

COLON CANCER TREATMENT REGIMENS (Part 1 of 5)

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 healthcare 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 only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes 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 National Comprehensive Cancer Network 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.

Advanced or Metastatic Disease¹

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

REGIMEN	DOSING
mFOLFOX6^{2,4}	Day 1: Oxaliplatin 85mg/m ² IV over 2 hours Day 1: Leucovorin 400mg/m ² * IV over 2 hours Days 1-3: 5-FU 400mg/m ² IV bolus 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^{3,5}	Day 1: Oxaliplatin 85mg/m ² IV over 2 hours Day 1: Leucovorin 400mg/m ² * IV over 2 hours Days 1-3: 5-FU 400mg/m ² IV bolus 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.
mFOLFOX6 + Panitumumab^{3,6}	Day 1: Oxaliplatin 85mg/m ² IV over 2 hours Day 1: Leucovorin 400mg/m ² * IV over 2 hours Days 1-3: 5-FU 400mg/m ² IV bolus 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: Panitumumab 6mg/kg IV over 60 minutes. Repeat cycle every 2 weeks.
CapeOX²	Day 1: Oxaliplatin 130mg/m ² IV over 2 hours Days 1-14: Capecitabine 850-1,000mg/m ² twice daily PO. Repeat cycle every 3 weeks.
CapeOX + Bevacizumab^{2,7}	Day 1: Oxaliplatin 130mg/m ² IV over 2 hours Days 1-14: Capecitabine 850-1,000mg/m ² PO twice daily Day 1: Bevacizumab 7.5mg/kg IV. Repeat cycle every 3 weeks.
FOLFIRI⁸	Day 1: Irinotecan 180mg/m ² IV over 30-90 minutes Day 1: Leucovorin 400mg/m ² * IV infusion to match duration of irinotecan infusion Days 1-3: 5-FU 400mg/m ² IV bolus day 1, then 1,200mg/m ² /day × 2 days (total 2,400mg/m ² over 46-48 hours) [†] continuous infusion. Repeat cycle every 2 weeks.
FOLFIRI⁸ + Bevacizumab⁹	Day 1: Irinotecan 180mg/m ² IV over 30-90 minutes Day 1: Leucovorin 400mg/m ² * IV infusion to match duration of irinotecan infusion Days 1-3: 5-FU 400mg/m ² IV bolus 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.
FOLFIRI⁸ + Cetuximab¹¹	Day 1: Irinotecan 180mg/m ² IV over 30-90 minutes Day 1: Leucovorin 400mg/m ² * IV infusion to match duration of irinotecan infusion Days 1-3: 5-FU 400mg/m ² IV bolus day 1, then 1,200mg/m ² /day × 2 days (total 2,400mg/m ² over 46-48 hours) [†] IV continuous infusion, plus Days 1 and 8: Cetuximab 400mg/m ² IV over 2 hours first infusion, then 250mg/m ² IV over 60 minutes. ¹⁰ OR Day 1: Cetuximab 500mg/m ² IV over 2 hours. Repeat cycle every 2 weeks

continued

COLON CANCER TREATMENT REGIMENS (Part 2 of 5)

Advanced or Metastatic Disease (continued)

REGIMEN	DOSING
FOLFIRI⁸ + Panitumumab¹²	Day 1: Irinotecan 180mg/m ² IV over 30–90 minutes Day 1: Leucovorin 400mg/m ² * IV infusion to match duration of irinotecan infusion Days 1–3: 5-FU 400mg/m ² IV bolus day 1, then 1,200mg/m ² /day × 2 days (total 2,400mg/m ² over 46–48 hours) [†] IV continuous infusion Day 1: Panitumumab 6mg/kg IV over 60 minutes. Repeat cycle every 2 weeks.
FOLFIRI + ziv-aflibercept¹³	Day 1: Irinotecan 180mg/m ² IV over 30–90 minutes Day 1: Leucovorin 400mg/m ² * IV infusion to match duration of irinotecan infusion Days 1–3: 5-FU 400mg/m ² IV bolus day 1, then 1,200mg/m ² /day × 2 days (total 2,400mg/m ² over 46–48 hours) [†] continuous infusion Day 1: Ziv-aflibercept 4mg/kg IV over 1 hour. Repeat cycle every 2 weeks.
Capecitabine¹⁴	Days 1–14: 850–1,250mg/m ² PO twice daily. Repeat cycle every 3 weeks.
Capecitabine¹⁴ + Bevacizumab⁷	Days 1–14: Capecitabine 850–1,250mg/m ² PO twice daily Day 1: Bevacizumab 7.5mg/kg IV. Repeat cycle every 3 weeks.
Bolus or infusional 5-FU/leucovorin Roswell Park regimen¹⁵	Days 1, 8, 15, 22, 29, and 36: Leucovorin 500mg/m ² IV over 2 hours Days 1, 8, 15, 22, 29, and 36: 5-FU 500mg/m ² IV bolus 1 hour after start of leucovorin. Repeat cycle every 8 weeks.
Simplified biweekly infusional 5-FU/LV (sLV5FU2)⁸	Day 1: Leucovorin 400mg/m ² * IV over 2 hours Days 1–3: 5-FU bolus 400mg/m ² and then 1,200mg/m ² /day × 2 days (total 2,400mg/m ² over 46–48 hours) [†] continuous infusion. Repeat cycle every 2 weeks.
Weekly infusional LV5FU2^{16, 17}	Day 1: Leucovorin 20mg/m ² IV over 2 hours Day 1: 5-FU 500mg/m ² IV bolus injection 1 hour after the start of leucovorin Day 1: 5-FU 2,600mg/m ² by 24-hour infusion plus leucovorin 500mg/m ² Repeat cycle every week.
IROX¹⁸	Day 1: Oxaliplatin 85mg/m ² IV over 2 hours, followed by irinotecan 200mg/m ² IV over 30 or 90 minutes. Repeat cycle every 3 weeks.
FOLFOXIRI ± bevacizumab^{19, 20}	Day 1: Irinotecan 165mg/m ² IV, plus oxaliplatin 85mg/m ² IV Day 1: Leucovorin 400mg/m ² * Days 1–3: Fluorouracil 1,600mg/m ² /day × 2 days (total 3,200mg/m ² over 48 hours) [†] continuous infusion starting on day 1, ± Day 1: Bevacizumab 5mg/kg IV. Repeat cycle every 2 weeks.
Irinotecan^{21, 22}	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. Repeat cycle every 3 weeks.
Cetuximab (KRAS/NRAS WT gene only) ± irinotecan^{11, 23}	Cetuximab 400mg/m ² first infusion, then 250mg/m ² IV weekly OR cetuximab 500mg/m ² IV every 2 weeks, ± Irinotecan 300–350mg/m ² IV every 3 weeks OR irinotecan 180mg/m ² IV every 2 weeks OR irinotecan 125mg/m ² on days 1 and 8 and repeat every 3 weeks.
Cetuximab (KRAS/NRAS WT gene only)¹¹	Day 1: Cetuximab 400mg/m ² first infusion, then 250mg/m ² IV weekly ²³ OR 500mg/m ² IV over 2 hours. Repeat cycle every 2 weeks.
Panitumumab²⁴ (KRAS/NRAS WT gene only)	Panitumumab 6mg/kg IV over 60 minutes every 2 weeks.
Regorafenib²⁵	Days 1–21: Regorafenib 160mg PO daily. Repeat cycle every 28 days.

continued

COLON CANCER TREATMENT REGIMENS (Part 3 of 5)

Adjuvant Chemotherapy Regimens

Principals of Adjuvant Therapy¹

Capecitabine appears to be equivalent to bolus 5-FU/leucovorin in patients with stage III colon cancer.²⁶

FOLFOX is superior to fluoropyrimidine therapy alone for patients with stage III colon cancer.^{27,28} FOLFOX is reasonable for high-risk or intermediate-risk stage II patients and is not indicated for good- or average-risk patients with stage II colon cancer. FLOX is an alternative to FOLFOX.²⁹

A survival benefit has not been demonstrated for the addition of oxaliplatin to 5-FU/leucovorin in stage II colon cancer.³⁰

A benefit for the addition of oxaliplatin to 5-FU/leucovorin in patients age 70 and older has not been proven.³⁰

Bolus 5-FU/leucovorin/irinotecan should not be used in adjuvant therapy,³¹ and infusional 5-FU/leucovorin/irinotecan (FOLFIRI) has not been shown to be superior to 5-FU/LV.^{32,33} Capecitabine/oxaliplatin is superior to bolus 5-FU/leucovorin.³⁴

Bevacizumab, cetuximab, panitumumab, or irinotecan should not be used in the adjuvant setting for patients with stage II or III colon cancer outside the setting of a clinical trial.

REGIMEN	DOSING
mFOLFOX6 ³⁵⁻³⁷	Day 1: Oxaliplatin 85mg/m ² IV over 2 hours Day 1: Leucovorin 400mg/m ² * IV over 2 hours Days 1-3: 5-FU 400mg/m ² IV bolus on day 1, then 1,200mg/m ² /day × 2 days (total 2,400mg/m ² over 46-48 hours) [†] continuous infusion. Repeat cycle every 2 weeks.
FLOX ³⁸	5-FU 500mg/m ² IV bolus weekly × 6 + leucovorin 500mg/m ² IV weekly × 6, each 8-week cycle × 3 with oxaliplatin 85mg/m ² IV administered on weeks 1, 3, and 5 of each 8-week cycle × 3.
Capecitabine ³⁹	Days 1-14: 1,250mg/m ² twice daily PO. Repeat cycle every 3 weeks for 24 weeks.
CapeOx ⁴⁰	Day 1: Oxaliplatin 130mg/m ² over 2 hours, day 1 Days 1-14: Capecitabine 1,000mg/m ² twice daily PO. Repeat cycle every 3 weeks for 24 weeks.
5-FU/leucovorin ^{41, 42}	Leucovorin 500mg/m ² given as a 2-hour infusion and repeated weekly × 6 weeks, plus 5-FU 500mg/m ² given IV bolus 1 hour after the start of leucovorin and repeated weekly × 6 weeks. Repeat cycle every 8 weeks for 4 cycles. OR Simplified biweekly infusional 5-FU/LV (sLV5FU2) Leucovorin 400mg/m ² * IV over 2 hours on day 1, followed by 5-FU bolus 400mg/m ² and then 1,200mg/m ² /day × 2 days (total 2,400mg/m ² over 46-48 hours) [†] continuous infusion. Repeat cycle every 2 weeks.

* Leucovorin 400mg/m² is the equivalent of levoleucovorin 200mg/m².

† NCCN recommends limiting chemotherapy orders to 24-hour units (i.e., 1,200mg/m²/day NOT 2,400mg/m² over 48 hours) to minimize medication errors.

‡ 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 larger dose of capecitabine. The relative efficacy of CapeOx with lower starting doses of capecitabine has not been addressed in large-scale randomized trials.

References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer V.2.2015. Available at: <http://www.nccn.org>. Accessed October 6, 2014.
2. deGramont A, Figer A, Seymour M, et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced rectal cancer. *J Clin Oncol*. 2000;18:2938-2947.
3. Cheeseman SL, Joel SP, Chester JD, et al. A "modified deGramont" regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer. *Br J Cancer*. 2002;87:393-399. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12177775>.
4. Maindault-Goebel F, deGramont A, Louvet C, et al. Evaluation of oxaliplatin dose intensity in bimonthly leucovorin and 48-hour 5-fluorouracil continuous infusion regimens (FOLFOX) in pretreated metastatic colorectal cancer. *Ann Oncol*. 2000;11:1477-1483.
5. Emmanouilides C, Sfakiotaki G, Androulakis N, et al. Front-line bevacizumab in combination with oxaliplatin, leucovorin and 5-fluorouracil (FOLFOX) in patients with metastatic colorectal cancer: a multicenter phase II study. *BMC Cancer*. 2007;7:91.
6. Douillard JY, Siena S, Cassidy J, et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: the PRIME study. *J Clin Oncol*. 2010;28:4697-4705.

continued

COLON CANCER TREATMENT REGIMENS (Part 4 of 5)

References (continued)

7. Saltz LB, Clarke S, Diaz-Rubio E, et al. Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: a randomized phase III study. *J Clin Oncol*. 2008;26:2013-2019. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18421054>.
8. Andre T, Louvet C, Maindrault-Goebel F, et al. CPT-11 (irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continuous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. *Eur J Cancer*. 1999;35(9):1343-1347.
9. Fuchs CS, Marshall J, Mitchell E, et al. Randomized, controlled trial of irinotecan plus infusional, bolus, or oral fluoropyrimidines in first-line treatment of metastatic colorectal cancer: results from the BICC-C Study. *J Clin Oncol*. 2007;25:4779-4786. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17947725>.
10. Cunningham D, Humblet Y, Siena S, et al. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. *N Engl J Med*. 2004;351:337-345.
11. Martin-Martorell P, Roselló S, Rodríguez-Braun E, et al. Biweekly cetuximab and irinotecan in advanced colorectal cancer patients progressing after at least one previous line of chemotherapy: results of a phase II single institution trial. *Br J Cancer*. 2008;99:455-458.
12. Peeters M, Price TJ, Cervantes A, et al. Randomized phase III study of panitumumab with fluorouracil, leucovorin, and irinotecan (FOLFIRI) compared with FOLFIRI alone as second-line treatment in patients with metastatic colorectal cancer. *J Clin Oncol*. 2010;28:4706-4713. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20921462>.
13. Van Cutsem E, Tabernero J, Lakomy R, et al. Addition of Afibercept to Fluorouracil, Leucovorin, and Irinotecan Improves Survival in a Phase III Randomized Trial in Patients With Metastatic Colorectal Cancer Previously Treated With an Oxaliplatin-Based Regimen. *J Clin Oncol*. 2012;30:3499-3506. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22949147>.
14. Van Cutsem E, Twelves C, Cassidy J, et al. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: results of a large phase III study. *J Clin Oncol*. 2001;19:4097-4106.
15. Wolmark N, Rockette H, Fisher B, et al. The benefit of leucovorin-modulated fluorouracil as postoperative adjuvant therapy for primary colon cancer: results from National Surgical Adjuvant Breast and Bowel Protocol C-03. *J Clin Oncol*. 1993;11:1879-1887.
16. Jäger E, Heike M, Bernhard H, et al. Weekly high-dose leucovorin plus low-dose leucovorin combined with fluorouracil in advanced colorectal cancer: results of a randomized multicenter trial. *J Clin Oncol*. 1996;14:2274-2279.
17. Douillard JY, Cunningham D, Roth AD, et al. Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomized trial. *The Lancet*. 2000;355:1041-1047.
18. Haller DG, Rothenberg ML, Wong AO, et al. Oxaliplatin plus irinotecan compared with irinotecan alone as second-line treatment after single agent fluoropyrimidine therapy for metastatic colorectal carcinoma. *J Clin Oncol*. 2008;26:4544-4550.
19. Falcone A, Ricci S, Brunetti I, et al. Phase III trial of infusional fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFIRI) compared with infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI) as first-line treatment for metastatic colorectal cancer: The Gruppo Oncologico Nord Ovest. *J Clin Oncol*. 2007;25(13):1670-1676.
20. Loupakis F, Cremolini C, Masi G, et al. FOLFIRI plus bevacizumab (bev) versus FOLFIRI plus bev as first-line treatment of metastatic colorectal cancer (MCRC): results of the phase III randomized TRIBE trial. *J Clin Oncol*. 2013;31(Suppl 4) Abstract 336.
21. Cunningham D, Pyrhonen S, James R, et al. Randomized trial of irinotecan plus supportive care versus supportive care alone after fluorouracil failure for patients with metastatic colorectal cancer. *The Lancet*. 1998;352:1413-1418.
22. Fuchs CS, Moore MR, Harker G, et al. Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer. *J Clin Oncol*. 2003;21:807-814.
23. Van Cutsem E, Tejpar S, Vanbeckevoort D, et al. Inpatient Cetuximab Dose Escalation in Metastatic Colorectal Cancer According to the Grade of Early Skin Reactions: The Randomized EVEREST Study. *J Clin Oncol*. 2012;30:2861-2868. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22753904>.
24. Van Cutsem E, Peeters M, Siena S, et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. *J Clin Oncol*. 2007;25:1658-1664.
25. Grothey A, Van Cutsem E, Sobrero A, et al. Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): an international, multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet*. 2013;381:303-312. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23177514>.
26. Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. *N Engl J Med*. 2005;352(26):2696-2704.
27. Andre T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. *N Engl J Med*. 2004;350:2343-2351.
28. Andre T, Boni C, Navarro M, et al. Improved overall survival with oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment in stage II or III colon cancer in the MOSAIC trial. *J Clin Oncol*. 2009;27:3109-3116 [Epub 2009 May 18].
29. Kuebler JP, Wiewand HS, O'Connell MJ, et al. Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07. *J Clin Oncol*. 2007;25:2198-2204.
30. Tournigand C, André T, Bonnetain F, et al. Adjuvant therapy with fluorouracil and oxaliplatin in stage II and elderly (between ages 70 and 75 years) with colon cancer: a subgroup analyses of the Multicenter International Study of oxaliplatin, fluorouracil, and leucovorin in the adjuvant treatment of colon cancer trial. *J Clin Oncol*. August 20, 2012 [Epub ahead of print].
31. Saltz LB, Niedzwiecki D, Hollis D, et al. Irinotecan fluorouracil plus leucovorin is not superior to fluorouracil plus leucovorin alone as adjuvant treatment for stage III colon cancer: results of CALGB C89803. *J Clin Oncol*. 2007;25:3546-3561.
32. Van Cutsem E, Labianca R, Bodoky G, et al. Randomized phase III trial comparing biweekly infusional fluorouracil/leucovorin alone or with irinotecan in the adjuvant treatment of stage III colon cancer: PETACC-3. *J Clin Oncol*. 2009;27:3117-3125. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19451425>.
33. Ychou M, Raoul JL, Douillard JY, et al. A phase III randomized trial of LV5FU2 + irinotecan versus LV5FU2 alone in adjuvant high-risk colon cancer (FNCLCC Accord02/FFCD9802). *Ann Oncol*. 2009;20:674-80 [Epub 2009 Jan 29].
34. Haller DG, Tabernero J, Maroun J, et al. Capecitabine plus oxaliplatin compared with fluorouracil and folinic acid as adjuvant therapy for stage III colon cancer. *J Clin Oncol*. 2011;29:1465-1471.
35. Andre T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. *N Engl J Med*. 2004;350:2343-2351.

continued

COLON CANCER TREATMENT REGIMENS (Part 5 of 5)

References (continued)

36. Cheeseman SL, Joel SP, Chester JD, et al. A "modified deGramont" regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer. *Br J Cancer*. 2002;87:393-399. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12177775>.
37. Maindrault-Goebel F, deGramont A, Louvet C, et al. Evaluation of oxaliplatin dose intensity in bimonthly leucovorin and 48-hour 5-fluorouracil continuous infusion regimens (FOLFOX) in pretreated metastatic colorectal cancer. *Annals of Oncology*. 2000;11:1477-1483.
38. Kuebler JP, Wieand HS, O'Connell MJ, et al. Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07. *J Clin Oncol*. 2007;25:2198-2204.
39. Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. *N Eng J Med*. 2005;352:2696-2704.
40. Schmoll HJ, Cartwright T, Tabernero J, et al. Phase III trial of capecitabine plus oxaliplatin as adjuvant therapy for stage III colon cancer: a planned safety analysis in 1,864 patients. *J Clin Oncol*. 2007;25:102-109. Hailer DG, Tabernero J, Maroun J, et al. Capecitabine Plus Oxaliplatin Compared With Fluorouracil and Folinic Acid As Adjuvant Therapy for Stage III Colon Cancer. *J Clin Oncol* 2011;29:1465-1471. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21383294>.
41. Haller DG, Catalano PJ, Macdonald JS, Mayer RJ. Phase III study of fluorouracil, leucovorin and levamisole in high risk stage II and III colon cancer: final report of Intergroup 0089. *J Clin Oncol*. 2005;23:8671-8678.
42. Andre T, Louvet C, Maindrault-Goebel F, et al. CPT-11 (irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continuous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. *Eur J Cancer*. 1999;35(9):1343-1347.

(Revised 10/2014)

© 2014 Haymarket Media, Inc.