Rectal Cancer Treatment Regimens

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced health care team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are provided only to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data become available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Note: All recommendations are category 2A unless otherwise indicated.

▶Systemic Therapy for Advanced or Metastatic Disease[1]

REGIMEN	DOSING
Capecitabine[2-4,a-d]	**Days 1-14:** Capecitabine 850-1,250mg/m^2 orally twice daily. Repeat cycle every 3 weeks.
Capecitabine + Bevacizumab[2,5-7,a,b,e]	**Day 1:** Bevacizumab 7.5mg/kg IV **Days 1-14:** Capecitabine 850-1,250mg/m^2 orally twice daily. Repeat cycle every 3 weeks.
CapeOX[2,8-10,a,c,d,f,g-j]	**Day 1:** Oxaliplatin 130mg/m^2 IV over 2 hours **Days 1-15:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat cycle every 3 weeks.
CapeOX + Bevacizumab[2,5,8,10,11,b,e,g,h,i,j]	**Day 1:** Bevacizumab 7.5mg/kg IV, **followed by:** **Day 1:** Oxaliplatin 130mg/m^2 IV over 2 hours **Days 1-15:** Capecitabine 1,000mg/m^2 orally twice daily.[e] Repeat cycle every 3 weeks.
Cetuximab (*KRAS/NRAS/BRAF* wild-type gene and left-sided tumor only) (Category 2B)[12-16,b]	**Day 1:** Cetuximab 400mg/m^2 IV over 2 hours first infusion, then 250mg/m^2 IV over 60 minutes weekly **OR** **Day 1:** Cetuximab 500mg/m^2 IV. Repeat cycle every 2 weeks.
Encorafenib + Cetuximab (*BRAF* V600E mutation positive)[12,17-19,j]	**Days 1-28:** Encorafenib 300mg orally once daily. Repeat cycle every 4 weeks, **with:** **Day 1:** Cetuximab 400mg/m^2 IV over 2 hours first infusion, then 250mg/m^2 IV over 60 minutes beginning with cycle 2. Repeat cycle weekly. **OR** **Days 1-28:** Encorafenib 300mg orally once daily. Repeat cycle every 4 weeks, **with:** **Day 1:** Cetuximab 500mg/m^2 IV. Repeat cycle every 2 weeks.
Encorafenib + Panitumumab (*BRAF* V600E mutation positive)[17-20,j]	**Days 1-28:** Encorafenib 300mg orally once daily. Repeat cycle every 4 weeks, **with:** **Day 1:** Panitumumab 6mg/kg IV over 60 minutes. Repeat cycle every 2 weeks.
Entrectinib (*NTRK* gene fusion positive)[21,22,k]	**Days 1-28:** Entrectinb 600mg orally daily. Repeat cycle every 4 weeks.
FOLFIRI[23-27,d,g,j,l]	**Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes **with:** **Day 1:** Leucovorin 400mg/m^2 IV infusion to match duration of irinotecan infusion, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks.
FOLFIRI + Bevacizumab[23-26,28,e,g,j,l]	**Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes **with:** **Day 1:** Leucovorin 400mg/m^2 IV infusion to match duration of irinotecan infusion, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion **Day 1:** Bevacizumab 5mg/kg IV. Repeat cycle every 2 weeks.

continued

Rectal Cancer Treatment Regimens

▶Systemic Therapy for Advanced or Metastatic Disease[1] (continued)

REGIMEN	DOSING
FOLFIRI + Cetuximab (*KRAS/NRAS/BRAF* wild-type gene and left-sided tumor only)[12,14,16,23,24,27,29,g,j,l]	**Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes, **with:** **Day 1:** Leucovorin 400mg/m^2 IV infusion to match duration of irinotecan infusion, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion Repeat cycle every 2 weeks, **with:** **Day 1:** Cetuximab 400mg/m^2 IV over 2 hours first infusion, then 250mg/m^2 IV over 60 minutes beginning with cycle 2. Repeat cycle weekly. **OR** **Day 1:** Cetuximab 500mg/m^2 IV, **followed by:** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes, **with:** **Day 1:** Leucovorin 400mg/m^2 IV infusion to match duration of irinotecan infusion, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push day 1, then 1,200,g/m^2/day x 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks.
FOLFIRI + Panitumumab (*KRAS/NRAS/BRAF* wild-type gene and left-sided tumor only)[20,23-25,27,30,g,j,l]	**Day 1:** Panitumumab 6mg/kg IV over 60 minutes, **followed by:** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes **with:** **Day 1:** Leucovorin 400mg/m^2 IV infusion to match duration of irinotecan infusion, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks.
FOLFIRI + Ramucirumab[23-25,31,32,j,m]	**Day 1:** Ramucirumab 8mg/kg IV over 60 minutes **followed by:** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes **with:** **Day 1:** Leucovorin 400mg/m^2 IV infusion to match duration of irinotecan infusion, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push day 1, then 1,200mg/m^2/day × 2 day (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks.
FOLFIRI + Ziv-aflibercept[23-25,33,34,j,l]	**Day 1:** Ziv-aflibercept 4mg/kg IV over 1 hour, **followed by:** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes, **with:** **Day 1:** Leucovorin 400mg/m^2 IV infusion to match duration of irinotecan infusion, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks.
FOLFOXIRI[8,23-25,35,d,g,h,l]	**Day 1:** Irinotecan 165mg/m^2 IV over 30 to 90 minutes **Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours to match the infusion time of oxaliplatin, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 (2,400mg/m^2 over 48 hours) IV continuous infusion. Repeat cycle every 2 weeks.
FOLFOXIRI + Bevacizumab[5,8,23-25,35,36,e,g,h,l]	**Day 1:** Irinotecan 165mg/m^2 IV over 30-90 minutes **Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **with:** **Day 1:** Leucovorin 400mg/m^2 IV to match infusion time of oxaliplatin, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 48 hours) continuous infusion starting on day 1 **Day 1:** Bevacizumab 5mg/kg IV. Repeat cycle every 2 weeks.
FOLFOXIRI + Cetuximab (*KRAS/NRAS/BRAF* wild-type gene and left-sided tumor only)[8,12,23-25,35,38,l] **(Category 2B)**	**Day 1:** Cetuximab 400mg/m^2 IV over 2 hours week 1, then 250mg/m^2 IV over 60 minutes starting week 2. Repeat cycle weekly, **with:** **Day 1:** Irinotecan 165mg/m^2 IV over 30-90 minutes **Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion daily (2,400mg/m^2 IV over 46-48 hours). Repeat cycle every 2 weeks. **OR** **Day 1:** Cetuximab 500mg/m^2 IV over 2 hours, **followed by:** **Day 1:** Irinotecan 165mg/m^2 IV over 30-90 minutes **Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion daily (2,400mg/m^2 IV over 46-48 hours). Repeat cycle every 2 weeks.

continued

Rectal Cancer Treatment Regimens

▶Systemic Therapy for Advanced or Metastatic Disease[1] (continued)

REGIMEN	DOSING
FOLFOXIRI + Panitumumab (*KRAS/NRAS/BRAF* wild-type gene and left-sided tumor only)[8,20,23-25,35,38,39,l] (Category 2B)	**Day 1:** Panitumumab 6mg/kg IV over 60 minutes, **followed by:** **Day 1:** Irinotecan 165mg/m^2 IV over 30-90 minutes **Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion daily (2,400mg/m^2 IV over 46-48 hours). Repeat cycle every 2 weeks.
Irinotecan[25,40,41,j,n]	**Days 1 and 8:** Irinotecan 125mg/m^2 IV over 30-90 minutes. Repeat cycle every 3 weeks. **OR** **Day 1:** Irinotecan 300-350mg/m^2 IV over 30-90 minutes.[n] Repeat cycle every 3 weeks. **OR** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes. Repeat cycle every 2 weeks.
Irinotecan + Bevacizumab[5,23,25,40,42,e,j,m]	**Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes **Day 1:** Bevacizumab 5mg/kg IV. Repeat cycle every 2 weeks. **OR** **Day 1:** Irinotecan 300-350mg/m^2 IV over 30-90 minutes[n] **Day 1:** Bevacizumab 7.5mg/kg IV. Repeat cycle every 3 weeks.
Irinotecan + Cetuximab (*KRAS/NRAS/BRAF* wild-type gene)[12,14,16,25,40,j]	**Day 1:** Cetuximab 400mg/m^2 IV first infusion, then 250mg/m^2 IV weekly, **with:** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Cetuximab 500mg/m^2 IV, **followed by:** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes. Repeat cycle every 2 weeks.
Irinotecan + Panitumumab (*KRAS/NRAS/BRAF* wild-type gene)[20,2530,43,44,j]	**Day 1:** Panitumumab 6mg/kg IV over 60 minutes, **followed by:** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes. Repeat cycle every 2 weeks
Irinotecan + Ramucirumab[25,31,32,j]	**Day 1:** Ramucirumab 8mg/m^2 over 60 minutes, **followed by:** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes. Repeat cycle every 2 weeks.
Irinotecan + Ziv-aflibercept[25,33,40,j]	**Day 1:** Ziv-aflibercept 4mg/kg IV over 60 minutes, **followed by:** **Day 1:** Irinotecan 180mg/m^2 IV over 30-90 minutes. Repeat cycle every 2 weeks.
IROX[8,25,45,h]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **followed by:** **Day 1:** Irinotecan 200mg/m^2 over 30-90 minutes. Repeat cycle every 3 weeks.
IROX + Bevacizumab[5,8,25,45-47,e,h]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Irinotecan 200mg/m^2 IV over 30-90 minutes **Day 1:** Bevacizumab 7.5mg/kg IV. Repeat cycle every 3 weeks.
Larotrectinib (*NTRK* gene fusion positive)[48,49,k]	**Days 1-28:** Larotrectinib 100mg orally twice daily. Repeat cycle every 4 weeks.
mFOLFOX6[8,23,24,50-53,c,d,f,g,h,j,l]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push on day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks.
mFOLFOX6 + Bevacizumab[5,23-25,54-57,e,g,h,j,l]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push on day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion **Day 1:** Bevacizumab 5mg/kg IV. Repeat cycle every 2 weeks.

continued

Rectal Cancer Treatment Regimens

▶Systemic Therapy for Advanced or Metastatic Disease[1] (continued)

REGIMEN	DOSING
mFOLFOX6 + Cetuximab (*KRAS/NRAS/BRAF* wild-type gene and left-sided tumor only when used as initial therapy)[8,12,23,24,56,g,h,j,l]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push on day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks, **with** **Day 1:** Cetuximab 400mg/m^2 IV over 2 hours for the first infusion, then 250mg/m^2 IV over 60 minutes weekly. **OR** **Day 1:** Cetuximab 500mg/m^2 IV over 2 hours every 2 weeks.
mFOLFOX6 + Panitumumab (*KRAS/NRAS/BRAF* wild-type gene and left-sided tumor only when used as initial therapy)[8,12,20,23,24,51,57,58,g,h,j,l]	**Day 1:** Panitumumab 6mg/kg IV over 60 minutes, **followed by:** **Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push on day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks.
mFOLFOX7[8,23,24,59,60,g,h,j,l]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours IV **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2/day (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat every 2 weeks.
Nivolumab (MSI-H/dMMR tumors only)[61,62,b,j]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat every 2 weeks. **OR** **Day 1:** Nivolumab 3mg/kg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks
Nivolumab + Ipilimumab (MSI-H/dMMR tumors only)[61,63,64,b,j]	**Day 1:** Nivolumab 3mg/kg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for 4 cycles, **followed by:** **Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 3mg/kg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for 4 cycles, **followed by:** **Day 1:** Nivolumab 3mg/kg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 3mg/kg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for 4 cycles, **followed by:** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.
Panitumumab (*KRAS/NRAS/BRAF* wild-type gene and left-sided tumor only; Category 2B)[20,65,b]	**Day 1:** Panitumumab 6mg/kg IV over 60 minutes. Repeat cycle every 2 weeks.
Pembrolizumab (MSI-H/dMMR tumors only)[66-68,b,g,j]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat every 3 weeks. **OR** **Day 1:** Pembrolizumab 2mg/kg IV over 30 minutes. Repeat cycle every 3 weeks. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat every 42 days up to 2 years of therapy.

continued

Rectal Cancer Treatment Regimens

▶Systemic Therapy for Advanced or Metastatic Disease[1] (continued)

REGIMEN	DOSING
Regorafenib[69-71,j,n]	**First Cycle** **Days 1-7:** Regorafenib 80mg orally once daily **Days 8-14:** Regorafenib 120mg orally once daily **Days 15-21:** Regorafenib 160mg orally once daily. **Subsequent Cycles:** **Days 1-21:** Regorafenib 160mg orally once daily. Repeat cycle every 4 weeks. **OR** **Days 1-21:** Regorafenib 160mg orally once daily. Repeat cycle every 4 weeks.
Roswell Park Fluorouracil/ Leucovorin[23,24,72-74,b-d,l]	**Days 1, 8, 15, 22, 29, and 36:** Leucovorin 500mg/m^2 IV over 2 hours **Days 1, 8, 15, 22, 29, and 36:** Fluorouracil 500mg/m^2 IV push 1 hour after start of leucovorin. Repeat cycle every 8 weeks (6 weeks on- followed by 2 weeks off-treatment).
Roswell Park Fluorouracil/ Leucovorin + Bevacizumab[5,23,24,72,73,b,e,l]	**Days 1, 8, 15, 22, 29, and 36:** Leucovorin 500mg/m^2 IV over 2 hours **Days 1, 8, 15, 22, 29, and 36:** Fluorouracil 500mg/m^2 IV push 1 hour after start of leucovorin infusion, **with:** Repeat cycle every 8 weeks (6 weeks on- followed by 2 weeks off-treatment). **Day 1:** Bevacizumab 5mg/kg IV. Repeat cycle every 2 weeks.
Simplified Biweekly Infusional Fluorouracil/Leucovorin[23,24,27,b,c,d,l]	**Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by**: **Day 1:** Fluorouracil 400 mg/m^2 IV push, **followed by**: **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion daily (2,400mg/m^2 IV over 46-48 hours). Repeat cycle every 2 weeks.
Simplified Biweekly Infusional Fluorouracil/Leucovorin + Bevacizumab[5,23,24,27,75,b,e,l]	**Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Day 1:** Fluorouracil 400 mg/m^2 IV push, **followed by:** **Days 1-3:** Fluorouracil 1,200mg/m^2 IV continuous infusion daily (2,400mg/m^2 IV over 46-48 hours) **Day 1:** Bevacizumab 5mg/kg IV. Repeat cycle every 2 weeks.
Trastuzumab + Lapatinib (HER2 amplified and *KRAS/HRAS/ BRAF* wild-type gene)[76-78,b,j,n]	**Day 1:** Trastuzumab 4mg/kg IV first infusion, then 2mg/kg IV beginning with cycle 2 Repeat cycle weekly, **with:** **Days 1-28:** Lapatinib 1,000mg orally daily. Repeat cycle every 4 weeks.
Trastuzumab + Pertuzumab (HER2 amplified and *KRAS/HRAS/ BRAF* wild-type gene[76,79,80,b,j,n]	**Day 1:** Trastuzumab 8mg/kg IV first infusion, then 6 mg/kg IV beginning with cycle 2 **Day 1:** Pertuzumab 840mg IV first infusion, then 420mg IV beginning with cycle 2. Repeat cycle every 3 weeks.
Trifluridine + Tipiracil[81,82,j,n]	**Days 1-5 and 8-12:** Trifluridine + Tipiracil 35mg/m^2 up to a maximum dose of 80mg/dose (based on the trifluridine component) orally twice daily. Repeat cycle every 4 weeks.
Weekly Fluorouracil/ Leucovorin[23,24,83,b,c,l]	**Day 1:** Leucovorin 20mg/m^2 IV over 2 hours **Day 1:** Fluorouracil 500mg/m^2 IV push 1 hour after the start of leucovorin infusion. Repeat cycle every week. **OR** **Day 1:** Leucovorin 500mg/m^2 IV over 2 hours **Day 1:** Fluorouracil 2,600mg/m^2 continuous infusion over 24 hours. Repeat cycle every week.
Weekly Fluorouracil/Leucovorin + Bevacizumab[23,24,75,83,b,e,l]	**Day 1:** Leucovorin 20mg/m^2 IV over 2 hours once weekly **Day 1:** Fluorouracil 500mg/m^2 IV push administered one hour after start of leucovorin infusion once weekly, **with:** **Day 1:** Bevacizumab 5mg/kg IV every 2 weeks. **OR** **Day 1:** Leucovorin 500mg/m^2 IV over 2 hours once weekly **Day 1:** Fluorouracil 2,600mg/m^2 IV continuous infusion over 24 hours once weekly, **with:** **Day 1:** Bevacizumab 5mg/kg IV every 2 weeks.

continued

Rectal Cancer Treatment Regimens

▶Preoperative/Postoperative Adjuvant Concurrent Chemotherapy/RT

REGIMEN	DOSING
Capecitabine + RT[2,84,85,p]	**Days 1-5:** Capecitabine 825mg/m^2 orally twice daily. Repeat weekly for 5 weeks with concurrent RT.
Continuous Infusion Fluorouracil + RT[24,86,p]	**Days 1-5 or 1-7:** Fluorouracil 225mg/m^2 IV continuous infusion over 24 hours daily. Repeat weekly for 5 weeks with concurrent RT.
Fluorouracil + Leucovorin + RT[23,24,87,p,q]	**Days 1-4 and 29-32:** Leucovorin 20mg/m^2 IV push **Days 1-4 and 29-32:** Fluorouracil 400mg/m^2 IV push. Administer for one 35-day cycle with concurrent RT.

▶Postoperative Adjuvant Chemotherapy Regimens[1]

Capecitabine[2,3,a]	**Days 1-14:** Capecitabine 1,000-1,250mg/m^2 orally twice daily. Repeat cycle every 3 weeks for 6 cycles following concurrent chemotherapy/RT for a total of 6 months of perioperative treatment including chemotherapy/RT **OR** **Days 1-14:** Capecitabine 1,000-1,250mg/m^2 orally twice daily. Repeat cycle every 3 weeks preceding and 3 cycles following chemotherapy/RT for a total of 6 months of perioperative treatment including concurrent chemotherapy/RT
CapeOx[2,8,9,a,h]	**Day 1:** Oxaliplatin 130mg/m^2 IV over 2 hours **Days 1-15:** Capecitabine 1,000mg/m^2 orally twice daily.[e] Repeat cycle every 3 weeks for 8 cycles following concurrent chemotherapy/RT for a total of 6 months of perioperative treatment including concurrent chemotherapy/RT. **OR** **Day 1:** Oxaliplatin 130mg/m^2 IV over 2 hours **Days 1-14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat cycle every weeks for 3 cycles preceding and 3 cycles following chemotherapy/RT for a total of 6 months of perioperative treatment including concurrent chemotherapy/RT.
mFOLFOX6[8,23,24,50-53,h,l]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push on day 1, then 1,200mg/m^2/day × 2 days (total 2,400mg/m^2 over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks for 8 cycles following concurrent chemotherapy/RT for a total of 6 months of perioperative treatment including concurrent chemotherapy/RT.
Roswell Park Fluorouracil/ Leucovorin[23,24,72,73,89,l]	**Days 1, 8, 15, 22, 29, and 36:** Leucovorin 500mg/m^2 IV over 2 hours **Days 1, 8, 15, 22, 29, and 36:** Fluorouracil 500mg/m^2 IV push 1 hour after start of leucovorin infusion. Repeat cycle every 8 weeks (6 weeks on followed by 2 weeks off treatment) for 2 cycles following concurrent chemotherapy/RT for a total of 6 months of perioperative treatment including concurrent chemotherapy/RT. **OR** **Days 1,8,15,22,29,36:** Leucovorin 500mg/m^2 IV over 2 hours **Days 1,8,15,22,29,36:** Fluorouracil 500mg/m^2 push administered 1 hour after start of Leucovorin infusion. Repeat cycle every 8 weeks (6 weeks on followed by 2 weeks off treatment) for 1 cycle preceding and 1 cycle following chemotherapy/RT for a total of 6 months of perioperative treatment including concurrent chemotherapy/RT.
Simplified Biweekly Infusional Fluorouracil/Leucovorin[23,24,27,l]	**Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Day 1:** Fluorouracil 400 mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion daily (2,400mg/m^2 IV over 46-48 hours). Repeat cycle every 2 weeks for 8 cycles following concurrent chemotherapy/RT for a total of 6 months of perioperative treatment including concurrent chemotherapy/RT. **OR** **Day 1:** Leucovorin 400mg/m2 IV over 2 hours, **followed by:** **Day 1:** Fluorouracil 400mg/m2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m2 IV continuous infusion daily (2,400mg/m^2 IV over 46-48 hours). Repeat cycle every 2 weeks for 4 cycles preceding and 4 cycles following chemotherapy/RT for a total of 6 months of perioperative treatment including concurrent chemotherapy/RT.

[a] The majority of safety and efficacy data for this regimen have been developed in Europe, where a capecitabine starting dose of 1,000mg/m2 twice daily for 14 days, repeated every 21 days, is standard. Evidence suggests that North American patients may experience greater toxicity with capecitabine (as well as with other fluoropyrimidines) than European patients, and may require a lower dose of capecitabine.

[b] Initial therapy option for patients with advanced or metastatic disease not appropriate for intensive therapy.

[c] Capecitabine, CapeOX (preferred), Fluorouracil/Leucovorin, and FOLFOX (preferred) are neoadjuvant chemotherapy options (for 2-3 months) and adjuvant chemotherapy options (6 months perioperative treatment) for resectable, metachronous metastases.

[d] Neoadjuvant (2-3 months) with FOLFOX (preferred) or CapeOX (preferred), FOLFIRI, (Category 2B) or FOLFOXIRI (Category 2B) and adjuvant therapy with FOLFOX (preferred, CapeOX (preferred), Capecitabine, or Fluorouracil/Leucovorin (6 months total perioperative treatment preferred) for resectable synchronous liver and/or lung metastases only.

continued

Rectal Cancer Treatment Regimens

[e] Bevacizumab may be safely given at a rate of 0.5mg/kg/min (5mg/kg over 10 minutes and 7.5mg/kg over 15 minutes). An FDA-approved biosimilar is an appropriate substitute for bevacizumab.

[f] FOLFOX and CapeOX are neoadjuvant chemotherapy options (2-3 months) and adjuvant chemotherapy (6 month total perioperative treatment) for treatment of resectable, synchronous liver and/or lung metastases only.

[g] Initial therapy option for patients with advanced or metastatic disease appropriate for intensive therapy.

[h] Oxaliplatin may be given either over 2 hours, or may be infused over a shorter time at a rate of 1mg/m^2/min. Leucovorin infusion should match time of oxaliplatin. (Cercek A, Park V, Yaeger R, et al. Faster FOLFOX: oxaliplatin can be safety infused at a rate of 1mg/m^2/min. *J Oncol Pract*. 2016;12:e548-553.)

[i] Beginning in the evening of day 1 until the morning of day 15 (28 total doses).

[j] Subsequent therapy option for selected patients with advanced or metastatic disease.

[k] Larotrectinib or entrectinib are treatment options for patients with metastatic colorectal cancer that is NTRK gene fusion positive.

[l] Leucovorin 400mg/m^2 is the equivalent of levoleucovorin 200mg/m^2.

[m] Irinotecan 300mg/m^2 is recommended for patients <70 years, prior pelvic irradiation, ECOG performance status or >2.

[n] Regorafenib or trifluridine + tipiracil are treatment options for patients who have progressed through all available regimens.

[o] An FDA-approved biosimilar is an appropriate substitute for tratuzumab

[p] This course may be followed by or preceded and followed by postoperative adjuvant chemotherapy.

[q] Bolus 5-Fluorouracil/RT is an option for patients not able to tolerate capecitabine or infusional 5-Fluorouracil.

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