

5-FLUOROURACIL – LEUCOVORIN (“ROSWELL PARK” REGIMEN)

Leucovorin	500 mg/m ²	IV*	Days 1, 8, 15, 22, 29 and 36
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One hour after starting the leucovorin administer

5-Fluorouracil	500 mg/m ²	IVB	Days 1, 8, 15, 22, 29 and 36
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*Administer over 2 hours.

Repeat cycle every 8 weeks for a total of 4 cycles for adjuvant therapy of colon cancer.

References: [Buroker TR, et al. J Clin Oncol 1994;12:14 – 20](#); [Haller DG, et al. J Clin Oncol 2005;23:8671 – 8](#).

5-FLUOROURACIL – LEUCOVORIN (“MAYO CLINIC” REGIMEN)

Leucovorin	20 mg/m ² /day	IVB*	Days 1 – 5
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Followed immediately by

5-Fluorouracil	425 mg/m ² /day	IVB*	Days 1 – 5
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*Both drugs administered by IV bolus daily.

Repeat courses at weeks 4 and 8, and then every 5 weeks thereafter for a total of 6 cycles for the adjuvant treatment of colon cancer.

References: [Buroker TR, et al. J Clin Oncol 1994;12:14 – 20](#); [Haller DG, et al. J Clin Oncol 2005;23:8671 – 8](#).

5-FLUOROURACIL – LEUCOVORIN – BEVACIZUMAB

Leucovorin	500 mg/m ²	IV*	Days 1, 8, 15, 22, 29 and 36
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One hour after starting the leucovorin administer

5-Fluorouracil	600 mg/m ²	IVB	Days 1, 8, 15, 22, 29 and 36
Bevacizumab	5 mg/kg	IV	Day 1, then repeated every 2 weeks thereafter

*Administer over 2 hours.

Repeat cycle every 8 weeks for up to 96 weeks.

References: [Kabbinavar FF, et al. J Clin Oncol 2005;23:3697 – 705](#); [Kabbinavar FF, et al. J Clin Oncol 2005;23:3706 – 12](#).

FLOX (5-FLUOROURACIL – LEUCOVORIN – OXALIPLATIN)

Leucovorin	500 mg/m ²	IV*	Days 1, 8, 15, 22, 29 and 36
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One hour after starting the leucovorin administer

5-Fluorouracil	500 mg/m ²	IVB	Days 1, 8, 15, 22, 29 and 36
Oxaliplatin	85 mg/m ²	IV*	Day 1, 15 and 29

*Administer over 2 hours.

Repeat cycle every 8 weeks for a total of 3 cycles for adjuvant therapy of colon cancer.

Reference: [Kuebler JP, et al. / J Clin Oncol 2007;25:2198 – 204.](#)**FOLFIRI (IRINOTECAN – LEUCOVORIN – 5-FLUOROURACIL)**

Irinotecan	180 mg/m ²	IV*	Day 1
Leucovorin	400 mg/m ²	IV*	Day 1

Followed by

5-Fluorouracil	400 mg/m ²	IVB**	Day 1
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Followed by

5-Fluorouracil	2400–3000 mg/m ²	CIVI#	Day 1
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*On Day 1, irinotecan and leucovorin are given at the same time in different bags using a Y-connector administered over 2 hours in D₅W; **Administer as an IV bolus over 2 – 4 minutes; #5-Fluorouracil 2400 mg/m² administered for 2 cycles and then increased to 3000 mg/m² from cycle 3 onwards in cases of no toxicity greater than Grade 1 during the first 2 cycles. 5-Fluorouracil administered as a continuous infusion over 46 hours.

Repeat cycle every 14 days.

Reference: [Tournigand C, et al. / J Clin Oncol 2004;22:229 – 37.](#)

FOLFOX 4 (OXALIPLATIN – 5-FLUOROURACIL – LEUCOVORIN)

Oxaliplatin	85 mg/m ²	IV*	Day 1
Leucovorin	200 mg/m ² /day	IV*	Days 1 and 2

Followed by

5-Fluorouracil	400 mg/m ² /day	IVB**	Days 1 and 2
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Followed by

5-Fluorouracil	600 mg/m ² /day	CIVI#	Days 1 and 2
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*On Day 1 oxaliplatin and leucovorin are given at the same time in different bags using a Y-line over 2 hours in D₅W; **Administer as an IV bolus over 2 – 4 minutes; #Administer as a continuous IV infusion over 22 hours.

Repeat cycle every 14 days. A total of 12 cycles administered for adjuvant treatment of colon cancer beginning within 7 weeks after surgery.

References: [Rothenberg ML, et al. *J Clin Oncol* 2003;21:2059 – 69](#); [de Gramont A, et al. *J Clin Oncol* 2000;18:2938 – 47](#); [Goldberg RM, et al. *J Clin Oncol* 2004;22:23 – 30](#). Adjuvant: [Andre T, et al. *N Engl J Med* 2004;350:2343 – 51](#).

FOLFOX 4 – BEVACIZUMAB (OXALIPLATIN– 5-FLUOROURACIL – LEUCOVORIN – BEVACIZUMAB) – METASTATIC ONLY

Bevacizumab	10 mg/kg ^ψ	IV	Day 1
Oxaliplatin	85 mg/m ²	IV*	Day 1
Leucovorin	200 mg/m ² /day	IV*	Days 1 and 2

Followed by

5-Fluorouracil	400 mg/m ² /day	IVB**	Days 1 and 2
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Followed by

5-Fluorouracil	600 mg/m ² /day	CIVI#	Days 1 and 2
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^ψClinical data supports a dose of 5 mg/kg [Reference: [Kabbinavar F, et al. *J Clin Oncol* 2003;21:60 – 5](#)]; *On Day 1 – oxaliplatin and leucovorin are given at the same time in different bags using a Y-line over 2 hours in D₅W; **Administer as an IV bolus over 2 – 4 minutes; #Administer as a CIVI over 22 hours.

Repeat cycle every 14 days.

Reference: [Giantonio BJ, et al. *J Clin Oncol* 2007;25:1539 – 44](#).

FOLFOX 6 (OXALIPLATIN – 5-FLUOROURACIL – LEUCOVORIN)

Oxaliplatin [‡]	100 mg/m ²	IV*	Day 1
Leucovorin [‡]	400 mg/m ²	IV*	Day 1

Followed by

5-Fluorouracil	400 mg/m ²	IVB**	Day 1
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Followed by

5-Fluorouracil	2400–3000 mg/m ²	CIVI #	Day 1
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*On Day 1 – oxaliplatin and leucovorin are given at the same time in different bags using a Y-line over 2 hours in D₅W; **Administer as an IV bolus over 2 – 4 minutes; #Administer as a continuous infusion over 46 hours. 5-Fluorouracil 2400 mg/m² given for 2 cycles and then increased to 3000 mg/m² from cycle 3 onwards in cases of no toxicity greater than Grade 1 during first 2 cycles.

Repeat cycle every 14 days.

NOTE: The modified FOLFOX 6 uses a dose of oxaliplatin of 85 mg/m².

References: [Tournigand C, et al. *J Clin Oncol* 2004;22:229 – 37](#); [Maindrault-Goebel F, et al. *Eur J Cancer* 1999;35:1338 – 42](#)

FOLFOX 7 (OXALIPLATIN – 5-FLUOROURACIL – LEUCOVORIN)

Oxaliplatin	130 mg/m ² *	IV*	Day 1
Leucovorin	400 mg/m ² *	IV*	Day 1

Followed by

5-Fluorouracil	400 mg/m ²	IVB**	Day 1
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Followed by

5-Fluorouracil	2400 mg/m ²	CIVI#	Day 1
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*On Day 1 – oxaliplatin and leucovorin are given at the same time in different bags using a Y-line over 2 hours in D₅W; **Administer as an IV bolus over 2 – 4 minutes; #Administer as a CIVI over 46 hours.

Repeat cycle every 14 days (for up to 8 cycles for patients who responded or were stable).

NOTE: Cycle 2 was administered at week 3, but all subsequent cycles are administered every 2 weeks.

DOSE MODIFICATION: The 5-Fluorouracil dose was reduced to 2000 mg/m² CIVI for any grade 3 or 4 stomatitis, diarrhea, neutropenia, thrombocytopenia, or skin toxicity or other grade 3 major organ drug-related toxicity. The oxaliplatin dose was reduced to 100 mg/m²/cycle for any grade 3 or 4 neutropenia or thrombocytopenia, grade 3 diarrhea or stomatitis, any other grade 3 major organ drug-related toxicity, or paresthesia associated with pain. Oxaliplatin was stopped until symptom improvement in case of persistent paresthesia associated with pain or functional impairment persisting between cycles.

References: [Maindrault-Goebel F, et al. *Eur J Cancer* 2001;37:1000 – 5](#); [Tournigand C, et al. *J Clin Oncol* 2006;24:394 – 400](#).

FOLFOXIRI (IRINOTECAN – OXALIPLATIN – LEUCOVORIN – 5-FLUOROURACIL)

Irinotecan	165 mg/m ²	IV*	Day 1
Oxaliplatin	85 mg/m ²	IV**	Day 1
Leucovorin	200 mg/m ²	IV**	Day 1
5-Fluorouracil	3200 mg/m ²	CIVI#	Days 1 and 2

*Administer over 1 hour; **Administer over 2 hours; #Administer as a continuous IV infusion over 48 hours.

Repeat cycle every 14 days until evidence of disease progression, unacceptable toxicity, patient refusal, or for a maximum of 12 cycles.

Reference: [Falcone A, et al. J Clin Oncol 2007;25:1670 – 6.](#)

IFL (IRINOTECAN – 5-FLUOROURACIL – LEUCOVORIN)

Irinotecan	125 mg/m ²	IV*	Days 1, 8, 15 and 22
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Followed by

Leucovorin	20 mg/m ²	IVB**	Days 1, 8, 15 and 22
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Followed by

5-Fluorouracil	500 mg/m ²	IVB**	Days 1, 8, 15 and 22
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*Administer over 90 minutes; **Administer as an IV bolus over 2 – 5 minutes.

Repeat cycle every 6 weeks (i.e., 2 weeks rest between cycles).

References: [Saltz LB, et al. N Engl J Med 2000;343:905 – 14;](#) [Goldberg RM, et al. J Clin Oncol 2004;22:23 – 30.](#)

IFL – BEVACIZUMAB (IRINOTECAN – 5-FLUOROURACIL – LEUCOVORIN – BEVACIZUMAB)

Bevacizumab	5 mg/kg	IV	Days 1, 15 and 29
Irinotecan	125 mg/m ²	IV*	Days 1, 8, 15 and 22

Followed by

Leucovorin	20 mg/m ²	IVB**	Days 1, 8, 15 and 22
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Followed by

5-Fluorouracil	500 mg/m ²	IVB**	Days 1, 8, 15 and 22
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*Administer over 90 minutes; **Administer as an IV bolus over 2 – 5 minutes.

Repeat cycle every 6 weeks.

Reference: [Hurwitz H, et al. N Engl J Med 2004;350:2335 – 42.](#)

IRINOTECAN MONOTHERAPY (EVERY 3 WEEKS)

Irinotecan	350 mg/m ²	IV*	Day 1
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*Administer over 30 minutes.

Repeat cycle every 21 days. Disease assessment after 3 cycles. Responders or SD after 3 cycles, continued treatment for 6 or more cycles.

NOTE: Data supports dose reduction to 300 mg/m² for prior pelvic or abdominal radiation or in patients aged greater than 65 years.

Reference: [Rougier P, et al. *J Clin Oncol* 1997;15:251 – 60.](#)

IRINOTECAN MONOTHERAPY (WEEKLY)

Irinotecan	125 mg/m ²	IV*	Days 1, 8, 15 and 22
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*Administer over 90 minutes.

Repeat cycle every 6 weeks (i.e., 2 week rest period between cycles).

Reference: [Saltz LB, et al. *N Engl J Med* 2000;343:905 – 14.](#)

PANITUMUMAB

Panitumumab	6 mg/kg	IV*	Every 2 weeks
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*Administer dose over 60 minutes. For doses greater than 1000 mg administer the dose over 90 minutes.

Administer until disease progression or unacceptable toxicity.

References: Amgen Package Insert, October 2006; [Van Cutsem E, et al. *J Clin Oncol* 2007;25:1658 – 64.](#)

XELIRI (CAPECITABINE – IRINOTECAN)

Capecitabine	1000 mg/m ² BID#	PO	Days 1 – 14*
Irinotecan	240 – 250 mg/m ² #	IV**	Day 1

#All doses were reduced by 25% if moderate renal impairment was present and/or if the patient was aged 65 years of older (i.e., capecitabine to 750 mg/m² PO BID and irinotecan to 200 mg/m²); *Start in the PM of Day 1 and continue through the AM of Day 15; **Administered over 90 minutes.

NOTE: Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

Repeat cycle every 21 days.

References: [Cartwright TH, et al. *ASCO GI Symposium 2004*:\[abstract 271\];](#) [Patt YZ, et al. *ASCO GI Symposium 2004*:\[abstract 228\];](#) [Park SH, et al. *Oncology* 2004;66:353 – 7.](#)

XELOX (CAPECITABINE – OXALIPLATIN)

Capecitabine	850 – 1000 mg/m ² BID	PO*	Days 1 – 14
Oxaliplatin	130 mg/m ²	IV	Day 1

*First dose day 1 in the evening, last dose Day 15 in the morning. The capecitabine dose was reduced to 75% of the standard starting dose in patients with moderate renal impairment (CrCL less than 50 mL/minute).

NOTE: Capecitabine dose should be rounded to nearest 150 mg or 500 mg tablet size.

Repeat cycle every 21 days.

References: [Schmoll HJ, et al. / Clin Oncol 2007;25:102 – 9](#); [Hochster HS, et al. ASCO GI Symposium 2005;\[Abstract 241\]](#).

XELOX (CAPECITABINE – OXALIPLATIN) – ELDERLY (≥ 70 YEARS)

Capecitabine	1000 mg/m ² BID	PO*	Days 2 – 15
Oxaliplatin	85 – 130 mg/m ² **	IV***	Day 1

*Administered at 12 hourly intervals, within 30 minutes of breakfast and the evening meal; **The initial study protocol called for dose escalation of capecitabine and oxaliplatin according to toxicity reported in the prior cycle – an interim analysis demonstrated greater than expected toxicity, so the protocol was amended to include only dose escalation of the oxaliplatin. If there were no Grade 2 or greater toxicities the dose of oxaliplatin was increased to 110 mg/m² in the second cycle and then to 130 mg/m² in the third cycle; ***Administer over 2 hours diluted in D₅W.

NOTE: Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

Repeat cycle every 21 days for a maximum of nine cycles.

Reference: [Comella P, et al. Cancer 2005;104:282 – 9](#).

XELOX – BEVACIZUMAB (CAPECITABINE – OXALIPLATIN – BEVACIZUMAB)

Capecitabine	850–1000 mg/m ² BID	PO	Days 1 – 14
Oxaliplatin	130 mg/m ²	IV	Day 1
Bevacizumab	7.5 mg/kg	IV	Day 1
		<i>OR</i>	
Bevacizumab	5 mg/kg	IV	Days 1 and 14

Repeat cycle every 21 days.

NOTE: Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

Reference: [Hochster HS, et al. Proc Am Soc Clin Oncol 2006;24\(18S\):146s: \[Abstract 3510\]](#).

RECTAL CANCER

CAPECITABINE – OXALIPLATIN (NEOADJUVANT)

Neoadjuvant chemotherapy:

Capecitabine	1000 mg/m ² BID	PO	Days 1 – 14
Oxaliplatin	130 mg/m ²	IV	Day 1

Repeat cycle every 21 days for 4 cycles.

Chemoradiotherapy:

Radiation Upon completion of neoadjuvant chemotherapy, radiation was delivered by a 2-phase technique. Phase 1 consisted of 45 Gy in 25 daily fractions (encompassing the primary tumor and the pelvic lymph nodes). Phase 2 involved the administration of 9 Gy in 5 fractions covering the tumor, either clinically palpable or visible on imaging with a 2cm margin in all directions.

	<i>Concurrent with</i>		
Capecitabine	825 mg/m ² BID*	PO	Twice daily without interruption during radiation

*If patients had a dose reduction of capecitabine during neoadjuvant therapy, then a proportional dose reduction should be made during the chemoradiotherapy component of the regimen.

Surgery:

Total mesorectal excision (TME) was performed 6 weeks after completion of chemoradiotherapy.

Postoperative adjuvant chemotherapy – following recovery from surgery initiate:

Capecitabine	1250 mg/m ² BID	PO	Days 1 – 14
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Repeat post-operative cycle every 21 days for a total of 4 cycles.

Reference: [Chau I, et al. J Clin Oncol 2006;24:668 – 74.](#)

5-FLUOROURACIL – RADIATION THERAPY (NEOADJUVANT)

Chemoradiotherapy:

Radiation	50.4 Gy delivered (as at least 6-MV photons) in 28 fractions of 1.8 Gy five times a week to the pelvis with individually shaped portals and the use of a three-field or four-field box technique.		
5-Fluorouracil	1000 mg/m ² /day	CIVI*	Days 1 – 5 during the 1 st and 5 th week of radiation therapy

Surgery Performed 6 weeks after completion of chemoradiotherapy

One month following surgery:

5-Fluorouracil	500 mg/m ² /day	IVB	Days 1 – 5
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Repeat cycle every 28 days for 4 cycles.

*Administer as a continuous 120 hour infusion.

Reference: [Sauer R, et al. N Engl J Med 2004;351:1731 – 40.](#)

5-FLUOROURACIL – LEUCOVORIN – RADIATION (ADJUVANT)

Chemotherapy to start between 21 and 42 days following definitive surgery:

Leucovorin	500 mg/m ²	IV*	Days 1, 8, 15, 22, 29 and 36
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Followed 1 hour after the start of the leucovorin infusion by

5-Fluorouracil Radiation therapy	500 mg/m ² Initiate 3 – 5 weeks following completion of cycle 1 of chemotherapy. The total radiation dose administered was 45 Gy in 25 fractions at 1.8 Gy per day. All fields were treated daily, 5 days per week. The boost volume was treated to a dose of 5.4 Gy in three fractions of 1.8 Gy per day.	IV**	Days 1, 8, 15, 22, 29 and 36
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*Administer over 2 hours; **Administer as an IV bolus.

Repeat systemic chemotherapy cycles every 8 weeks for a total of 6 cycles.

Reference: [Wolmark N, et al. J Natl Cancer Inst 2000;92:388 – 96.](#)

5-FLUOROURACIL – RADIATION (ADJUVANT)

5-Fluorouracil	500 mg/m ² /day	IV*	Days 1 – 5 and 36 – 40
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Followed by

Radiation	To start on Day 64. Radiation via 3 or 4 field technique at 1.8 Gy/fraction/day on Monday to Friday to 45 Gy total over approximately 5 weeks with additional 5.4 Gy ± 3.6 Gy boost
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With concurrent

5-Fluorouracil	225 mg/m ² /day	CIVI	During entire radiation course
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Followed by

5-Fluorouracil	450 mg/m ² /day	IV*	Days 134– 138 and 169 – 173
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*Administer as an IV bolus over 3 – 5 minutes.

Reference: [O'Connell MJ, et al. N Engl J Med 1994;331:502 – 7.](#)