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.*

Note: Consider Clinical Trials as treatment options for eligible patients. For adenomatous polyp with high-grade dysplasia, recommendations are the same as for colon cancer. Refer to Colon Cancer algorithm.

EVALUATION

Tumor within 12 cm from anal verge

- Pathology review[1]
- CEA
- Complete MSI analysis
- Proctoscopic evaluation by surgeon
- High-resolution rectal staging MRI without contrast (endorectal ultrasound may be performed if MRI not possible or to facilitate classification of cT1 vs T2 disease)
- CT of chest/abdomen/pelvis (with and without contrast) or MRI with contrast of abdomen/pelvis
- Colonoscopy (with biopsy if no pathology or pathology nondiagnostic)
- Lifestyle risk assessment[2]

PRIMARY TREATMENT

Resectable primary, no metastasis

- Stage I eligible for TAE **or** TAMIS/TEM resection[3] → TAE **or** TAMIS/TEM[3] → Excision complete?
  - Yes → Surveillance, see Page 7
  - No → Radical surgical resection: LAR, CAA **or** APR, with or without temporary fecal diversion (ileostomy) → Surveillance, see Page 7
- Stage I not eligible for TAE **or** TAMIS/TEM resection[3] → Radical surgical resection: LAR, CAA **or** APR, with or without temporary fecal diversion (ileostomy) → Surveillance, see Page 7
- Stage II and Stage III → Neoadjuvant therapy[4] (consider clinical trial if available) → Radical surgical resection: LAR, protectomy with CAA or APR → Consider adjuvant chemotherapy[5] (consider clinical trial if available) → Surveillance, see Page 7

Unresectable primary, no metastasis

Multidisciplinary management including medical oncology, surgical oncology, radiation oncology, and GI endoscopy. → Consider chemoradiation therapy (before or following systemic chemotherapy) → Individualized systemic therapy → Surveillance, see Page 7

Metastatic disease, intact primary

Are primary tumor and metastases resectable?

- Yes → **Multidisciplinary management:**
  - Recommendations include the surgeon, medical oncologist, and radiation oncologist
  - Refer to Principles of Rectal Surgery, Adjuvant Therapy and Radiation Therapy
  - Choice and timing of systemic chemotherapy, consideration of surgery, and radiation are to be individualized based on multidisciplinary management discussion between the medical oncologist, surgeon and radiations oncologist. In all cases, surgical resection should be performed with the intent for cure rather than palliation.

  → Individualized systemic therapy → Surveillance, see Page 7
- No →
  - First line chemotherapy with/without chemoradiation, refer to Page 3
  - If symptomatic, consider chemoradiation therapy, endoscopic intervention (e.g. endoscopic ablation), resection of primary tumor or diverting colostomy

  → Surveillance, see Page 7

[1] Consider MD Anderson approved GI biomarkers (Click here)
[2] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
[3] Criteria for eligibility for transanal excision: cT1 (EUS or MRI), less than 3 cm, low grade, no lymphovascular or perineural invasion
[4] See Principles of Neoadjuvant Therapy
[5] Capecitabine or 5-flourouracil/leucovorin or 5-flourouracil/leucovorin/oxaliplatin or capecitabine/oxaliplatin

LAR = low anterior resection
APR = abdominoperineal resection
CAA = coloanal anastomosis
TAE = transanal excision
TAMIS = transanal minimally invasive surgery
TEM = transanal endoscopic microsurgery

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Rectal Cancer

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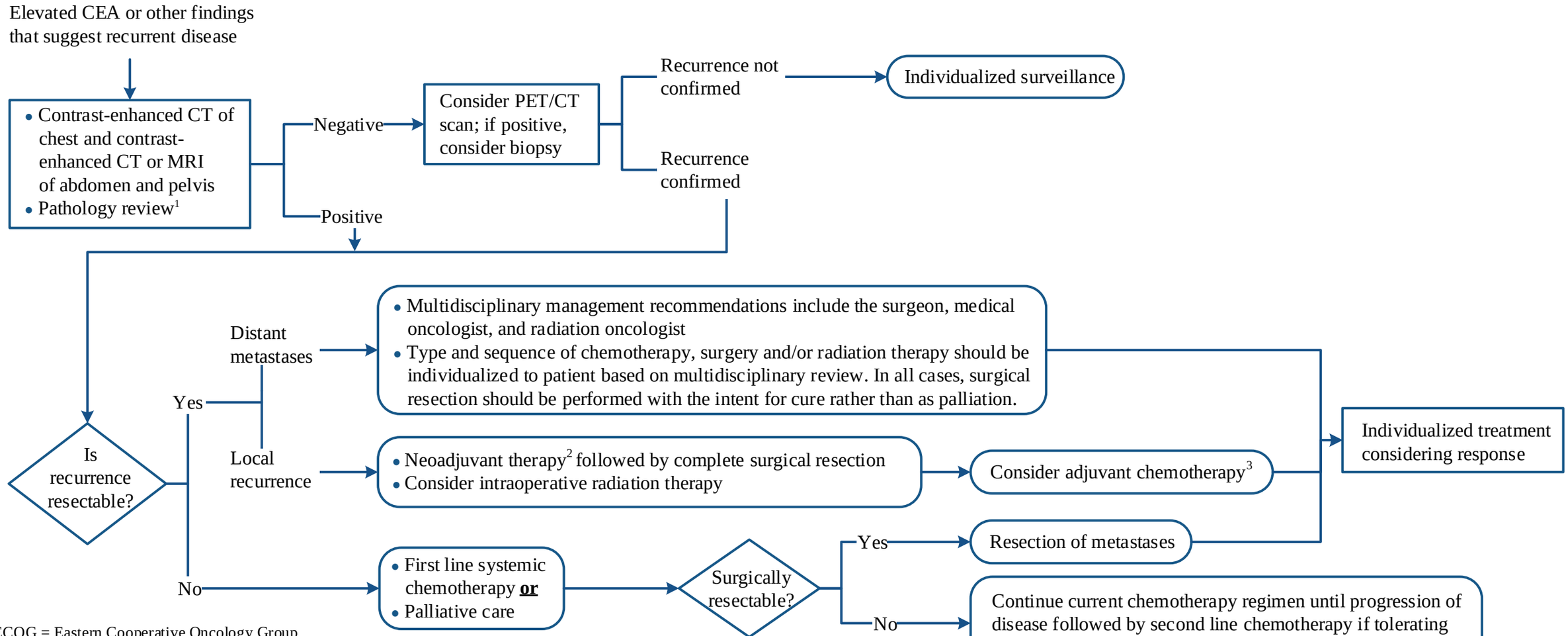
EVALUATION AND MANAGEMENT OF SUSPECTED OR DOCUMENTED RECURRENT RECTAL CANCER



ECOG = Eastern Cooperative Oncology Group

[1] Confirm biomarker studies include expanded *RAS*, *BRAF V600E*, and MSI status upon diagnosis of stage IV. Refer to MD Anderson approved GI biomarkers (Click here)

[2] See Principles of Neoadjuvant Therapy

[3] Capecitabine or 5-fluorouracil/leucovorin or 5-fluorouracil/leucovorin/oxaliplatin based on multidisciplinary review

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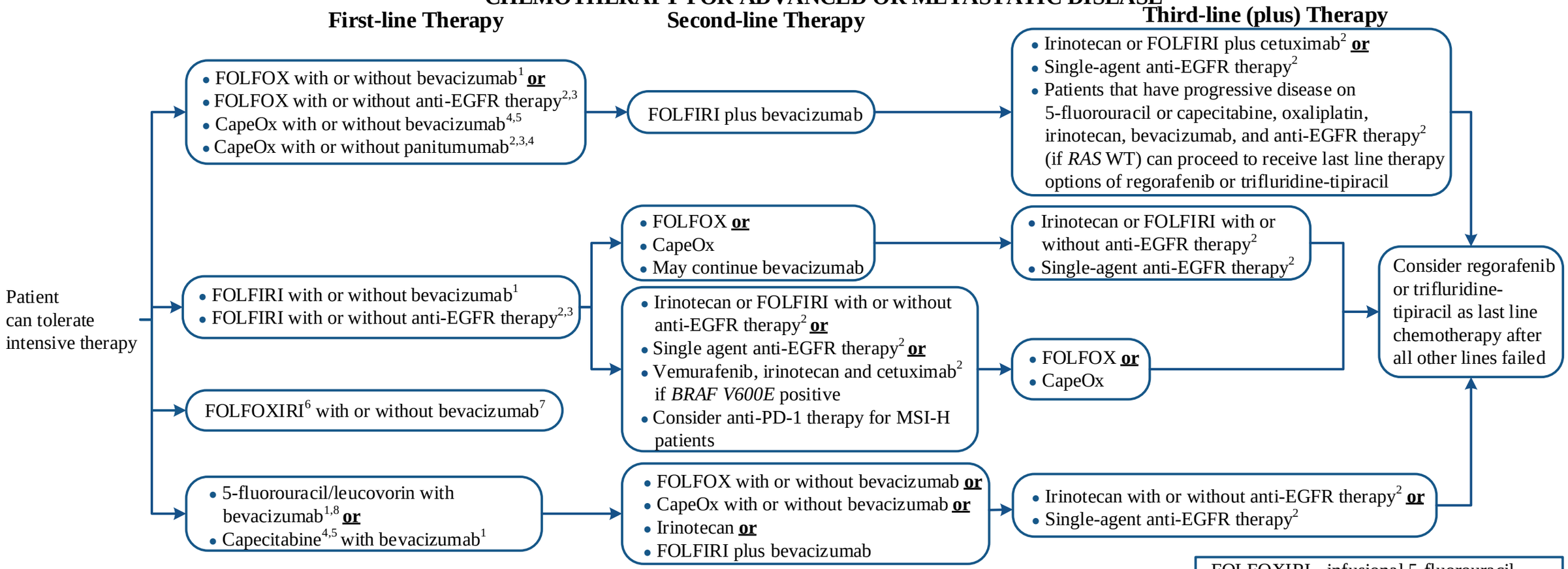
Rectal Cancer

Note: Consider Clinical Trials as treatment options for eligible patients. For adenomatous polyp with high-grade dysplasia, recommendations are the same as for colon cancer. Refer to Colon Cancer algorithm.

CHEMOTHERAPY FOR ADVANCED OR METASTATIC DISEASE



[1] Bevacizumab used in combination with IV 5-fluorouracil-based chemotherapy is approved for first-line therapy. 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.
[2] A *RAS* mutation indicates resistance to cetuximab and panitumumab
[3] Consider anti-EGFR therapy only if primary tumor is left sided/rectal cancer
[4] Patients with diminished creatinine clearance 30-50 mL/minute will require dose reduction. All patients with a creatinine clearance of less than 30 mL/minute will not be eligible to receive capecitabine.
[5] If the patient is taking warfarin or phenytoin while on capecitabine, the patient must be monitored regularly due to potential drug-drug interaction
[6] Consider regimen only in patients with adequate ECOG. Check blood counts regularly. May be best used for neoadjuvant therapy.
[7] Best suited for surgically resectable patients. Once progression, consider:
- Clinical trial
- *RAS* WT: irinotecan or FOLFIRI plus cetuximab or panitumumab
- Regorafenib
- Trifluridine-tipiracil

[8] A treatment option for patients not able to tolerate oxaliplatin or irinotecan

FOLFOXIRI - infusional 5-fluorouracil, leucovorin, oxaliplatin, and irinotecan
FOLFOX - infusional 5-fluorouracil, leucovorin and oxaliplatin
FOLFIRI - infusional 5-fluorouracil, leucovorin and irinotecan
CapeOx - capecitabine[4,5] and oxaliplatin

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Rectal Cancer

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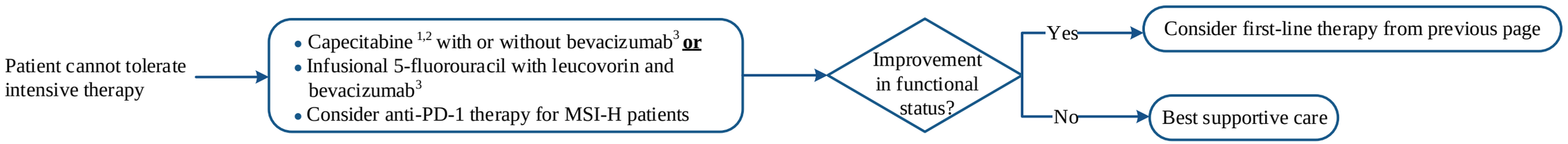
CHEMOTHERAPY FOR ADVANCED OR METASTATIC DISEASE



[1] Patients with diminished creatinine clearance 30-50 mL/minute will require dose reduction. All patients with a creatinine clearance of less than 30 mL/minute will not be eligible to receive capecitabine.
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Rectal Cancer

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CHEMOTHERAPY FOR ADVANCED OR METASTATIC DISEASE

CapeOx (XELOX)
- Oxaliplatin 100-130 mg/m^2 IV on Day 1
- Capecitabine 850-1000 mg/m^2 PO twice daily for 14 days
- With or without bevacizumab 7.5 mg/kg IV
- Repeat every 3 weeks
- With or without panitumumab* 9 mg/kg every 3 weeks

mFOLFOX 6
- Oxaliplatin 85 mg/m^2 IV over 2 hours on Day 1
- Leucovorin 400 mg/m^2 IV over 2 hours on Day 1
- 5-fluorouracil 400 mg/m^2 IV bolus on Day 1, then 5-fluorouracil 2400 mg/m^2 over 46 hours IV continuous infusion
- With or without bevacizumab 5 mg/kg IV
- Repeat every 2 weeks
- With or without panitumumab* 6 mg/kg every 2 weeks or cetuximab*

mFOLFIRI
- Irinotecan 180 mg/m^2 IV over 90 minutes on Day 1
- Leucovorin 400 mg/m^2 IV over 2 hours during irinotecan on Day 1
- 5-fluorouracil 400 mg/m^2 IV bolus, then 5-fluorouracil 2400 mg/m^2 over 46 hours IV continuous infusion
- With or without bevacizumab 5 mg/kg IV
- Repeat every 2 weeks
- With or without cetuximab* 400 mg/m^2 IV for the first infusion followed by 250 mg/m^2 IV weekly or 500 mg/m^2 IV every 2 weeks or panitumumab* 6 mg/kg IV 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 one to two months, then dose escalate as appropriate.)

Trifluridine-tipiracil
- Trifluridine-tipiracil 35 mg/m^{2}of trifluridine component (max 80 mg) PO twice a day on Days 1-5 and 8-12 of a 28 day cycle

5-Fluorouracil, Leucovorin or Capecitabine
- Capecitabine 1000 mg/m^2 PO twice daily for 14 days, every 3 weeks
- With or without bevacizumab 7.5 mg/kg IV every 3 weeks

or
- Leucovorin 400 mg/m^2 IV over 2 hours on Day 1
- 5-fluorouracil 400 mg/m^2 IV on Day 1, then 2400 mg/m^2 over 46 hours IV continuous infusion
- With or without bevacizumab 5 mg/kg IV
- Repeat 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

* A *RAS* mutation indicates resistance to cetuximab and panitumumab

Note: Consider Clinical Trials as treatment options for eligible patients. For adenomatous polyp with high-grade dysplasia, recommendations are the same as for colon cancer. Refer to Colon Cancer algorithm.

CHEMOTHERAPY FOR ADVANCED OR METASTATIC DISEASE

Anti-EGFR* plus Irinotecan

- Cetuximab* 400 mg/m^2 IV for the first infusion, then 250 mg/m^2 IV weekly with
- Irinotecan 350 mg/m^2 IV every 3 weeks or 180 mg/m^2 IV every 2 weeks

or

- Cetuximab* 500 mg/m^2 IV every 2 weeks or panitumumab* 6 mg/kg IV every 2 weeks
- With or without irinotecan 180 mg/m^2 IV every 2 weeks

Panitumumab*

- Panitumumab 6 mg/kg IV every 2 weeks
- Panitumumab 9 mg/kg IV every 3 weeks

FOLFOXIRI**

Consider dosing as FOLFIRINOX for toxicity

- Oxaliplatin 85 mg/m^2 IV Day 1
- Irinotecan 180 mg/m^2 IV Day 1
- 5-fluorouracil 2400 mg/m^2 IV continuous infusion over 46 hours
- Repeat every 2 weeks

***BRAF* Mutation**

- Vemurafenib 960 mg PO twice daily, irinotecan 180 mg/m^2 IV every 2 weeks, and anti-EGFR therapy with cetuximab* 500 mg/m^2 IV every 2 weeks

Microsatellite instability (MSI-H)

- Nivolumab 240 mg IV every 2 weeks
- Pembrolizumab 200 mg IV every 3 weeks

* A *RAS* mutation indicates resistance to cetuximab and panitumumab. (Refer to Principles of Chemotherapy on Page 10)
** Consider regimen only in patients with adequate ECOG. Check blood counts regularly. May be best used for neoadjuvant therapy.

Rectal Cancer

Note: Consider Clinical Trials as treatment options for eligible patients. For adenomatous polyp with high-grade dysplasia, recommendations are the same as for colon cancer. Refer to Colon Cancer algorithm.

OBSERVATION/SURVEILLANCE[1,2]

Stage I	• Physical exam: every 6-12 months for 3 years • CEA: every 6-12 months for 3 years • Proctoscopic examination following local excision: 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 • 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)	• Physical exam: every 3-6 months for 2 years, then every 6 months for 3 years • CEA: every 3-6 months for 2 years, then every 6 months for 3 years • CT scan of chest and contrast-enhanced CT or MRI of abdomen/pelvis: every 12 months for 3-5 years • 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) and Stage III	• Physical exam: every 3-6 months for 3 years, then every 6 months for 2 years • CEA: every 3-6 months for 3 years, then every 6 months for 2 years • Proctoscopic examination: every 6-12 months for 5 years[3] • CT scan of chest and contrast-enhanced CT or MRI of abdomen/pelvis: every 12 months for at least 5 years • 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 • Patients with rectal cancer treated with neoadjuvant chemoradiation (particularly those with significant residual tumor burden) may experience late failures (beyond 5 years). The follow-up of these patients should be individualized but may include continue annual follow-up for up 8 years
Stage IV - NED	• Physical exam: every 3-4 months for 2 years, then every 6 months for 3 years • CEA: every 3-4 months for 2 years, then every 6 months for 3 years • CT scan of chest and CT (with and without contrast) or MRI of abdomen/pelvis: every 3-4 months for 2 years, every 6 months for 2 years, then annually after 5 years • Colonoscopy: at one year from rectal resection, then (if normal) after 3 years, and then once every 5 years or sooner if indicated based on findings of prior colonoscopy
Stage IV	• 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 3-6 months if primary tumor is intact (or sooner if clinically indicated) • CEA: every 3-4 months for 3 years, then every 6 months for 3 years • CT of chest and contrast-enhanced CT or MRI of abdomen/pelvis: every 3 months. • Colonoscopy: patients with unresected, intact primary tumors, endoscopic surveillance is recommended every 4-6 months to ensure luminal patency

[1]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.
[2]Note: Surveillance imaging with PET/CT alone is not recommended as primary imaging modality when there is no contraindication to conventional contrast-enhanced CT scan
[3]When surgical resection has been performed according to the principals outlined, patients with good pathological response to neoadjuvant chemoradiation are at low risk and routine proctoscopic evaluation may be selectively omitted.
NED = no evidence of disease

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PRINCIPLES OF RECTAL SURGERY

Transanal Excision (Including Transanal Minimally Invasive Surgery (TAMIS) or Transanal Endoscopic Microsurger (TEM))

Criteria (must meet all)

- T1N0 staging on ultrasound or high resolution MRI and cross-sectional imaging
- Able to completely remove tumor with 1 cm margin (full-thickness)
- No lymphovascular invasion
- No perineural invasion
- Less than 30% circumference
- Well- to moderately-differentiated histology
- Less than 3 cm in greatest dimension

Transabdominal Resection (Low anterior resection or coloanal anastomosis using total or tumor-specific mesorectal excision.)

General Management Principles

- The treating surgeon should perform an endoscopic evaluation (e.g. proctosigmoidoscopy) before initiating treatment in order to assess the full extent of primary tumor involvement.
- Primary tumor resection should include adequate margins of resection and be en bloc with the mesorectum and involved adjacent viscera. Tumor transection or resection that leaves gross residual tumor in the operative field (R2) should be avoided.
- Treatment of draining lymphatics is accomplished by en bloc resection of both the proximally ascending and distally descending nodal basins.
- Function restorative reconstruction (e.g. sphincter preservation) performed when possible and deemed appropriate based on an assessment of the underlying functional status of the anal sphincter.

Distal and Circumferential Resection Margins

- The distal resection margin should not be involved by tumor and ideally be greater than 1 cm below the distal extent of the tumor when a total mesorectal excision has been performed. Intramural tumor spread may be present up to 1-2 cm distal to the tumor.
- Determination of the level of distal transection should be based on the level of tumor involvement prior to neoadjuvant therapy.
- In cases of proximal rectal location, the distal margin of resection should be at least 4-5 cm below the distal extent of the tumor en bloc with the mesorectum (see Lymphadenectomy Principles below).
- Full rectal mobilization allows for a negative distal margin and adequate mesorectal excision.
- A negative circumferential resection margin (greater than 1 mm on microscopic evaluation) should be obtained (R0). Resection margins less than or equal to 1 mm should be considered microscopically positive (R1) and will be at higher risk for recurrence.

Lymphadenectomy and Mesorectal Excision

- Routine radical lymphadenectomy should be achieved with proximal lymphovascular resection to the origin of the superior hemorrhoidal vessels (include IMA level lymph nodes when clinically suspected to be involved) and distal complete mesorectal excision to include the entire mesorectum or the tumor-specific mesorectum at least 5 cm below the distal extent of the tumor (so called "tumor specific mesorectal excision).
- The mesorectal dissection should be performed sharply within the mesorectal fascial plane to ensure a complete mesorectal excision.
- Clinically suspicious nodes beyond the field of resection should be biopsied or removed if possible.
- Resection of lateral lymph nodes (internal iliac and obturator lymph node basins) should be considered in the presence of clinically suspected nodes.

Total Mesorectal Excision (TME)

- A minimally invasive approach (e.g. laparoscopic or robotic) should adhere to the same principles of cancer surgery as for open resection.

Continued on next page

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PRINCIPLES OF RECTAL SURGERY - continued

Transabdominal Resection (continued)

Abdominoperineal Resection

- Tumors located in the distal rectum requiring an abdominoperineal resection are at an increased risk for circumferential resection margin positivity.
- In addition to the TME principles as outlined above, the division of the pelvic floor (levator muscles) should be wide around the level of tumor to avoid narrowing or coning of the resection. For anterior or posterior tumors, this could require en bloc resection of the adjacent structure such as the vagina or coccyx in order to ensure a clear margin.
- The approach to the pelvic floor may be trans-abdominal (from above) or trans-perineal (from below) in either a lithotomy or prone position as long as a complete resection with clear margins can be achieved.

Liver

- Complete resection or ablative therapy must be feasible based on anatomic grounds and extent of disease. Maintenance of normal hepatic function is required.
- Resectable extrahepatic sites of 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 otherwise unresectable patients.
- Primary tumor should be resected with curative intent (R0). Consider completion with radical lymphadenectomy at time of liver resection if synchronous metastasis at presentation and a non-oncologic 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 residual 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 a subsequent 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 with or without intra-peritoneal hyperthermic chemotherapy may be considered in the setting of a clinical trial.

Note: Consider Clinical Trials as treatment options for eligible patients. For adenomatous polyp with high-grade dysplasia, recommendations are the same as for colon cancer. Refer to Colon Cancer algorithm.

PRINCIPLES OF CHEMOTHERAPY

- The presence of the *BRAF* mutation indicates anti-EGFR resistance.
- The presence of microsatellite instability (MSI-H) status regardless if due to somatic or germline mutation may benefit from immune checkpoint inhibition.

PRINCIPLES OF NEOADJUVANT THERAPY

- Neoadjuvant chemoradiation therapy is provided to the patient prior to surgical resection followed by adjuvant chemotherapy. However, in select situations where surgery was initially provided, adjuvant chemoradiation therapy is then considered followed by adjuvant chemotherapy.
- All patients with locally advanced (stage II and III) rectal cancer should be evaluated for neoadjuvant therapy. Standard neoadjuvant treatment should include combination **chemoradiation therapy** (see Principles of Radiation Therapy), however a number of alternative approaches may be considered in a multidisciplinary setting including neoadjuvant chemotherapy alone, induction chemotherapy followed by chemoradiation therapy, or chemoradiation therapy followed by consolidation chemotherapy (total neoadjuvant therapy).
- The decision for which approach should take into consideration the tumor characteristics, extent of lymph node involvement, and predicted status of the circumferential resection margin. In an effort to optimize the chance for sphincter preservation, neoadjuvant chemoradiation therapy may also be considered for selected patients with earlier stage (e.g. T2N0) tumors that are very low-lying within the rectum.
- In some instances of low risk tumors (proximal rectal cancers with wide radial margins, no extramural vascular invasion on MRI), radiation therapy may be omitted altogether.

Dosing Schedule for Concurrent Chemotherapy and Radiation Therapy:

- Radiation therapy plus infusional 5-fluorouracil 250-300 mg/m2/day IV continuous infusion, Monday through Friday on days of radiation therapy
- Radiation therapy plus capecitabine 825 mg/m^2 PO twice daily, Monday through Friday on days of radiation therapy

PRINCIPLES OF ADJUVANT THERAPY

Postoperative adjuvant chemotherapy for patients receiving preoperative chemotherapy/radiation therapy:

mFOLFOX 6

- Oxaliplatin 85 mg/m^2 IV over 2 hours on Day 1
- Leucovorin 400 mg/m^2 IV over 2 hours on Day 1
- 5-fluorouracil 400 mg/m^2 IV bolus on Day 1, then 2400 mg/m^2 IV over 46 hours continuous infusion
- Repeat every 2 weeks

Capecitabine 1000 mg/m^2 PO twice daily on Days 1-14, followed by 7 days rest

- Repeat every 3 weeks

CapeOx (XELOX)

- Oxaliplatin 100-130 mg/m^2 IV on Day 1
- Capecitabine 850-1000 mg/m^2 PO twice daily on Days 1-14, followed by 7 days rest
- Repeat every 3 weeks

Infusional 5-fluorouracil/leucovorin

- Leucovorin 400 mg/m^2 IV over 2 hours on Day 1
- 5-fluorouracil 400 mg/m^2 IV bolus on Day 1, then 2400 mg/m^2 IV over 46 hours continuous infusion
- Repeat every 2 weeks

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PRINCIPLES OF RADIATION THERAPY

- Radiation therapy fields should include the tumor, the presacral nodes, the mesorectal region and the internal iliac nodes.
- Multiple radiation therapy fields should be used (generally a 3 or 4 field technique). Positioning and other techniques to minimize the volume of small bowel in the fields should be encouraged.
- For postoperative patients treated by abdominoperineal resection, the perineal scar should be included within the fields.
- Radiation doses: 45 Gy in 25 fractions to the pelvis, followed by a boost to the tumor bed and presacral region, with a dose of 5.4 Gy in 3 fractions for preoperative treatments, and a dose of 5.4-9 Gy in 3-5 fractions for postoperative treatments.
- Short course (5 Gy in 5 fractions) preoperative radiation therapy may be appropriate in certain situations such as preoperative treatment of patients with resectable metastatic disease. For treatment with this approach, reducing dose to normal tissue is very important. We recommend treating prone with a belly board and with a full bladder, using IMRT and daily image guidance.
- Intraoperative radiation therapy (IORT), if available, should be considered for very close or positive margins after resection as an additional boost, especially for patients with T4 or recurrent cancers.
- For unresectable cancers, doses higher than 54 Gy may be required.
- 5-fluorouracil based chemotherapy should be delivered concurrently with radiation.
- IMRT may be considered in selected cases to reduce toxicity. For IMRT cases, careful attention should be given to appropriate contouring, such as that recommended by the RTOG consensus panel.

SUGGESTED READINGS

Abdalla, E. K., Vauthey, J. N., Ellis, L. M., Ellis, V., Pollock, R., Broglio, K. R., ... & Curley, S. A. (2004). Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. *Annals of Surgery*, *239*(6), 818.

Adam, R., Avisar, E., Ariche, A., Giachetti, S., Azoulay, D., Castaing, D., ... & Bismuth, F. (2001). Five-year survival following hepatic resection after neoadjuvant therapy for nonresectable colorectal [liver] metastases. *Annals of Surgical Oncology*, *8*(4), 347-353.

Alberts, S. R., Horvath, W. L., Sternfeld, W. C., Goldberg, R. M., Mahoney, M. R., Dakhil, S. R., ... & Donohue, J. H. (2005). Oxaliplatin, fluorouracil, and leucovorin for patients with unresectable liver-only metastases from colorectal cancer: a North Central Cancer Treatment Group phase II study. *Journal of Clinical Oncology*, *2*3(36), 9243-9249.

Aloia, T. A., Vauthey, J. N., Loyer, E. M., Ribero, D., Pawlik, T. M., Wei, S. H., ... & Abdalla, E. K. (2006). Solitary colorectal liver metastasis: resection determines outcome. *Archives of Surgery*, *141*(5), 460-467..

Ambiru, S., Miyazaki, M., Ito, H., Nakagawa, K., Shimizu, H., Kato, A., ... & Nakajima, N. (1998). Resection of hepatic and pulmonary metastases in patients with colorectal carcinoma. *Cancer*, *82*(2), 274-278.

Aschele, C., Cionini, L., Lonardi, S., Pinto, C., Cordio, S., Rosati, G., ... & Bonetti, A. (2011). Primary tumor response to preoperative chemoradiation with or without oxaliplatin in locally advanced rectal cancer: pathologic results of the STAR-01 randomized phase III trial. *Journal of Clinical Oncology*, *29*(20), 2773-2780.

Aschele, C., Pinto, C., Cordio, S., Rosati, G., Tagliagambe, A., Artale, S., ... & Cionini, L. (2009). Preoperative fluorouracil (FU)-based chemoradiation with and without weekly oxaliplatin in locally advanced rectal cancer: Pathologic response analysis of the Studio Terapia Adiuvante Retto (STAR)-01 randomized phase III trial. *Journal of Clinical Oncology*, *27*(18S), CRA4008-CRA4008.

Bonjer, H. J., Deijen, C. L., Abis, G. A., Cuesta, M. A., van der Pas, M. H., de Lange-de Klerk, E. S., ... & Rosenberg, J. (2015). A randomized trial of laparoscopic versus open surgery for rectal cancer. *New England Journal of Medicine*, *372*(14), 1324-1332.

Brouquet, A., Abdalla, E. K., Kopetz, S., Garrett, C. R., Overman, M. J., Eng, C., ... & Vauthey, J. N. (2011). High survival rate after two-stage resection of advanced colorectal liver metastases: response-based selection and complete resection define outcome. *Journal of Clinical Oncology*, *29*(8), 1083-1090.

Blazer III, D. G., Kishi, Y., Maru, D. M., Kopetz, S., Chun, Y. S., Overman, M. J., ... & Zorzi, D. (2008). Pathologic response to preoperative chemotherapy: a new outcome end point after resection of hepatic colorectal metastases. *Journal of Clinical Oncology*, *26*(33), 5344-5351.

Breugom, A. J., Van Gijn, W., Muller, E. W., Berglund, Å., van den Broek, C. B. M., Fokstuen, T., ... & Martijn, H. (2014). Adjuvant chemotherapy for rectal cancer patients treated with preoperative (chemo) radiotherapy and total mesorectal excision: a Dutch Colorectal Cancer Group (DCCG) randomized phase III trial. *Annals of Oncology*, *26*(4), 696-701.

Chang, G. J., You, Y. N., Park, I. J., Kaur, H., Hu, C. Y., Rodriguez-Bigas, M. A., ... & Ernst, R. D. (2012). Pre-treatment high-resolution rectal MRI and treatment response to neoadjuvant chemoradiation. *Diseases of the Colon and Rectum*, *55*(4), 371.

Chang, G. J., Rodriguez-Bigas, M. A., Eng, C., & Skibber, J. M. (2009). Lymph node status after neoadjuvant radiotherapy for rectal cancer is a biologic predictor of outcome. *Cancer, 115*(23), 5432-5440.

Continued on next page

SUGGESTED READINGS - continued

Chun, Y. S., Vauthey, J. N., Boonsirikamchai, P., Maru, D. M., Kopetz, S., Palavecino, M., ... & Loyer, E. M. (2009). Association of computed tomography morphologic criteria with pathologic response and survival in patients treated with bevacizumab for colorectal liver metastases. *JAMA, 302*(21), 2338-2344.

Crane, C. H., Skibber, J. M., Feig, B. W., Vauthey, J. N., Thames, H. D., Curley, S. A., ... & Lin, E. H. (2003). Response to preoperative chemoradiation increases the use of sphincter-preserving surgery in patients with locally advanced low rectal carcinoma. *Cancer*, *97*(2), 517-524.

Cremolini, C., Loupakis, F., & Falcone, A. (2015). TRIBE trial. FOLFOXIRI and bevacizumab for metastatic colorectal cancer. *New England Journal of Medicine*, *372*(3), 291-292.

Cunningham, D., Humblet, Y., Siena, S., et al. (2004). Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. *New England Journal of Medicine*, *351*(4), 337-345.

Das, P., Delclos, M. E., Skibber, J. M., et al. (2010). Hyperfractionated accelerated radiotherapy for rectal cancer in patients with prior pelvic irradiation. *International Journal of Radiation Oncology* Biology* Physics, 77*(1), 60-65.

Das, P., Lin, E. H., Bhatia, S., et al. (2006). Preoperative chemoradiotherapy with capecitabine versus protracted infusion 5-fluorouracil for rectal cancer: a matched-pair analysis. *International Journal of Radiation Oncology* Biology* Physics, 66*(5), 1378-1383.

Douillard, J., Cunningham, D., Roth, A. D., et al. (2000). Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomised trial. *The Lancet*, *355*(9209), 1041-1047.

Douillard, J.Y., Oliner, K.S., Siena, S., et al. (2013). Panitumab-FOLFOX4 treatment and RAS mutations in colorectal cancer. *New England Journal of Medicine*. 369(11),1023-34.

Fleshman, J., Branda, M., Sargent, D. J., Boller, A. M., George, V., Abbas, M., ... & Fichera, A. (2015). Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial. *Jama*, *314*(13), 1346-1355.

Goldberg, R. M., Sargent, D. J., Morton, R. F., et al. (2004). A randomized controlled trial of fluorouracil plus leucovorin, irinotecan, and oxaliplatin combinations in patients with previously untreated metastatic colorectal cancer. *Journal of Clinical Oncology*, *22*(1), 23-30.

Haller, D.G., Tabernero, J., Maroun, J., et al. (2011). Capecitabine plus oxaliplatin compared with fluorouracil and folinic acid as adjuvant therapy for stage III colon cancer. *Journal of Clinical Oncology*, *9*(11),1465-1471.

Heald, R. J., and Ryall, R. D. H. (1986). Recurrence and survival after total mesorectal excision for rectal cancer. *The Lancet*, *327*(8496), 1479-1482.

Heinemann, V., von Weikersthal, L. F., Decker, T., et al. (2014). FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial. *The Lancet Oncology, 15*(10), 1065-1075.

Hofhinz, R., Wenz, S., Post, A. (2011). Capecitabine (Cape) versus 5-fluorouracil (5-FU)–based (neo)adjuvant chemoradiotherapy (CRT) for locally advanced rectal cancer (LARC): Long-term results of a randomized, phase III trial. 2011 ASCO Annual Meeting. *Journal of Clinical Oncology*, abst 3504.

Hong, Y. S., Nam, B. H., Kim, K. P., Kim, J. E., Park, S. J., Park, Y. S., ... & Ahn, J. B. (2014). Oxaliplatin, fluorouracil, and leucovorin versus fluorouracil and leucovorin as adjuvant chemotherapy for locally advanced rectal cancer after preoperative chemoradiotherapy (ADORE): an open-label, multicentre, phase 2, randomised controlled trial. *The Lancet Oncology, 15*(11), 1245-1253.

Inoue, M., Kotake, Y., Nakagawa, K., et al. (2000). Surgery for pulmonary metastases from colorectal carcinoma. *The Annals of Thoracic Surgery*, *70*(2), 380-383.

Ikoma, N., You, Y. N., Bednarski, B. K., Rodriguez-Bigas, M. A., Eng, C., Das, P., ... & Chang, G. J. (2017). Impact of Recurrence and Salvage Surgery on Survival After Multidisciplinary Treatment of Rectal Cancer. *Journal of Clinical Oncology*, JCO-2016.

Continued on next page

SUGGESTED READINGS - continued

Jayne, D. G., Guillou, P. J., Thorpe, H., Quirke, P., Copeland, J., Smith, A. M., ... & Brown, J. M. (2007). Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. J*ournal of Clinical Oncology, 25*(21), 3061-3068.

Kang, S. B., Park, J. W., Jeong, S. Y., Nam, B. H., Choi, H. S., Kim, D. W., ... & Chang, H. J. (2010). Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. *The Lancet Oncology, 11*(7), 637-645.

Kapiteijn, E., Marijnen, C. A., Nagtegaal, I. D., Putter, H., Steup, W. H., Wiggers, T., ... & Leer, J. W. (2001). Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *New England Journal of Medicine, 345*(9), 638-646.

Kopetz, S., McDonough S.L., Morris, V.K., Lenz, H., Magliocco, A.M., Atreya, C.E., … & Hochester, H.S. (2017) Randomized trial of irinotecan and cetuximab with or without vemurafenib in *BRAF*-mutant metastatic colorectal cancer (SWOG 1406). *Journal of Clinical Oncology, 35*(Suppl 4S), Abstract 520.

Le, D. T., Uram, J. N., Wang, H., Bartlett, B. R., Kemberling, H., Eyring, A. D., ... & Biedrzycki, B. (2015). PD-1 blockade in tumors with mismatch-repair deficiency. *New England Journal of Medicine, 372*(26), 2509-2520.

Locker, G. Y., Hamilton, S., Harris, J., Jessup, J. M., Kemeny, N., Macdonald, J. S., ... & Bast Jr, R. C. (2006). ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. *Journal of Clinical Oncology, 24*(33), 5313-5327.

Marijnen, C. A. M., Nagtegaal, I. D., Kapiteijn, E., Kranenbarg, E. K., Noordijk, E. M., Van Krieken, J. H. J. M., ... & Cooperative Investigators of the Dutch Colorectal Cancer Group. (2003). Radiotherapy does not compensate for positive resection margins in rectal cancer patients: report of a multicenter randomized trial. *International Journal of Radiation Oncology* Biology* Physics, 55*(5), 1311-1320.

Mayer, R. J., Van Cutsem, E., Falcone, A., Yoshino, T., Garcia-Carbonero, R., Mizunuma, N., ... & Sobrero, A. (2015). Randomized trial of TAS-102 for refractory metastatic colorectal cancer. *New England Journal of Medicine, 372*(20), 1909-1919.

MERCURY Study Group. (2006). Diagnostic accuracy of preoperative magnetic resonance imaging in predicting curative resection of rectal cancer: prospective observational study. *BMJ, 333*(7572), 779.

Meyerhardt, J. A., Mangu, P. B., Flynn, P. J., Korde, L., Loprinzi, C. L., Minsky, B. D., ... & Benson III, A. B. (2013). Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer: American Society of Clinical Oncology clinical practice guideline endorsement. *Journal of Clinical Oncology, 31*(35), 4465-4470.

Monson, J. R. T., Weiser, M. R., Buie, W. D., Chang, G. J., Rafferty, J. F., Buie, W. D., ... & Feingold, D. (2013). Practice parameters for the management of rectal cancer (revised). *Diseases of the Colon & Rectum, 56*(5), 535-550.

Myerson, RJ., Outlaw, ED., Chang, A. (2009). Radiotherapy for epidermoid carcinoma of the anus; thirty years 'experience. *International Journal of Radiatiation Oncology *Biology* Physics, 75*(2), 428-435.

National Comprehensive Cancer Network. Rectal Cancer (Version 3.2017). https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed June 2017.

Nordlinger, B., Sorbye, H., Glimelius, B., Poston, G. J., Schlag, P. M., Rougier, P., ... & Jaeck, D. (2008). Perioperative chemotherapy with FOLFOX4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup trial 40983): a randomised controlled trial. *The Lancet, 371*(9617), 1007-1016.

Ngan, S. Y., Burmeister, B., Fisher, R. J., Solomon, M., Goldstein, D., Joseph, D., ... & McKendrick, J. (2012). Randomized trial of short-course radiotherapy versus long-course chemoradiation comparing rates of local recurrence in patients with T3 rectal cancer: Trans-Tasman Radiation Oncology Group trial 01.04. *Journal of Clinical Oncology, 30*(31), 3827-3833.

Continued on next page

SUGGESTED READINGS - continued

Overman, M. J., McDermott, R., Leach, J. L., Lonardi, S., Lenz, H. J., Morse, M. A., ... & Goldberg, M. V. (2017). Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): an open-label, multicentre, phase 2 study. *The Lancet Oncology*, *18*(9), 1182-1191.

Park, I. J., You, Y. N., Agarwal, A., Skibber, J. M., Rodriguez-Bigas, M. A., Eng, C., ... & Hu, C. Y. (2012). Neoadjuvant treatment response as an early response indicator for patients with rectal cancer. *Journal of Clinical Oncology*, *30*(15), 1770-1776.

Peeters, K. C., Marijnen, C. A., Nagtegaal, I. D., Kranenbarg, E. K., Putter, H., Wiggers, T., ... & van de Velde, C. J. (2007). The TME trial after a median follow-up of 6 years: increased local control but no survival benefit in irradiated patients with resectable rectal carcinoma. *Annals of Surgery*, *246*(5), 693-701.

Peeters, M., Cervantes-Ruiperez, A., Strickland, A., Ciuleanu, T., Mainwaring, P. N., Tzekova, V. I., ... & Gansert, J. L. (2010). Randomized phase III study of panitumumab (pmab) with FOLFIRI versus FOLFIRI alone as second-line treatment (tx) in patients (pts) with metastatic colorectal cancer (mCRC): Analysis by tumor epidermal growth factor receptor (EGFR) staining. *Journal of Clinical Oncology*, *28*(15_suppl), 3565-3565.

Quirke, P., Steele, R., Monson, J., Grieve, R., Khanna, S., Couture, J., ... & Parmar, M. (2009). Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial. *The Lancet*, *373*(9666), 821-828.

Regnard, J. F., Grunenwald, D., Spaggiari, L., Girard, P., Elias, D., Ducreux, M., ... & Levasseur, P. (1998). Surgical treatment of hepatic and pulmonary metastases from colorectal cancers. *The Annals of Thoracic Surgery*, *66*(1), 214-218.

Rena, O., Casadio, C., Viano, F., Cristofori, R., Ruffini, E., Filosso, P. L., & Maggi, G. (2002). Pulmonary resection for metastases from colorectal cancer: factors influencing prognosis. Twenty-year experience. *European Journal of Cardio-thoracic Surgery*, *21*(5), 906-912.

Rödel, C., Graeven, U., Fietkau, R., Hohenberger, W., Hothorn, T., Arnold, D., ... & Raab, H. R. (2015). Oxaliplatin added to fluorouracil-based preoperative chemoradiotherapy and postoperative chemotherapy of locally advanced rectal cancer (the German CAO/ARO/AIO-04 study): final results of the multicentre, open-label, randomised, phase 3 trial. *The Lancet Oncology*, *16*(8), 979-989.

Roh, Mark S., Linda H. Colangelo, Michael J. O'Connell, Greg Yothers, Melvin Deutsch, Carmen J. Allegra, Morton S. Kahlenberg et al. "Preoperative multimodality therapy improves disease-free survival in patients with carcinoma of the rectum: NSABP R-03." *Journal of Clinical Oncology* 27, no. 31 (2009): 5124-5130.

Roh, M. S., Yothers, G. A., O'Connell, M. J., Beart, R. W., Pitot, H. C., Shields, A. F., ... & Landry, J. C. (2011). The impact of capecitabine and oxaliplatin in the preoperative multimodality treatment in patients with carcinoma of the rectum: NSABP R-04. *Journal of Clinical Oncology*, *29*(15_suppl), 3503-3503.

Sauer, R., Becker, H., Hohenberger, W., Rödel, C., Wittekind, C., Fietkau, R., ... & Karstens, J. H. (2004). Preoperative versus postoperative chemoradiotherapy for rectal cancer. *New England Journal of Medicine*, *351*(17), 1731-1740.

Sauer, R., Liersch, T., Merkel, S., Fietkau, R., Hohenberger, W., Hess, C., ... & Wittekind, C. (2012). Preoperative versus postoperative chemoradiotherapy for locally advanced rectal cancer: results of the German CAO/ARO/AIO-94 randomized phase III trial after a median follow-up of 11 years. *Journal of Clinical Oncology*, *30*(16), 1926-1933.

Sebag-Montefiore, D., Stephens, R. J., Steele, R., Monson, J., Grieve, R., Khanna, S., ... & Bessell, E. (2009). Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. *The Lancet*, *373*(9666), 811-820.

Siena, S., Tabernero, J., Cunningham, D., Koralewski, P., Ruff, P., Rother, M., ... & Douillard, J. (2010). Randomized phase III study of panitumumab (pmab) with FOLFOX4 compared to FOLFOX4 alone as first-line treatment (tx) for metastatic colorectal cancer (mCRC): PRIME trial analysis by epidermal growth factor receptor (EGFR) tumor staining. *Journal of Clinical Oncology*, *28*(15_suppl), 3566-3566.

Continued on next page

SUGGESTED READINGS - continued

Silberfein, E. J., Kattepogu, K. M., Hu, C. Y., Skibber, J. M., Rodriguez-Bigas, M. A., Feig, B., ... & Eng, C. (2010). Long-term survival and recurrence outcomes following surgery for distal rectal cancer. *Annals of Surgical Oncology*, *17*(11), 2863-2869.

Skibber, J.M. (2005). Local excision for rectal cancer. *Journal of the National Comprehensive Cancer Network*, *3*(4), 531-539.

Taylor, F. G. M., Quirke, P., Heald, R. J., Moran, B., Blomqvist, L., Swift, I., ... & Brown, G. (2011). One millimetre is the safe cut-off for magnetic resonance imaging prediction of surgical margin status in rectal cancer. *British Journal of Surgery*, *98*(6), 872-879.

Twelves, C.J. (2006). Xeloda in Adjuvant Colon Cancer Therapy (X-ACT) trial: overview of efficacy, safety, and cost-effectiveness. *Clinical Colorectal Cancer*, *6*(4), 278-87.

Van Cutsem, E., Köhne, C. H., Hitre, E., Zaluski, J., Chang Chien, C. R., Makhson, A., ... & Roh, J. K. (2009). Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer. *New England Journal of Medicine*, *360*(14), 1408-1417.

Van Cutsem, E., Siena, S., Humblet, Y., Canon, J. L., Maurel, J., Bajetta, E., ... & Spadafora, S. (2007). An open-label, single-arm study assessing safety and efficacy of panitumumab in patients with metastatic colorectal cancer refractory to standard chemotherapy. *Annals of Oncology*, *19*(1), 92-98.

Vauthey, J. N., Pawlik, T. M., Ribero, D., Wu, T. T., Zorzi, D., Hoff, P. M., ... & Risio, M. (2006). Chemotherapy regimen predicts steatohepatitis and an increase in 90-day mortality after surgery for hepatic colorectal metastases. *Journal of Clinical Oncology*, *24*(13), 2065-2072.

Venook, A. P., Niedzwiecki, D., Lenz, H. J., Innocenti, F., Fruth, B., Meyerhardt, J. A., ... & Berry, S. (2017). Effect of First-Line Chemotherapy Combined With Cetuximab or Bevacizumab on Overall Survival in Patients With KRAS Wild-Type Advanced or Metastatic Colorectal Cancer: A Randomized Clinical Trial. *JAMA*, *317*(23), 2392-2401.

Wibe, A., Eriksen, M. T., Syse, A., Tretli, S., Myrvold, H. E., & Søreide, O. (2005). Effect of hospital caseload on long-term outcome after standardization of rectal cancer surgery at a national level. *British Journal of Surgery*, *92*(2), 217-224.

DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Gastrointestinal Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

Thomas Aloia, MD (Surgical Oncology)
Tharakeswara Bathala, MD (Diagnostic Radiology – Body Imaging)
Brian K Bednarski, MD (Surgical Oncology)
George J. Chang, MD, MS (Surgical Oncology)[Ŧ]
Prajnan Das, MD (Radiation Oncology)[Ŧ]
Arvind Dasari, MD (GI Medical Oncology)
Lee M. Ellis, MD (Surgical Oncology)
Cathy Eng, MD (GI Medical Oncology)[Ŧ]
Barry W. Feig, MD (Surgical Oncology)
David Fogelman MD (GI Medical Oncology)
Stanley Hamilton, MD (Pathology/Lab Medicine)
Shonice Holdman, MBA[♦]
Benny Johnson, DO (GI Medical Oncology)
Bryan Kee, MD (GI Medical Oncology)
Scott Kopetz, MD (GI Medical Oncology)
Sunil Krishnan, MD (Radiation Oncology)
Craig Messick, MD (Surgical Oncology)
Bruce Minsky, MD (Radiation Oncology)
Michael Overman, MD (GI Medical Oncology)
Amy Pai, PharmD[♦]
Dina Patel, PharmD (Pharmacy Clinical Programs)
Miguel A. Rodriguez-Bigas, MD (Surgical Oncology)
Jane Rogers, PharmD (Pharmacy Clinical Programs)
Tara Sagebiel, MD (Diagnostic Radiology – Body Imaging)
Imad Shureiqi, MD (GI Medical Oncology)
John M. Skibber, MD (Surgical Oncology)
Jean Nicolas Vauthey, MD (Surgical Oncology)
Eduardo Vilar-Sanchez, MD (Clinical Cancer Prevention)
Robert Wolff, MD (GI Medical Oncology)
Y. Nancy You, MD (Surgical Oncology)

[Ŧ] Core Development Team
[♦] Clinical Effectiveness Development Team