COLORECTAL CANCER

CAPECITABINE
Capecitabine 1250 mg/m²* BID PO Days 1 – 14

*Total daily dose is 2500 mg/m², divided into 1250 mg/m² BID.

NOTE: Dose rounded to nearest 150 mg or 500 mg tablet size. Patient to take medication within 30 minutes of ingestion of food.

Repeat cycle every 21 days until disease progression/unacceptable toxicity. For adjuvant treatment continue for 24 weeks only.


CETUXIMAB
Cetuximab* 400 mg/m² IV* Day 1, Week 1

Followed by
Cetuximab* 250 mg/m² IV** Weekly, starting Day 1, Week 2

*Routine premedication given, at least prior to the first dose; ¯Loading dose administered over 2 hours (per package insert); **Administer over 1 hour.

NOTE: EGFR status of tumor must be verified.


CETUXIMAB – IRINOTECAN
Cetuximab* 400 mg/m² IV* Day 1

Followed by
Cetuximab* 250 mg/m² IV** Weekly, starting Day 1, Week 2

In addition to ONE of the following

Irinotecan (weekly)*; Irinotecan (Q3W)*; IFL*; FOLFIRI*

*Appropriate premedication given, at least prior to the first infusion; ¯Loading dose administered over 2 hours (per package insert); **Administer over 1 hour.

NOTE: EGFR status of tumor must be verified.

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

Leucovorin 500 mg/m² IV Days 1, 8, 15, 22, 29 and 36

*Administer over 2 hours.

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


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

Leucovorin 20 mg/m²/day IVB Days 1 – 5

Followed immediately by

5-Fluorouracil 425 mg/m²/day IVB Days 1 – 5

*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.


5-FLUOROURACIL – LEUCOVORIN – BEVACIZUMAB

Leucovorin 500 mg/m² IV Days 1, 8, 15, 22, 29 and 36

One hour after starting the leucovorin administer

5-Fluorouracil 600 mg/m² 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.

**FLOX (5-FLUOROURACIL – LEUCOVORIN – OXALIPLATIN)**

Leucovorin  
500 mg/m²  
IV  
Days 1, 8, 15, 22, 29 and 36

*One hour after starting the leucovorin administer*

5-Fluorouracil  
500 mg/m²  
IVB  
Days 1, 8, 15, 22, 29 and 36

Oxaliplatin  
85 mg/m²  
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:  

**FOLFIRI (IRINOTECAN – LEUCOVORIN – 5-FLUOROURACIL)**

Irinotecan  
180 mg/m²  
IV*  
Day 1

Leucovorin  
400 mg/m²  
IV*  
Day 1

Followed by

5-Fluorouracil  
400 mg/m²  
IVB**  
Day 1

Followed by

5-Fluorouracil  
2400–3000 mg/m²  
CIVI#  
Day 1

*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:  
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

Followed by

5-Fluorouracil 600 mg/m^2/day CIVI # Days 1 and 2

*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.


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

Followed by

5-Fluorouracil 600 mg/m^2/day CIVI # Days 1 and 2

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.

FOLFOX 6 (OXALIPLATIN – 5-FLUOROURACIL – LEUCOVORIN)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxaliplatin</td>
<td>100 mg/m²</td>
<td>IV*</td>
<td>Day 1</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>400 mg/m²</td>
<td>IV*</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

Followed by

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>400 mg/m²</td>
<td>IVB**</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

Followed by

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>2400-3000 mg/m²</td>
<td>CIVI #</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

*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.


FOLFOX 7 (OXALIPLATIN – 5-FLUOROURACIL – LEUCOVORIN)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxaliplatin</td>
<td>130 mg/m²²</td>
<td>IV*</td>
<td>Day 1</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>400 mg/m²²</td>
<td>IV*</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

Followed by

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>400 mg/m²</td>
<td>IVB**</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

Followed by

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>2400 mg/m²</td>
<td>CIVI #</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

*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.

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irinotecan</td>
<td>165 mg/m²</td>
<td>IV*</td>
<td>Day 1</td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>85 mg/m²</td>
<td>IV**</td>
<td>Day 1</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>200 mg/m²</td>
<td>IV**</td>
<td>Day 1</td>
</tr>
<tr>
<td>5-Fluorouracil</td>
<td>3200 mg/m²</td>
<td>CIVI#</td>
<td>Days 1 and 2</td>
</tr>
</tbody>
</table>

*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.


IFL (IRINOTECAN – 5–FLUOROURACIL – LEUCOVORIN)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irinotecan</td>
<td>125 mg/m²</td>
<td>IV*</td>
<td>1, 8, 15, 22</td>
</tr>
<tr>
<td>Followed by</td>
<td>Leucovorin</td>
<td>20 mg/m²</td>
<td>IVB**</td>
</tr>
<tr>
<td>Followed by</td>
<td>5-Fluorouracil</td>
<td>500 mg/m²</td>
<td>IVB**</td>
</tr>
</tbody>
</table>

*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).


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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab</td>
<td>5 mg/kg</td>
<td>IV</td>
<td>1, 15, 29</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>125 mg/m²</td>
<td>IV*</td>
<td>1, 8, 15, 22</td>
</tr>
<tr>
<td>Followed by</td>
<td>Leucovorin</td>
<td>20 mg/m²</td>
<td>IVB**</td>
</tr>
<tr>
<td>Followed by</td>
<td>5-Fluorouracil</td>
<td>500 mg/m²</td>
<td>IVB**</td>
</tr>
</tbody>
</table>

*Administer over 90 minutes; **Administer as an IV bolus over 2 – 5 minutes.

Repeat cycle every 6 weeks.

**IRINOTECAN MONOTHERAPY (EVERY 3 WEEKS)**

Irinotecan  350 mg/m²  IV  Day 1

*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.


**IRINOTECAN MONOTHERAPY (WEEKLY)**

Irinotecan  125 mg/m²  IV  Days 1, 8, 15 and 22

*Administer over 90 minutes.

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


**PANITUMUMAB**

Panitumumab  6 mg/kg  IV  Every 2 weeks

*Administer dose over 60 minutes. For doses greater than 1000 mg administer the dose over 90 minutes.

Administer until disease progression or unacceptable toxicity.


**XELIRI (CAPECITABINE – IRINOTECAN)**

Capecitabine  1000 mg/m² BID  PO  Days 1 – 14
Irinotecan  240 –250 mg/m²  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.

**XELOX (CAPECITABINE – OXALIPLATIN)**

Capecitabine  
850 – 1000 mg/m² BID PO*  Days 1 – 14

Oxaliplatin  
130 mg/m² 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:  

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

Capecitabine  
1000 mg/m² BID PO*  Days 2 – 15

Oxaliplatin  
85 – 130 mg/m²** 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:  

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**XELOX – BEVACIZUMAB (CAPECITABINE – OXALIPLATIN – BEVACIZUMAB)**

Capecitabine  
850–1000 mg/m² BID PO  Days 1 – 14

Oxaliplatin  
130 mg/m² IV  Day 1

Bevacizumab  
7.5 mg/kg IV  Day 1

OR

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:  
RECTAL CANCER

**CAPECITABINE – OXALIPLATIN (NEOADJUVANT)**

Neoadjuvant chemotherapy:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine</td>
<td>1000 mg/m² BID PO</td>
<td></td>
<td>1 – 14</td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>130 mg/m² IV</td>
<td></td>
<td>Day 1</td>
</tr>
</tbody>
</table>

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.

Concurrent with Capecitabine

825 mg/m² 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:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine</td>
<td>1250 mg/m² BID PO</td>
<td></td>
<td>1 – 14</td>
</tr>
</tbody>
</table>

Repeat post-operative cycle every 21 days for a total of 4 cycles.


**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/m²/day CIVI* Days 1 – 5 during the 1st and 5th week of radiation therapy

Surgery: Performed 6 weeks after completion of chemoradiotherapy

One month following surgery:

5-Fluorouracil 500 mg/m²/day IVB Days 1 – 5

Repeat cycle every 28 days for 4 cycles.

*Administer as a continuous 120 hour infusion.

**5-FLUOROURACIL – LEUCOVORIN – RADIATION (ADJUVANT)**

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin</td>
<td>500 mg/m²</td>
<td>IV*</td>
<td>1, 8, 15, 22, 29, 36</td>
</tr>
<tr>
<td>5-Fluorouracil</td>
<td>500 mg/m²</td>
<td>IV**</td>
<td>1, 8, 15, 22, 29, 36</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td></td>
<td></td>
<td>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.</td>
</tr>
</tbody>
</table>

*Administer over 2 hours; **Administer as an IV bolus.

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


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**5-FLUOROURACIL – RADIATION (ADJUVANT)**

5-Fluorouracil 500 mg/m²/day IV* Days 1 – 5 and 36 – 40

*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

*With concurrent*

5-Fluorouracil 225 mg/m²/day CIVI During entire radiation course

*Followed by*

5-Fluorouracil 450 mg/m²/day IV* Days 134 – 138 and 169 – 173

*Administer as an IV bolus over 3 – 5 minutes.