

《大腸直腸癌抗癌藥物治療指引》

115 年版與上一版差異

114 年版 修訂日 113/12/18	115 年版 修訂日 114/12/03
Adjuvant Therapy of Colon Cancer	Adjuvant Therapy of Colon Cancer ◎ 增加 • Atezolizumab + FOLFOX • Atezolizumab + CapeOx
	Total Neoadjuvant Therapy of Rectal Cancer ◎ 增加 • XRT + 5-FU • XRT + 5-FU/LV • XRT + Capecitabine • FOLFOX • CapeOx/Xelox

《大腸直腸癌抗癌藥物治療指引》

Adjuvant Therapy of Colon Cancer

* Infusional 5-FU may be administrated with Infusor (輸液器 / 奶瓶): 2400 mg/m² over 46 hrs on d1

mFOLFOX6

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	12	1-3
Leucovorin	400	≥ 90 mins	d1	Q2W	12	
5-FU	400	5 mins	d1	Q2W	12	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	12	

FOLFOX4

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	12	8
Leucovorin	200	≥ 90 mins	d1, 2	Q2W	12	
5-FU	400	5 mins	d1, 2	Q2W	12	
5-FU	600 [#]	22-24 hrs [#]	d1-2 [#]	Q2W	12	

[#] may be administrated with Infusor(輸液器 / 奶瓶): 1200 mg/m² over 46 hrs on d1

FOLFOX7

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W		11
Leucovorin	400	≥ 90 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

Capecitabine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Capecitabine	1250 PO BID	d1-14	Q3W	8	4

CapeOx/Xelox

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	2 hrs	d1	Q3W	8 [#]	5, 13
Capecitabine	1000 PO BID		d1-14	Q3W	8 [#]	

[#]4 cycles for low-risk patients

5-FU+LV

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Leucovorin	500	≥ 90 mins	d1, 8, 15, 22, 29, 36	Q8W	4	6
5-FU	500	1 hr	d1, 8, 15, 22, 29, 36	Q8W	4	

sLV5FU2

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Leucovorin	400	≥ 90 mins	d1	Q2W	12	7
5-FU	400	5 min	d1	Q2W	12	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	12	

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
TS-1	40 PO BID	d1-28	Q6W	4	10

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
UFUR	300-350/day PO	d1-28	Q4W	6	9
± Leucovorin	50-150 mg PO QD	d1-28	Q4W	6	

Atezolizumab + FOLFOX (dMMR)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Atezolizumab	840 mg	60 → 30 mins	d1	Q2W	25	12
Oxaliplatin	85	2 hrs	d1	Q2W	12	
Leucovorin	400	≥ 90 mins	d1	Q2W	12	
5-FU	400	5 mins	d1	Q2W	12	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	12	

Atezolizumab + CapeOx/Xelox (dMMR)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Atezolizumab	1200 mg	60 → 30 mins	d1	Q3W	16	12
Oxaliplatin	130	2 hrs	d1	Q3W	8	
Capecitabine	1000 PO BID		d1-14	Q3W	8	

Neoadjuvant Therapy of Colon Cancer

同 1st line therapy of metastatic colon cancer

參考文獻

1. 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.
2. Cheeseman SL, Joel SP, Chester JD, et al. A 'modified de Gramont' regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer. *Br J Cancer* 2002;87:393-399.
3. 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.
4. Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. *N Engl J Med* 2005;352:2696-2704.
5. Schmoll HJ, Cartwright T, Taerner 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.
6. Haller DG, Catalano P, 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.
7. 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):1343-7.
8. deGramont A, Figuer A, Seymour M, et al. Leucovorin and Fluorouracil With or Without Oxaliplatin as First-Line Treatment in Advanced Colorectal Cancer. *J Clin Oncol* 2000;18:2938-2947.
9. Sulkes A, Benner SE, Canetta RM. Uracil-ftorafur: an oral fluoropyrimidine active in colorectal cancer. *J Clin Oncol*. Oct 1998;16(10):3461-3475.
10. Hamaguchi, Tetsuya et al. Capecitabine versus S-1 as adjuvant chemotherapy for patients with stage III colorectal cancer (JCOG0910): an open-label, non-inferiority, randomised, phase 3, multicentre trial. *The Lancet Gastroenterology &*

- Hepatology , Volume 3 , Issue 1 , 47 – 56.
11. Tezuka T, Hamada C, Ishida H, et al. Phase II clinical study of modified FOLFOX7 (intermittent oxaliplatin administration) plus bevacizumab in patients with unresectable metastatic colorectal cancer-CRAFT study. Invest New Drugs. 2013 Oct;31(5):1321-9.
 12. Fang-Shu Ou, Dirk Arnold, Walter Peters, et al. Randomized trial of standard chemotherapy alone or combined with atezolizumab as adjuvant therapy for patients with stage III deficient DNA mismatch repair (dMMR) colon cancer (Alliance A021502; ATOMIC). Journal of Clinical Oncology 2025 43:17_suppl, LBA1-LBA1
 13. Schmoll HJ, Cartwright T, 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 Jan 1;25(1):102-9. doi: 10.1200/JCO.2006.08.1075. PMID: 17194911.

Adjuvant Therapy of Rectal Cancer

Chemotherapy

* Infusional 5-FU may be administrated with Infusor(輸液器 / 奶瓶): 2400 mg/m² over 46 hrs on d1

mFOLFOX6

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	12	1-3
Leucovorin	400	≥ 90 mins	d1	Q2W	12	
5-FU	400	5 mins	d1	Q2W	12	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	12	

sLV5FU2

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Leucovorin	400	≥ 90 mins	d1	Q2W	12	4, 13
5-FU	400	5 min	d1	Q2W	12	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	12	

Capecitabine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Capecitabine	1250 PO BID	d1-14	Q3W	8	5

CapeOx/Xelox

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	2 hrs	d1	Q3W	8	6, 7
Capecitabine	1000 PO BID		d1-14	Q3W	8	

5-FU+LV

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Leucovorin	500	≥ 90 mins	d1, 8, 15, 22, 29, 36	Q8W	4	8
5-FU	500	1 hr	d1, 8, 15, 22, 29, 36	Q8W	4	

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Uracil-Tegafur (UFUR)	300-350/day PO	d1-28	Q4W	6	14
± Leucovorin	50-150 mg PO QD	d1-28	Q4W	6	

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Tegafur/Gimeracil/ Oteracil (TS-1)	40 PO BID	d1-28	Q42D	4	15

CCRT of Rectal Cancer

XRT + continuous infusion 5-FU

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
5-FU	225	22-24 hrs	d1-5 or d1-7	QW	5 weeks during XRT	9

XRT + 5-FU/LV

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
5-FU	400	5 mins	d1-4	Q4W	During week 1, 5 of XRT	10
Leucovorin	20	5 mins	d1-4	Q4W		

XRT + Capecitabine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Capecitabine	825 PO BID	d1-5	QW	5	11, 12

Neoadjuvant Therapy of Rectal Cancer

FOLFOX

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	6	16
Leucovorin	400	≥ 90 mins	d1	Q2W	6	
5-FU	400	5 mins	d1	Q2W	6	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	6	

CapeOx/Xelox

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	2 hrs	d1	Q3W	4	17
Capecitabine	1000 PO BID		d1-14	Q3W	4	

FOLFIRINOX (T4, N+)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	6	20
Leucovorin	400	≥ 90 mins	d1	Q2W	6	
Irinotecan	180	≥ 90 mins	d1	Q2W	6	
5-FU	400	5 mins	d1	Q2W	6	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	6	

mFOLFIRINOX (T4, N+)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	6	20, 21
Leucovorin	400	≥ 90 mins	d1	Q2W	6	
Irinotecan	150	≥ 90 mins	d1	Q2W	6	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	6	

Therapy after CCRT

Oral Uracil-Tegafur + LV

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Uracil-Tegafur (UFUR)	250 mg/m ² PO QD				18, 19
Leucovorin (Folina)	45 mg PO QD				

Total Neoadjuvant Therapy of Rectal Cancer

CCRT

XRT + continuous infusion 5-FU

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
5-FU	225	22-24 hrs	d1-5 or d1-7	QW	5 weeks during XRT	9

XRT + 5-FU/LV

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
5-FU	400	5 mins	d1-4	Q4W	Week 1, 5	10
Leucovorin	20	5 mins	d1-4	Q4W	of XRT	

XRT + Capecitabine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Capecitabine	825 PO BID	d1-5	QW	5 weeks during XRT	11, 12

Chemotherapy**FOLFOX**

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	6-8	16
Leucovorin	400	≥ 90 mins	d1	Q2W	6-8	
5-FU	400	5 mins	d1	Q2W	6-8	
5-FU	1200 [#]	22-24 hrs [#]	d1-2 [#]	Q2W	6-8	

[#]may be administrated with Infusor(輸液器 / 奶瓶): 2400 mg/m² over 46 hrs on d1

CapeOx/Xelox

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	2 hrs	d1	Q3W	4-5	17
Capecitabine	1000 PO BID		d1-14	Q3W	4-5	

參考文獻

1. 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.
2. Cheeseman SL, Joel SP, Chester JD, et al. A 'modified de Gramont' regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer. *Br J Cancer* 2002;87:393-399.
3. 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.
4. 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):1343-7.
5. Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. *N Engl J Med* 2005;352:2696-2704.
6. Schmoll HJ, Cartwright T, Taerner 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.
7. 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.
8. Petrelli N, Douglass Jr HO, Herrare L, et al. The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: 40 a prospective randomized phase III trial. *J Clin Oncol* 1989;7:1419-1426.
9. O'Connell MJ, Martenson JA, Wieand HS, et al. Improving adjuvant therapy for rectal cancer by combining protracted-infusion fluorouracil with radiation therapy after curative surgery. *N Engl J Med* 1994;331:502-507.
10. Tepper JE, O'Connell M, Niedzwiecki D, et al. Adjuvant therapy in rectal cancer: analysis of stage, sex, and local control—final report of Intergroup 0114. *J Clin Oncol* 2002;20:1744-1750.
11. O'Connell MJ, Colangelo LH, Beart RW, et al. Capecitabine and oxaliplatin in the preoperative multimodality treatment of rectal cancer: surgical end points from National Surgical Adjuvant Breast and Bowel Project trial R-04. *J Clin Oncol*

- 2014;32:1927-1934.
12. Hofheinz R, Wenz FK, Post S, et al. Chemoradiotherapy with capecitabine versus fluorouracil for locally advanced rectal cancer: A randomized, multicenter, non-inferiority, phase 3 trial. *Lancet Oncol* 2012;13:579-588.
13. Shikina A, Shinto E, Hashiguchi Y, et al. Differential clinical benefits of 5-fluorouracil-based adjuvant chemotherapy for patients with stage III colorectal cancer according to CD133 expression status. *Jpn J Clin Oncol*. Jan 2014;44(1):42-48.
14. Sulkes A, Benner SE, Canetta RM. Uracil-ftorafur: an oral fluoropyrimidine active in colorectal cancer. *J Clin Oncol*. Oct 1998;16(10):3461-3475.
15. Hamaguchi, Tetsuya et al. Capecitabine versus S-1 as adjuvant chemotherapy for patients with stage III colorectal cancer (JCOG0910): an open-label, non-inferiority, randomised, phase 3, multicentre trial. *The Lancet Gastroenterology & Hepatology* , Volume 3 , Issue 1 , 47 – 56.
16. Koizumi M, Yamada T, Shinji S, et al. Feasibility of Neoadjuvant FOLFOX Therapy Without Radiotherapy for Baseline Resectable Rectal Cancer. *In Vivo*. 2018; 32(4): 937–943.
17. Hata T, Takahashi H, Sakai D, et al. Neoadjuvant CapeOx therapy followed by sphincter-preserving surgery for lower rectal cancer. *Surg Today* (2017) 47: 1372.
18. Wang LW, Yang SH, Lin JK, et al. Pre-operative chemoradiotherapy with oral tegafur-uracil and leucovorin for rectal cancer. *J Surg Oncol*. 2005 Mar 15;89(4):256-63; discussion 263-4. doi: 10.1002/jso.20168. Erratum in: *J Surg Oncol*. 2005 May 1;90(2):106. PMID: 15726610.
19. Fokas E, Schlenska-Lange A, Polat B, et al. Chemoradiotherapy Plus Induction or Consolidation Chemotherapy as Total Neoadjuvant Therapy for Patients With Locally Advanced Rectal Cancer: Long-term Results of the CAO/ARO/AIO-12 Randomized Clinical Trial. *JAMA Oncol*. Published online November 18, 2021. doi:10.1001/jamaoncol.2021.5445
20. Conroy T, Bosset JF, Etienne PL, et al.,. Neoadjuvant chemotherapy with FOLFIRINOX and preoperative chemoradiotherapy for patients with locally advanced rectal cancer (UNICANCER-PRODIGE 23): a multicentre, randomised, open-label, phase 3 trial. *The Lancet Oncology* 2021;22;702-715.
21. Bennouna J, André T, Campion L, et al., Rationale and Design of the IROCAS Study: Multicenter, International, Randomized Phase 3 Trial Comparing Adjuvant Modified (m) FOLFIRINOX to mFOLFOX6 in Patients With High-Risk Stage III (pT4 and/or N2) Colon Cancer-A UNICANCER GI-PRODIGE Trial. *Clin Colorectal Cancer*. 2019 Mar;18(1):e69-e73.

Chemotherapy for Metastatic Colon and Rectal Cancer

First-line therapy

* Infusional 5-FU may be administrated with Infusor(輸液器 / 奶瓶): 2400 mg/m² over 46 hrs on d1

mFOLFOX6

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	8-12	1, 2, 3
Leucovorin	400	≥ 90 mins	d1	Q2W	8-12	
5-FU (optional)	400	5 mins	d1	Q2W	8-12	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	8-12	

mFOLFOX7

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	8-12	28
Leucovorin	200	≥ 90 mins	d1	Q2W	8-12	
5-FU	1200*	22-24 hrs*	d1-2*	Q2W	8-12	

FOLFOX + Bevacizumab

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Bevacizumab	5 mg/kg	≥ 30 mins	d1	Q2W		4
Oxaliplatin	85	2 hrs	d1	Q2W		
Leucovorin	400	≥ 90 mins	d1	Q2W		
5-FU (optional)	400	5 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

FOLFOX + Panitumumab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Panitumumab	6 mg/kg	≥ 1 hr	d1	Q2W		5
Oxaliplatin	85	2 hrs	d1	Q2W		
Leucovorin	400	≥ 90 mins	d1	Q2W		
5-FU (optional)	400	5 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

FOLFOX + Cetuximab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Cetuximab	500(400 [#] → 250)	≥ 90 mins	d1	Q2W (QW [#])		6
Oxaliplatin	85	2 hrs	d1	Q2W		
Leucovorin	400	≥ 90 mins	d1	Q2W		
5-FU (optional)	400	5 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

#Loading 400 mg/m² then 250 mg/m² QW**CapeOx/Xelox (Q2W)**

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	2 hrs	d1	Q2W	Max 12	34, 36
Capecitabine	1000 PO BID		d1-7	Q2W	Max 12	

CapeOx/Xelox

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	2 hrs	d1	Q3W	Max 16	7
Capecitabine	1000 PO BID		d1-14	Q3W	Max 16	

CapeOx/Xelox + Bevacizumab

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Bevacizumab	7.5 mg/kg	≥ 30 mins	d1	Q3W	Max 16	7
Oxaliplatin	130	2 hrs	d1	Q3W	Max 16	
Capecitabine	1000 PO BID		d1-14	Q3W	Max 16	

FOLFIRI

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Irinotecan	180	≥ 90 mins	d1	Q2W		8
Leucovorin	400	≥ 90 mins	d1	Q2W		
5-FU (optional)	400	5 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

FOLFIRI + Bevacizumab

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Bevacizumab	5 mg/kg	≥ 30 mins	d1	Q2W		10
Irinotecan	180	≥ 90 mins	d1	Q2W		
Leucovorin	400	≥ 90 mins	d1	Q2W		
5-FU (optional)	400	5 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

FOLFIRI + Cetuximab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Cetuximab	500 (400 → 250)	≥ 90 mins	d1	Q2W (QW)		11, 12
Irinotecan	180	≥ 90 mins	d1	Q2W		
Leucovorin	400	≥ 90 mins	d1	Q2W		
5-FU (optional)	400	5 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

FOLFIRI + Panitumumab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Panitumumab	6 mg/kg	≥ 1 hr	d1	Q2W		13
Irinotecan	180	≥ 90 mins	d1	Q2W		
Leucovorin	400	≥ 90 mins	d1	Q2W		
5-FU (optional)	400	5 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

Capecitabine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Capecitabine	1000 (825-1250) PO BID	d1-14	Q3W		16

Capecitabine + Bevacizumab

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Bevacizumab	7.5 mg/kg	≥ 30 mins	d1	Q3W		16
Capecitabine	1000 (825-1250) PO BID		d1-14	Q3W		

CapeOx/Xelox + Cetuximab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Cetuximab	500 (400 → 250)	≥ 90 mins	d1	Q2W (QW)	#	39
Oxaliplatin	130	2 hrs	d1	Q3W		
Capecitabine	1000 PO BID		d1-14	Q3W		

#12 weeks before & after surgery

CapeOx/Xelox + Panitumumab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Panitumumab	6 mg/kg	≥ 1 hr	d1	Q2W	#	39
Oxaliplatin	130	2 hrs	d1	Q3W		
Capecitabine	1000 PO BID		d1-14	Q3W		

#12 weeks before & after surgery

FOLFOXIRI ± Bevacizumab

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
± Bevacizumab	5 mg/kg	≥ 30 mins	d1	Q2W		21, 22, 43
Oxaliplatin	85	2 hrs	d1	Q2W		
Leucovorin	400	≥ 90 mins	d1	Q2W		
Irinotecan	150	≥ 90 mins	d1	Q2W		
± 5-FU	400	5 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

Cetuximab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Cetuximab	400 → 250 [#]	≥ 90 mins	d1	QW*		12, 25

[#] Loading 400 mg/m² then 250 mg/m² QW, or 500 mg/m² Q2W

Panitumumab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Panitumumab	6 mg/kg	≥ 1 hr	d1	Q2W		26

Pembrolizumab (MSI-H)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Pembrolizumab	2 mg/kg	≥ 1 hr	d1	Q3W		29

Pembrolizumab (MSI-H)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Pembrolizumab	200 mg	≥ 30 mins	d1	Q3W		29

Nivolumab (MSI-H)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Nivolumab	3 mg/kg	≥ 30 mins	d1	Q2W		30

Nivolumab (MSI-H)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Nivolumab	240 mg	≥ 30 mins	d1	Q2W		30

Nivolumab + Ipilimumab (MSI-H)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Nivolumab	3 mg/kg	≥ 30 mins	d1	Q3W	4	33
Ipilimumab	1 mg/kg	≥ 30 mins	d1	Q3W		
Followed by Nivolumab	3 mg/kg or 240 mg	≥ 30 mins	d1	Q2W		

Bolus or Infusional 5FU/Leucovorin

Roswell Park

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Leucovorin	500	≥ 90 mins	d1, 8, 15, 22, 29, 36	Q8W		17
5-FU	500	1 hr	d1, 8, 15, 22, 29, 36	Q8W		

Simplified biweekly infusional 5-FU/LV (sLV5FU2)

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Leucovorin	400	≥ 90 mins	d1	Q2W		9
5-FU	400	5 min	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

Infusional 5-FU/LV (sLV5FU2) + Bevacizumab

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Bevacizumab	5 mg/kg	≥ 30 mins	d1	Q2W		38
Leucovorin	400	≥ 90 mins	d1	Q2W		
5-FU	400	5 mins	d1	Q2W		
5-FU	1200*	22-24 hrs*	d1-2*	Q2W		

Weekly

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Leucovorin	20	≥ 90 mins	d1	QW		18
5-FU	500	1 hr	d1	QW		

藥品名	劑量 mg/m ²	輸注時間	給藥日	頻率	週期	參考文獻
Leucovorin	500	≥ 90 mins	d1	QW		19
5-FU	2600	22-24 hrs	d1	QW		

參考文獻

1. deGramont A, Figer A, Seymour M, et al. Leucovorin and Fluorouracil With or Without Oxaliplatin as First-Line Treatment in Advanced Colorectal Cancer. J Clin Oncol 2000;18:2938-2947.
2. Cheeseman SL, Joel SP, Chester JD, et al. A 'modified de Gramont' regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer. Br J Cancer 2002;87:393-399.
3. 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.
4. 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.
5. 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.
6. Venook AP, Niedzwiecki D, Lenz H-J, et al. CALGB/SWOG 80405: Phase III trial of irinotecan/5-FU/leucovorin (FOLFIRI) or oxaliplatin/5-FU/leucovorin (mFOLFOX6) with bevacizumab (BV) or cetuximab (CET) for patients (pts) with KRAS wild-

- type (wt) untreated metastatic adenocarcinoma of the colon or rectum [abstract]. ASCO Meeting Abstracts 2014;32:LBA3.
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.
 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):1343-7.
 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.
 10. Heinemann V, von Weikersthal LF, Decker T, et al. FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial. *Lancet Oncol* 2014.
 11. 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.
 12. Martin-Martorell P, Rosello S, Rodriguez-Braun E, et al. Biweekly cetuximab and irinotecan in advanced colorectal cancer 50 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.
 13. Peeters M, Prince 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.
 14. Van Cutsem E, Tabernero J, Lakomy R, et al. Addition of Aflibercept 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.
 15. Tabernero J, Yoshino T, Cohn AL, et al. Ramucirumab versus placebo in combination with second-line FOLFIRI in patients with metastatic colorectal carcinoma that progressed during or after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine (RAISE): a randomized, double-blind, multicentre, phase 3 study. *Lancet Oncol* 2015;16:499-508.

16. Cunningham D, Lang I, Marcuello E, et al. Bevacizumab plus capecitabine versus capecitabine alone in elderly patients with previously untreated metastatic colorectal cancer (AVEX): an open-label, randomised phase 3 trial. *Lancet Oncol* 2013;14:1077-1085.
17. 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 Project protocol C-03. *J Clin Oncol* 1993;11:1879-1887.
18. Jäger E, Heike M, Bemhard H, et al. Weekly high-dose leucovorin versus low-dose leucovorin combined with fluorouracil in advanced colorectal cancer: results of a randomized multicenter trial. *J Clin Oncol* 1996;14:2274-2279.
19. 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 randomised trial. *The Lancet* 2000;355:1041-47.
20. 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.
21. Conroy T, Bosset JF, Etienne PL, et al. Neoadjuvant chemotherapy with FOLFIRINOX and preoperative chemoradiotherapy for patients with locally advanced rectal cancer (UNICANCER-PRODIGE 23): a multicentre, randomised, open-label, phase 3 trial. *The Lancet Oncology* 2021;22:702-715.
22. Cremolini C, Loupakis F, Antoniotti C, et al. FOLFOXIRI plus bevacizumab versus FOLFIRI plus bevacizumab as first-line treatment of patients with metastatic colorectal cancer: updated overall survival and molecular subgroup analyses of the open-label, phase 3 TRIBE study. *Lancet Oncol* 2015;16:1306-1315.
23. Cunningham D, Pyrhonen S, James R, et al. Randomised 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.
24. 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.
25. 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.
26. 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.
27. 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.
 28. Hochster HS, Grothey A, Hart L, et al. Improved time to treatment failure with an intermittent oxaliplatin strategy: results of CONcePT. *Ann Oncol* 2014;25:1172-1178.
 29. Le DT, Uram JN, Wang H, et al. PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. *N Engl J Med*. Jun 25 2015;372(26):2509-2520.
 30. Overman MJ KS, McDermott RS, et al. Nivolumab {+/-} ipilimumab in treatment of patients with metastatic colorectal cancer (mCRC) with and without high microsatellite instability (MSI-H): CheckMate-142 interim results [abstract]. *ASCO Meeting Abstracts* 2016;34:3501. 2016.
 31. Product Information: UFUR Capsule. tegafur, uracil oral capsules. 2015.
 32. Product Information: TS-1 capsules. Tegafur, Gimeracil, Oteracil potassium oral capsules. 2015.
 33. Overman MJ, Lonardi S, Wong K, et al. Durable Clinical Benefit With Nivolumab Plus Ipilimumab in DNA Mismatch Repair–Deficient/Microsatellite Instability–High Metastatic Colorectal Cancer. *J Clin Oncol* 2018;36:773-779.
 34. Grande C, Quintero G, Candamio S, et al. Biweekly XELOX (capecitabine and oxaliplatin) as first-line treatment in elderly patients with metastatic colorectal cancer. *Journal of Geriatric Oncology* 2013;4: 114-121.
 35. Bekaii-Saab TS, Ou F-S, Anderson DM, et al. Regorafenib dose optimization study (ReDOS): Randomized phase II trial to evaluate dosing strategies for regorafenib in refractory metastatic colorectal cancer (mCRC)-An ACCRU Network study. *J Clin Oncol* 2018;36(suppl 4S;abstr 611).
 36. Grande C, Quintero G, Candamio S, et al. Biweekly XELOX (capecitabine and oxaliplatin) as first-line treatment in elderly patients with metastatic colorectal cancer. *Journal of Geriatric Oncology* 2013;4: 114-121.
 37. Meric-Bernstam F, Hurwitz H, et al. Pertuzumab plus trastuzumab for HER2-amplified metastatic colorectal cancer (MyPathway): an updated report from a multicentre, open-label, phase 2a, multiple basket study. *Lancet Oncol*. 2019;20(4):518-530.

38. Nakayama N, Sato A, Tanaka S, Shimada K, et al. A phase II study of bevacizumab with modified OPTIMOX1 as first-line therapy for metastatic colorectal cancer: the TCOG-GI 0802 study. Invest New Drugs. 2015 Aug;33(4):954-62.
39. Bridgewater JA, Pugh SA, Maishman T, et al., Systemic chemotherapy with or without cetuximab in patients with resectable colorectal liver metastasis (New EPOC): long-term results of a multicentre, randomised, controlled, phase 3 trial. Lancet Oncol. 2020 Mar;21(3):398-411. doi: 10.1016/S1470-2045(19)30798-3.