RECTAL CANCER TREATMENT REGIMENS (Part 1 of 4)

The selection, dosing, and administration of anticancer agents and the management of associated toxicities are complex. Drug dose modifications and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and because of individual patient variability, prior treatment, and comorbidities. Thus, the optimal delivery of anticancer agents requires a healthcare delivery team experienced in the use of such agents and the management of associated toxicities in patients with cancer. The cancer treatment regimens below may include both FDA-approved and unapproved uses/regimens and are provided as references only to the latest treatment strategies. Clinicians must choose and verify treatment options based on the individual patient.

NOTE: GREY SHADED BOXES CONTAIN UPDATED REGIMENS.

Principles of adjuvant therapy:

- Consists of regimens that also include both concurrent chemotherapy and radiotherapy.
- Chemotherapy/radiotherapy can be administered either pre- or post-operatively, although later studies use post-operative regimens for patients not receiving preoperative therapy.
- Six months of perioperative therapy is preferred.
- In response to the shortage of leucovorin over the last few years, the FDA recently approved levoleucovorin (Fusilev) in combination with 5-FU for the palliative treatment of patients with advanced metastatic colorectal cancer. Levoleucovorin 200mg/m^2 is the equivalent of leucovorin 400mg/m^2.[1]

REGIMEN	DOSING
Postoperative Adjuvant Therapy for Patients Not Receiving Preoperative Therapy	
mFOLFOX6 (oxaliplatin [Eloxatin] + leucovorin + 5-fluorouracil [5-FU])[1,2] NOTE: Preferred	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hrs **+** leucovorin 400mg/m^2 IV over 2 hrs, **followed by** 5-FU 400mg/m^2 IV bolus, **followed by** 5-FU 1,200mg/m^2/day IV x 2 days (total 2,400mg/m^2) as a 46–48 hr continuous infusion. Repeat every 2 weeks for 6 months.
Capecitabine (Xeloda)[1,3]	**Days 1–14:** Capecitabine 1,250mg/m^2 orally twice daily. Repeat cycle every 3 weeks for 6 months.
CapeOX (also called XELOX) (oxaliplatin + capecitabine)[1,4] NOTE: Preferred	**Day 1:** Oxaliplatin 130mg/m^2 IV. **Days 1–14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat cycle every 3 weeks for 6 months.
Simplified biweekly infusional 5-FU/LV (sLV5FU2)[1,6]	**Day 1:** Leucovorin 400mg/m^2 IV, **followed by** 5-FU 400mg/m^2 IV bolus, **followed by** 5-FU 1,200mg/m^2/day IV x 2 days (total 2,400mg/m^2) as a 46–48 hr continuous infusion. Repeat every 2 weeks for 6 months.
FLOX (5-FU + leucovorin + oxaliplatin)[1,7]	**Days 1, 8, 15, 22, 29 and 36:** Leucovorin 500mg/m^2 IV, **followed by** 5-FU 500mg/m^2 IV bolus. **Days 1, 15 and 29:** Oxaliplatin 85mg/m^2 IV. Repeat cycle every 8 weeks for 6 months.
5-FU + leucovorin[1,8]	**Days 1, 8, 15, 22, 29 and 36:** Leucovorin 500mg/m^2 IV, **followed by** 5-FU 500mg/m^2 IV bolus. Repeat cycle every 8 weeks for 6 months.
Concurrent Chemotherapy + Radiotherapy	
External beam radiotherapy [XRT] **+ 5-FU**[1,9]	**Days 1–5 OR 1–7:** 5-FU 225mg/m^2 IV over 24 hrs during XRT.
XRT + 5-FU + leucovorin[1,10]	**Days 1–4:** Leucovorin 20mg/m^2 IV bolus, **followed by** 5-FU 400g/m^2 IV bolus during XRT. Repeat during weeks 1 and 5 of XRT.
XRT + capecitabine[1,11,12]	**Days 1–5 OR 1–7:** Capecitabine 825mg/m^2 twice daily **+** XRT. Repeat weekly for 5 weeks.
Advanced or Metastatic Rectal Disease	
mFOLFOX6 (oxaliplatin + leucovorin + 5-FU)[1,2,13]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hrs **+** leucovorin 400mg/m^2 IV over 2 hrs, **followed by** 5-FU 400mg/m^2 IV bolus, **followed by** 5-FU 1,200mg/m^2/day IV x 2 days (total 2,400mg/m^2) as a 46–48 hr continuous infusion. Repeat every 2 weeks.
mFOLFOX6 + bevacizumab (Avastin)[1,13,14]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hrs **+** leucovorin 400mg/m^2 IV over 2 hrs, **followed by** 5-FU 400mg/m^2 IV bolus, **followed by** 5-FU 1,200mg/m^2/day IV x 2 days (total 2,400mg/m^2) as a 46–48 hr continuous infusion. **Day 1:** Bevacizumab 5mg/kg. Repeat every 2 weeks.

continued

RECTAL CANCER TREATMENT REGIMENS (Part 2 of 4)	
REGIMEN	**DOSING**
Advanced or Metastatic Rectal Disease (continued)	
mFOLFOX 6 + panitumumab (Vectibix)[1,13,15] (KRAS wild-type gene only)	**Day 1:** Oxaliplatin 85mg/m² IV over 2 hrs **+** leucovorin 400mg/m² IV over 2 hrs, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48 hr continuous infusion. **Day 1:** Panitumumab 6mg/kg IV over 1 hr. Repeat every 2 weeks.
CapeOX (also called XELOX) (oxaliplatin + capecitabine)[1,2,16]	**Day 1:** Oxaliplatin 130mg/m² IV. **Days 1–14:** Capecitabine 850–1,000mg/m² orally twice daily. Repeat cycle every 3 weeks.
CapeOX + bevacizumab[1,2,16,17]	**Day 1:** Oxaliplatin 130mg/m² IV. **Days 1–14:** Capecitabine 850–1,000mg/m² orally twice daily. **Day 1:** Bevacizumab 7.5mg/kg IV. Repeat cycle every 3 weeks.
FOLFIRI (irinotecan [Camptosar] + leucovorin + 5-FU)[1,6]	**Day 1:** Irinotecan 180mg/m² IV **+** leucovorin 400mg/m² IV, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48 hr continuous infusion. Repeat every 2 weeks.
FOLFIRI + bevacizumab[1,6,18]	**Day 1:** Irinotecan 180mg/m² IV **+** bevacizumab 5mg/kg IV **+** leucovorin 400mg/m² IV, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48 hr continuous infusion. Repeat cycle every 2 weeks.
FOLFIRI + ziv-aflibercept (Zaltrap)[1,19]	**Day 1:** Irinotecan 180mg/m² IV **+** leucovorin 400mg/m² IV, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48 hr continuous infusion. **Day 1:** Ziv-aflibercept 4mg/kg IV. Repeat cycle every 2 weeks.
FOLFIRI + cetuximab (Erbitux)[1,6,20,21] (KRAS wild-type gene only)	**Day 1:** Irinotecan 180mg/m² IV **+** leucovorin 400mg/m² IV, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48 hr continuous infusion. Repeat every 2 weeks. **Day 1:** Cetuximab 400mg/m² IV over 2 hrs first infusion, then cetuximab 250mg/m² IV over 1 hr once weekly. **OR** Cetuximab 500mg/m² IV over 2 hrs every 2 weeks.
FOLFIRI + panitumumab[1,6,22] (KRAS wild-type gene only)	**Day 1:** Irinotecan 180mg/m² **+** leucovorin 400mg/m² IV, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48 hr continuous infusion. **Day 1:** Panitumumab 6mg/kg IV over 1 hr. Repeat every 2weeks.
Capecitabine[1,23]	**Days 1–14:** Capecitabine 1,250mg/m² orally twice daily. Repeat cycle every 3 weeks.
Capecitabine + bevacizumab[1,17,23]	**Days 1–14:** Capecitabine 850–1,250mg/m² orally twice daily. **Day 1:** Bevacizumab 7.5mg/kg IV. Repeat every 3 weeks.
Bolus or infusional 5-FU + leucovorin[1,24] (Roswell-Park Regimen)	**Days 1, 8, 15, 22, 29 and 36:** Leucovorin 500mg/m² IV, **followed by** 5-FU 500mg/m² IV bolus. Repeat every 8 weeks.
Simplified biweekly infusional 5-FU/LV (sLV5FU2)[1,6]	**Day 1:** Leucovorin 400mg/m² IV, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48 hr continuous infusion. Repeat every 2 weeks.
Weekly 5-FU/LV[1,25,26]	**Day 1:** Leucovorin 20mg/m² IV, **followed by** 5-FU 500mg/m² IV bolus. Repeat weekly. **OR** **Day 1:** Leucovorin 500mg/m² IV, **followed by** 5-FU 2,600mg/m² continuous infusion. Repeat weekly.

continued

RECTAL CANCER TREATMENT REGIMENS (Part 3 of 4)

REGIMEN	DOSING
Advanced or Metastatic Rectal Disease (continued)	
IROX (oxaliplatin + irinotecan)[1,27]	Oxaliplatin 85mg/m² IV **+** irinotecan 200mg/m² IV. Repeat cycle every 3 weeks.
FOLFOXIRI (irinotecan + oxaliplatin + leucovorin + 5-FU)[1,28]	**Day 1:** Irinotecan 165mg/m² IV **+** oxaliplatin 85mg/m² IV **+** leucovorin 400mg/m² IV **plus** **Days 1 and 2:** 5-FU 1,600mg/m²/day continuous infusion IV over 48 hrs (total 5-FU=3,200mg/m²). Repeat every 2 weeks.
Irinotecan ± bevacizumab[1,29,30]	**Days 1 and 8:** Irinotecan 125mg/m² IV. **Day 1:** Bevacizumab. Repeat cycle every 3 weeks. **OR** **Day 1:** Irinotecan 300–350mg/m² IV. **Day 1:** Bevacizumab. Repeat cycle every 3 weeks.
Cetuximab (KRAS wild-type gene only) **± irinotecan**[1,21,31]	**Day 1:** Cetuximab 400mg/m² IV, then 250mg/m² IV every 7 days. **OR** **Day 1:** Cetuximab 500mg/m² IV every 2 weeks **±** » Irinotecan 300–350mg/m² IV every 3 weeks, **OR** » Irinotecan 180mg/m² IV every 2 weeks, **OR** » On Days 1 and 8, irinotecan 125mg/m² IV. Repeat cycle every 3 weeks.
Panitumumab (KRAS wild-type gene only)[1,32]	**Day 1:** Panitumumab 6mg/kg IV. Repeat cycle every 2 weeks.

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RECTAL CANCER TREATMENT REGIMENS (Part 4 of 4)

REGIMEN	DOSING

References (continued)

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