

# 大腸直腸癌診療指引

## 一、參與討論同仁

主席	彭汪嘉康院士 (血腫科)	
	邱仲峯副院長 (放腫科)	
附設醫院	謝政毅主任 (血腫科)	陳嘉哲醫師 (直腸外科)
	李婉玫副主任 (癌症中心)	林家伶個管師 (癌症中心)
萬芳醫院	陳建信主任 (直腸外科)	林香蘭個管師 (癌症中心)
雙和醫院	張東晟主任 (大腸直腸外科)	林嘉琦個管師 (癌症中心)
臺北癌症中心	廖裕民醫師	曾慧恩醫師 (血液腫瘤科)

二、討論日期：107 年 10 月 24 日

三、校稿人員：廖裕民醫師、謝政毅主任 / 林家伶個管師

## 107 年版與上一版差異：

106 年版	107 年修訂版
直腸癌診療指引共識 -2 初步評估： 1. 必要檢查 <ul style="list-style-type: none"> <li>· CXR</li> <li>· Abdominal/pelvic CT 或 MRI</li> </ul> 2. 選擇性檢查 <ul style="list-style-type: none"> <li>· Chest CT</li> </ul>	直腸癌診療指引共識 -2 初步評估 1. CXR 刪除 2. 修訂及新增 <ul style="list-style-type: none"> <li>· Chest CT and Abdominal CT or MRI ( 必要檢查 )</li> <li>· pelvic MRI ( 選擇性檢查 )</li> </ul> 3. 新增 <ul style="list-style-type: none"> <li>· 疑似或證實性轉移直腸癌 (suspect or proven metastatic synchronous adenocarcinoma) 治療路徑</li> </ul>
直腸癌診療指引共識 -4 1. 處置治療 前導性放射線治療 ± 化學治療→手術切除	直腸癌診療指引共識 -4 1. 新增 前導性放射線治療 ± 化學治療後增列無法手術切除路徑→化學治療 ± 放射線治療
直腸癌診療指引共識 -3、4、5、6、7	直腸癌診療指引共識 -3、4、5、6、7 1. 新增附註 For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy
直腸癌診療指引共識 -5、6、7	直腸癌診療指引共識 -5、6、7 1. 新增附註 If d-MMR,MSI-H consider Immunotherapy

## 106 年版

見直腸癌診療指引共識 -6

直腸癌診療指引共識 -8

1. Chest /Abdomen + pelvic CT:

High risk patients：每半年一次。

大腸癌診療指引共識 -2

1. 診斷

阻塞性→腸造口手術→手術切除

大腸癌診療指引共識 - 2、3、4、5、6

大腸癌診療指引共識 -5

## 107 年修訂版

直腸癌診療指引共識 -6

1. 新增

疑似或證實性轉移直腸癌 (suspect or proven metastatic synchronous adenocarcinoma) 治療路徑 (詳見直腸癌共識 -6)

直腸癌診療指引共識 -8

1. 修訂

Chest /Abdomen + pelvic CT: Stage II 病人每 6-12 個月做一次 T

大腸癌診療指引共識 -2

1. 新增

阻塞性→腸造口手術或分流 或 支架 (選擇性) →手術切除  
Diversion or stan (optional)

大腸癌診療指引共識 - 2、3、4、5、6

1. 新增附註

For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy

大腸癌診療指引共識 -5

2. 新增

疑似或證實性轉移大腸癌 (suspect or proven metastatic synchronous adenocarcinoma) 治療路徑 (詳見大腸癌共識 -5)

## 106 年版

大腸癌診療指引共識 -3、4、5、6

大腸癌診療指引共識 -7

1. Chest /Abdomen + pelvic CT:

High risk patients：每半年一次。

## 107 年修訂版

大腸癌診療指引共識 -3、4、5、6

1. 新增附註

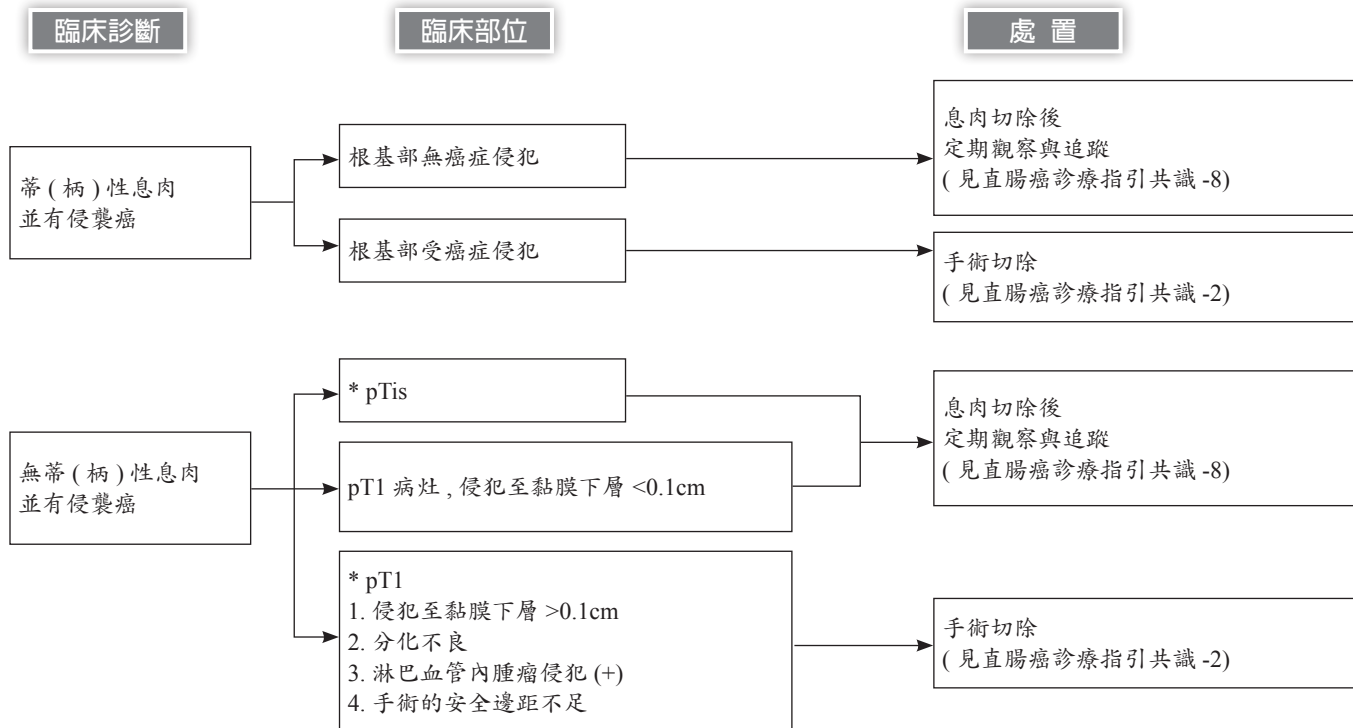
If d-MMR,MSI-H consider Immunotherapy

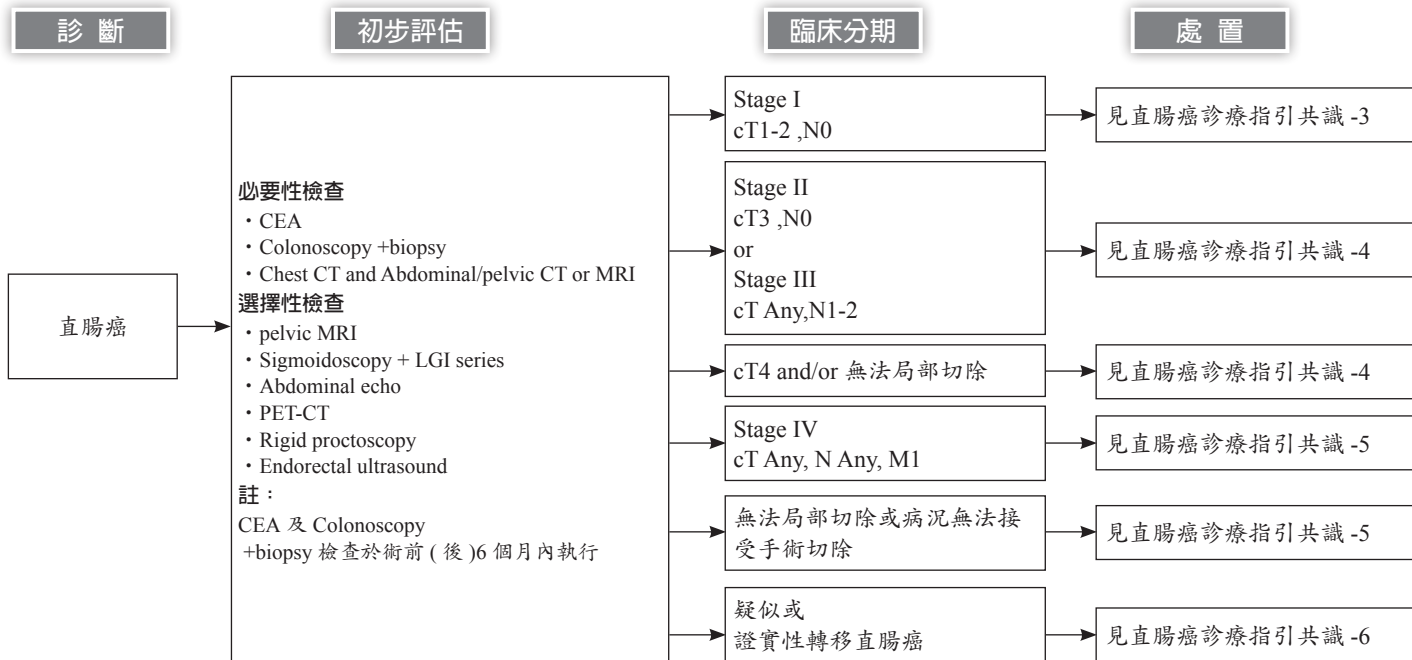
大腸癌診療指引共識 -7

1. 修訂

Chest /Abdomen + pelvic CT: Stage II 病人每 6-12 個月做一次

# 《直腸癌診療指引共識 -1》

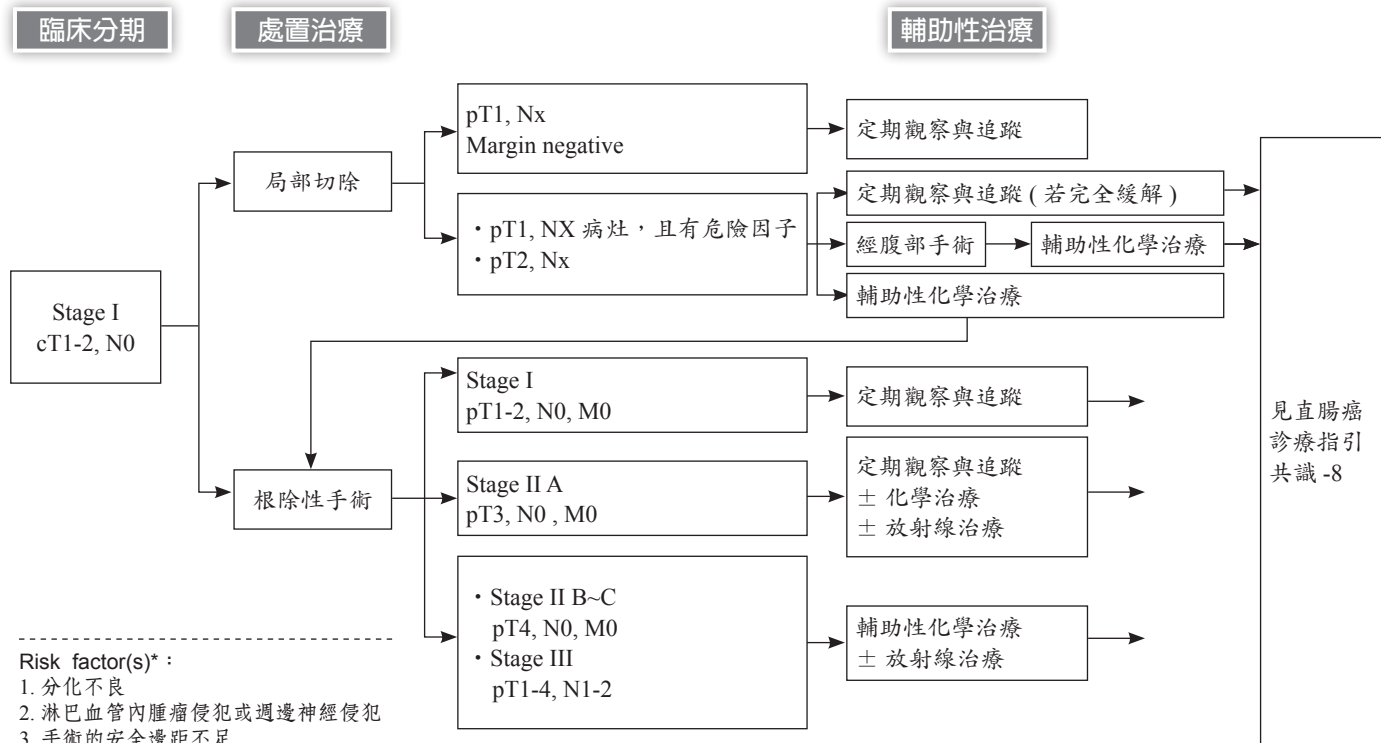




### 直腸癌定義：

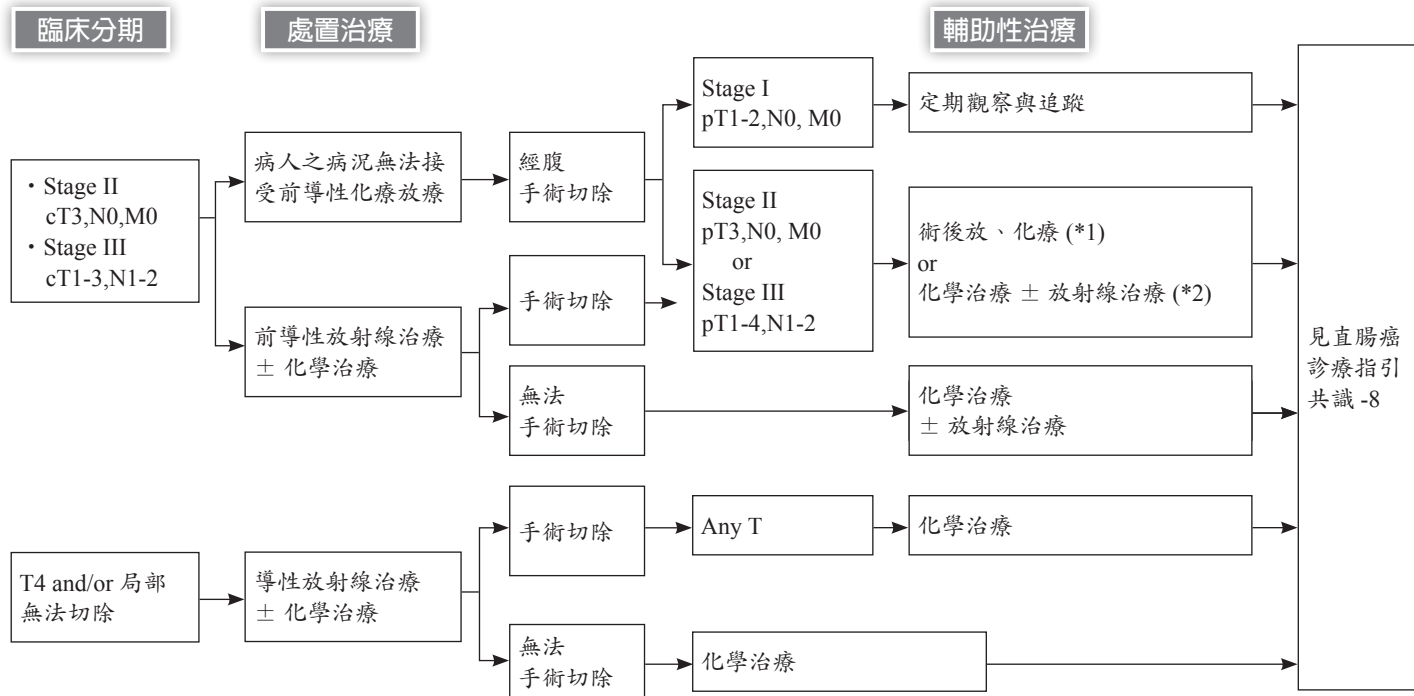
距離肛門口 15 公分以內之直腸，依病灶下緣距肛門口的距離分為上 (>11cm)、中 (>7cm & ≤ 11 cm)、下 (≤ 7 cm) 三段。對於中、下段局部廣泛性的癌症，且年齡介於 18 至 75 歲的病人，可接受手術前放射及化學治療，之後再實施根治性手術切除。對於上段直腸癌患者，則建議由臨床醫師視患者狀況而定，可直接進行手術，或採用手術前放射及化學治療，之後再實施根治性手術切除。

## 《直腸癌診療指引共識 -3》



Risk factor(s)\* :

1. 分化不良
2. 淋巴血管內腫瘤侵犯或週邊神經侵犯
3. 手術的安全邊距不足
4. SM3(Submucosa layer 3) invasion
5. StageIIA,pT3N0M0 : (without risk factor) added inspection MSI or MMR (optional),if MSI low adjuvant chemotherapy
6. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy



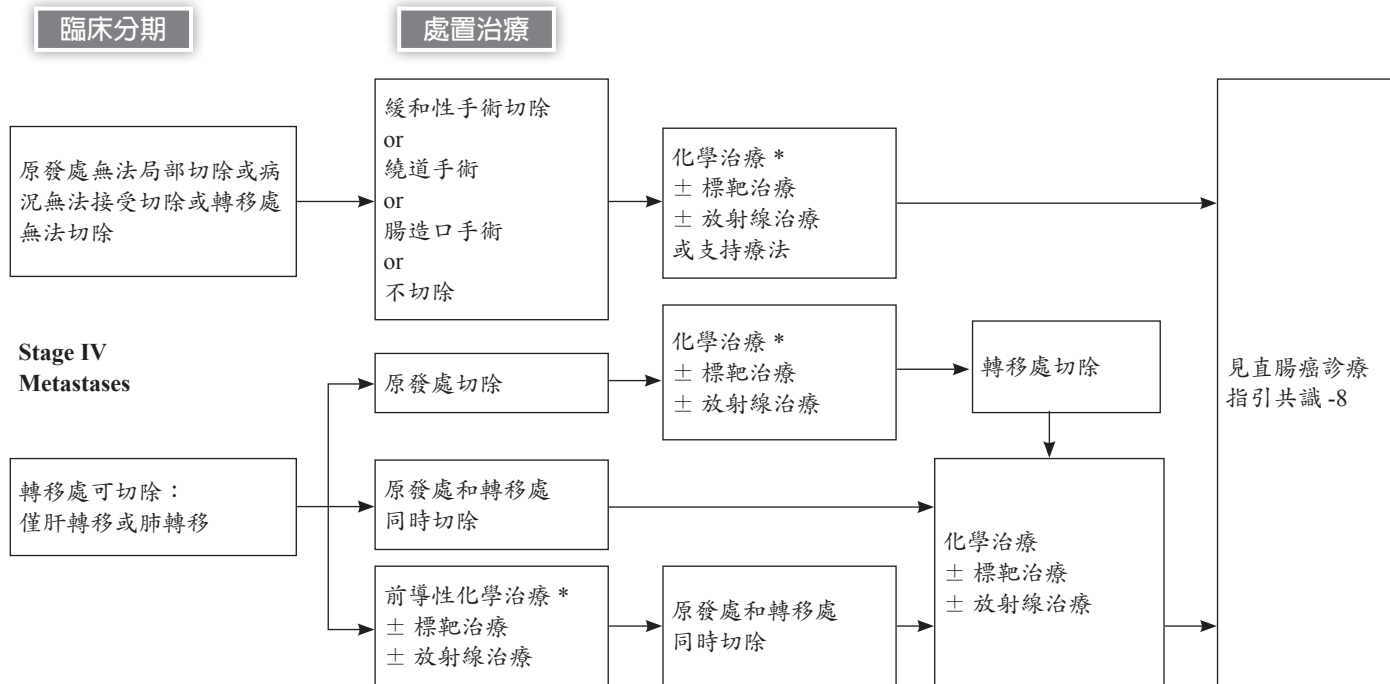
\*1. 若所選擇的化療藥物非為 Fluoropyrimidines 類 (如: oxaliplatin), 則不建議同步接受放射線治療。

\*2. 若病人的分期接近 T3,N0 且手術的安全邊距足夠, 以及預後特徵良好, RT 的治療成效較小, 建議單獨使用化學治療。

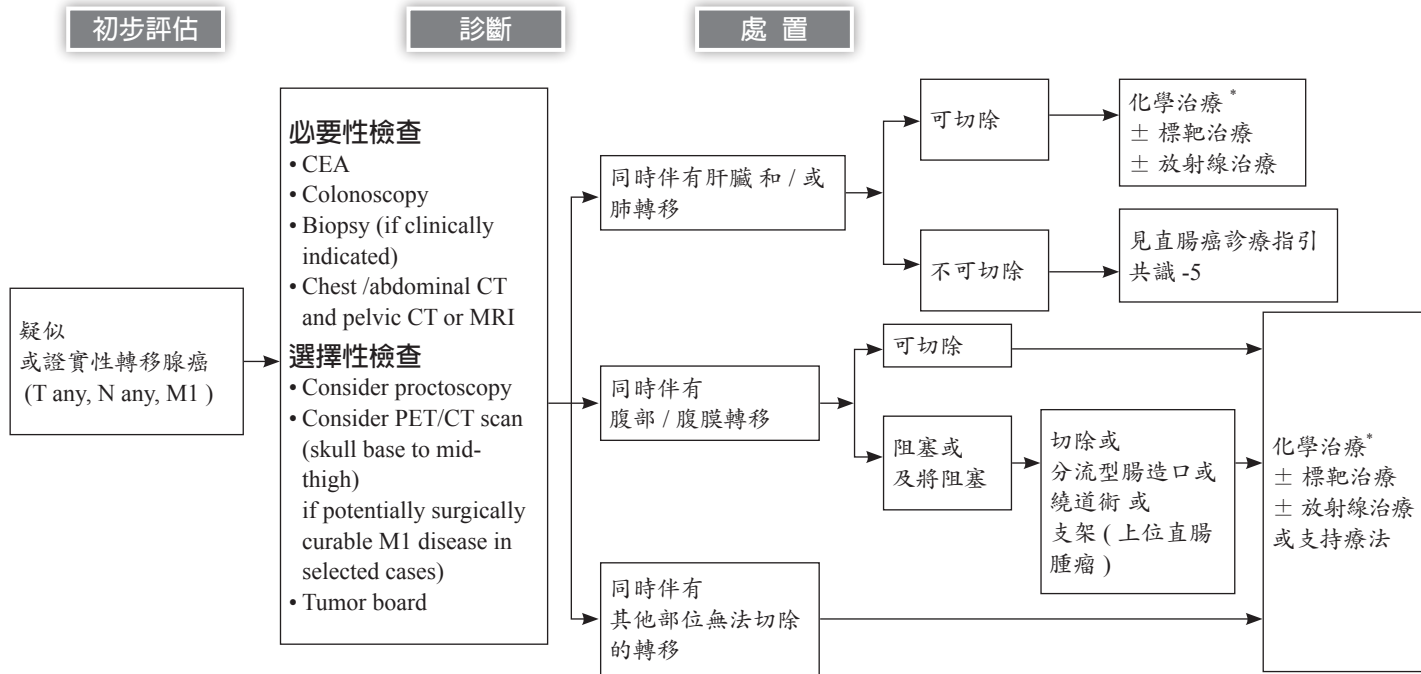
3. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy



## 《直腸癌診療指引共識 -5》

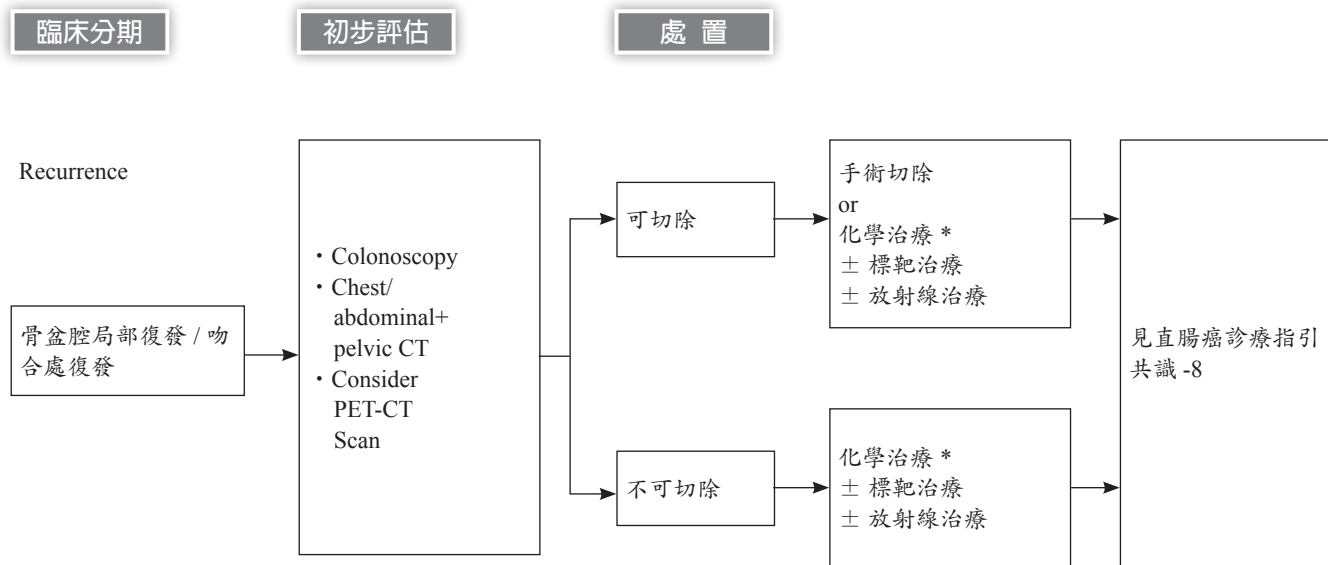


1. Stage IV 化學治療前加驗 RAS Mutation or BRAF,NGS (其餘 Stage Optional, optional 項目包括: B-RAF,MSI,MMR)
2. If d-MMR,MSI-H consider Immunotherapy
3. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy



1. Stage IV 化學治療前加驗 RAS Mutation or BRAF,NGS (其餘 Stage Optional , optional 項目包括 :B-RAF,MSI,MMR)
2. Iff d-MMR,MSI-H consider Immunotherapy
3. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy

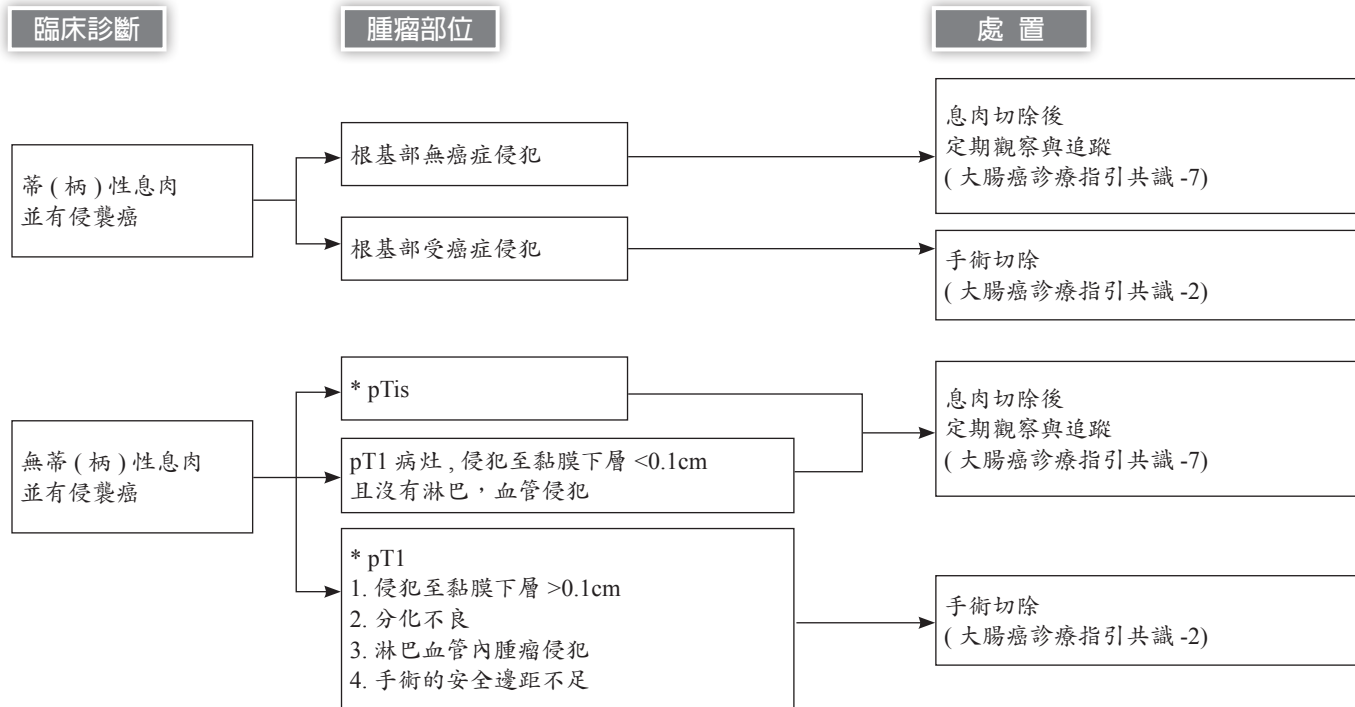
## 《直腸癌診療指引共識 -7》

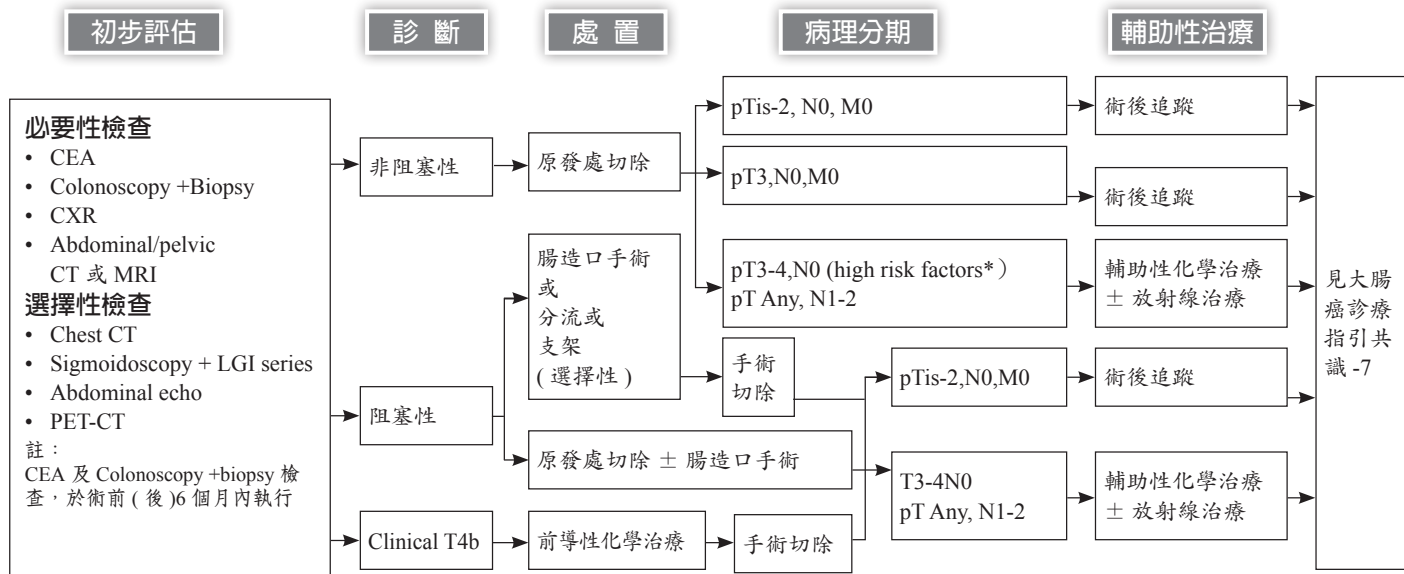


1. Stage IV 化學治療前加驗 RAS Mutation or BRAF,NGS (其餘 Stage Optional , optional 項目包括 :B-RAF,MSI,MMR )
2. If d-MMR,MSI-H consider Immunotherapy
3. For patients who are under 70 years old of age and ECOG: 0-2 points,suggested standard combination chemotherapy

Follow up Program for Rectal Cancer Patients ( at least 5 years )	
CEA	術後第一個月，兩年內每 3-6 個月一次，以後每 6 個月一次。
Chest /Abdomen + pelvic CT	(1) Stage II~III patients : 每 6-12 個月一次。
	(2) Stage IV patients : 兩年內每 3-6 個月一次，以後每 6-12 個月一次
Colonoscopy or Barium enema + Sigmoidoscopy	<p>第一年一次，之後每隔一年一次。</p> <ol style="list-style-type: none"> <li>1. 術前為阻塞型病灶，未全程做完大腸鏡檢者，術後 3-6 個月內即應再施檢一次。</li> <li>2. 若為 advanced adenoma，追蹤 1 年。</li> <li>3. 若非為 advance adenoma，追蹤 3 年而後追蹤 5 年</li> </ol>
Rigid proctoscopy ( 選擇性 )	每 6 個月一次。
Abdomen sono ( 選擇性 )	每 6 個月一次。
PET-CT scan ( 選擇性 )	臨床評估需要時

## 《大腸癌診療指引共識 -1》

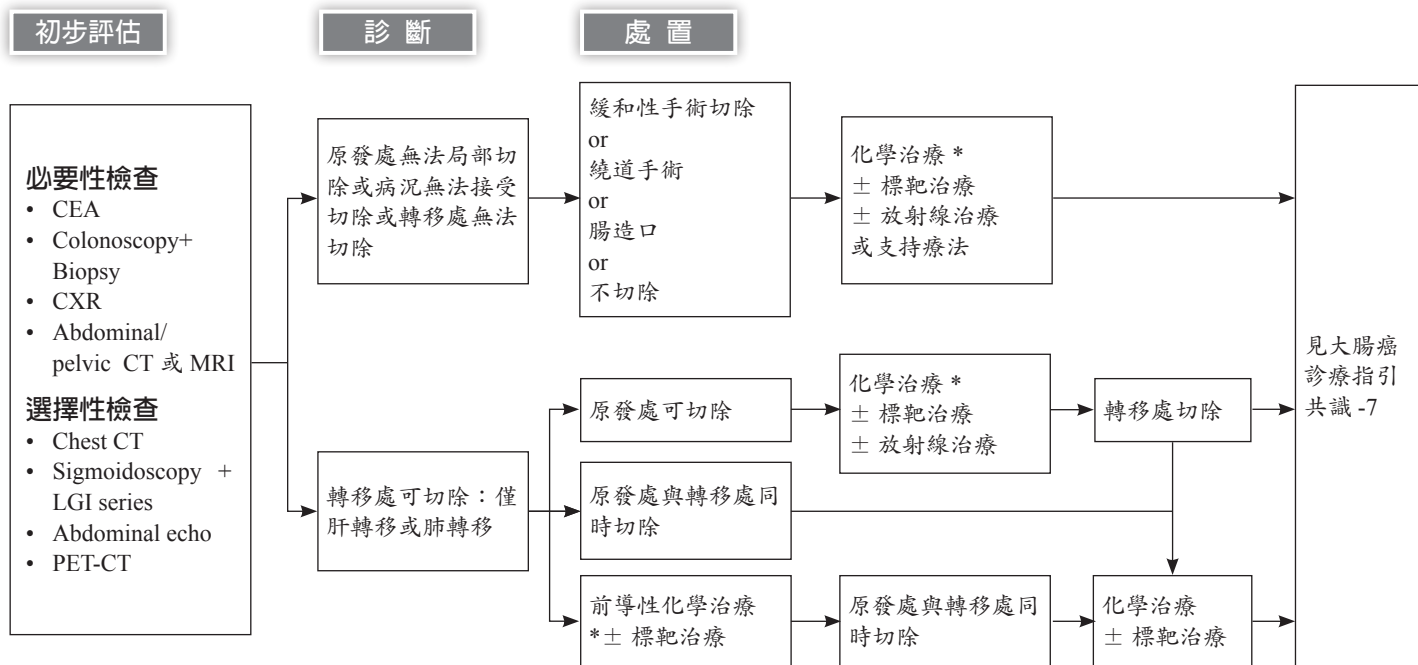




\*High risk factors :

1. 分化不良 (poorly differentiated)
2. 淋巴血管內腫瘤侵犯或神經週圍浸潤 (lymphatic/vascular/perineural invasion)
3. 淋巴摘除 <12 顆 (<12 lymph nodes examined)
4. 局部穿孔 (localized perforation)
5. 完全腸道阻塞 (bowel obstruction)
6. 手術的安全邊距不足、無法界定或手術邊距有癌細胞侵犯 (close, indeterminate or positive margins)
7. StageIIA,pT3N0M0 : (without risk factor) 加驗 MSI or MMR (optional),if MSI low → adjuvant chemotherapy
8. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy

## 《大腸癌診療指引共識 -3》



1. Stage IV 化學治療前加驗 RAS Mutation (其餘 Stage Optional, optional 項目包括 :B-RAF、MSI、MMR)。
2. If d-MMR, MSI-H consider Immunotherapy
3. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy

## 初步評估

## 診斷

## 處置

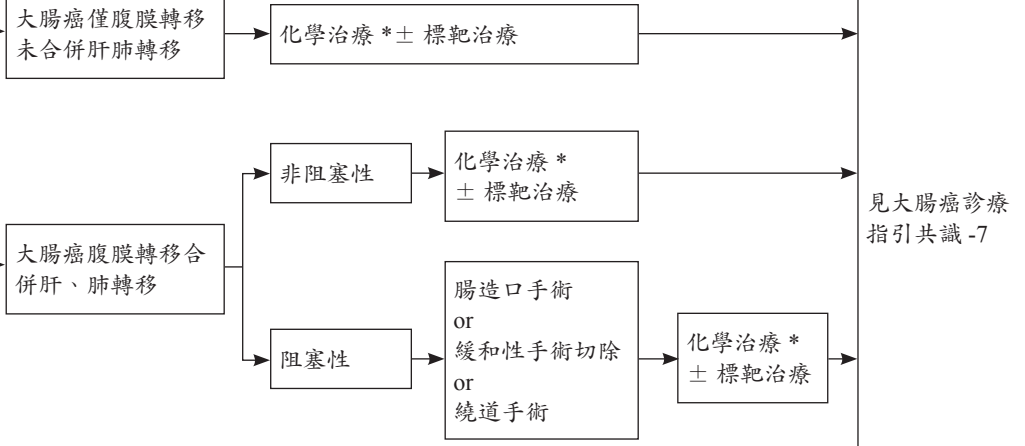
Metastases

### 必要性檢查

- CEA
- Colonoscopy +Biopsy
- CXR
- Abdominal/pelvic CT 或 MRI
- KRAS gene status

### 選擇性檢查

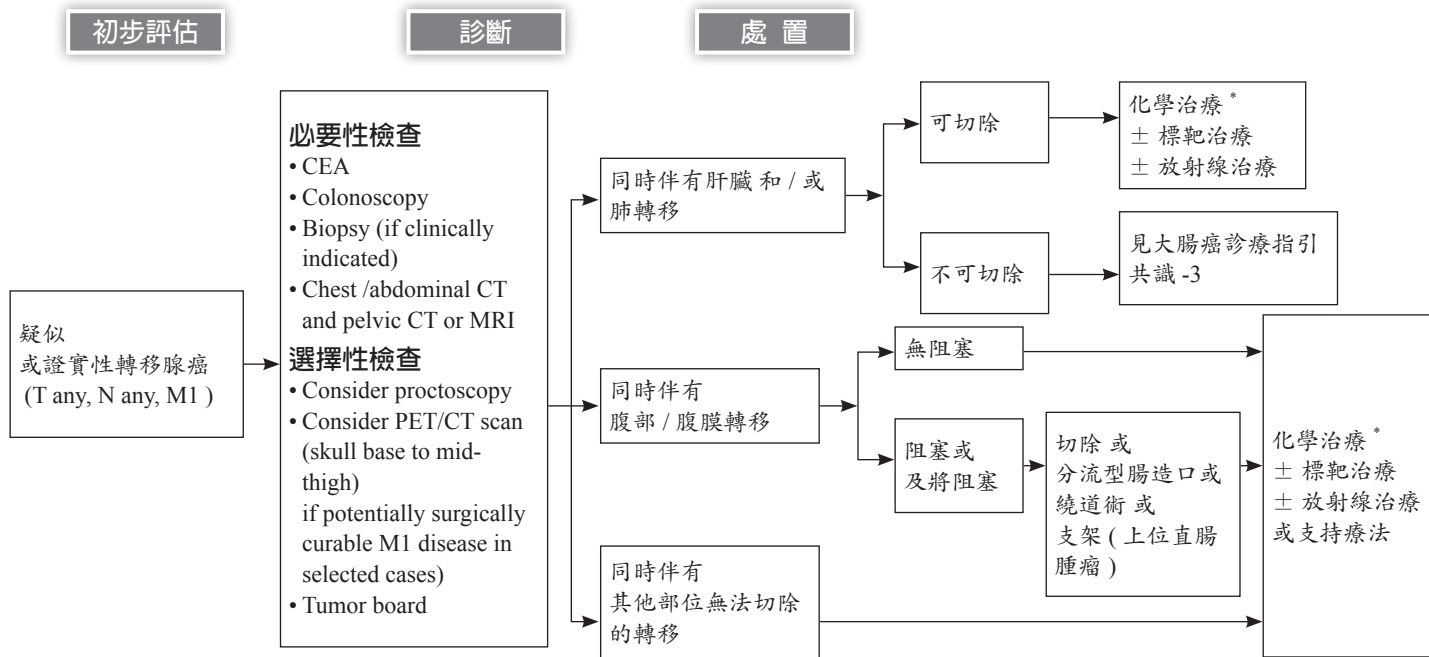
- Chest CT
- Sigmoidoscopy + LGI series
- Abdominal echo
- PET-CT
- Needle biopsy, if clinically indicated
- Multidisciplinary team evaluation, including a surgeon experienced in the resection of hepatobiliary and lung metastases



1. Stage IV 化學治療前加驗 RAS Mutation (其餘 Stage Optional, optional 項目包括: B-RAF、MSI、MMR)。
2. If d-MMR, MSI-H consider Immunotherapy
3. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy
4. 大腸癌僅腹膜轉移未合併肝肺轉移, 且 ECOG: 0-1, 心臟、肺、腎功能正常者, → 癌細胞減積手術 ± 腹腔內溫熱化學治療 (選擇性)。



## 《大腸癌診療指引共識 -5》



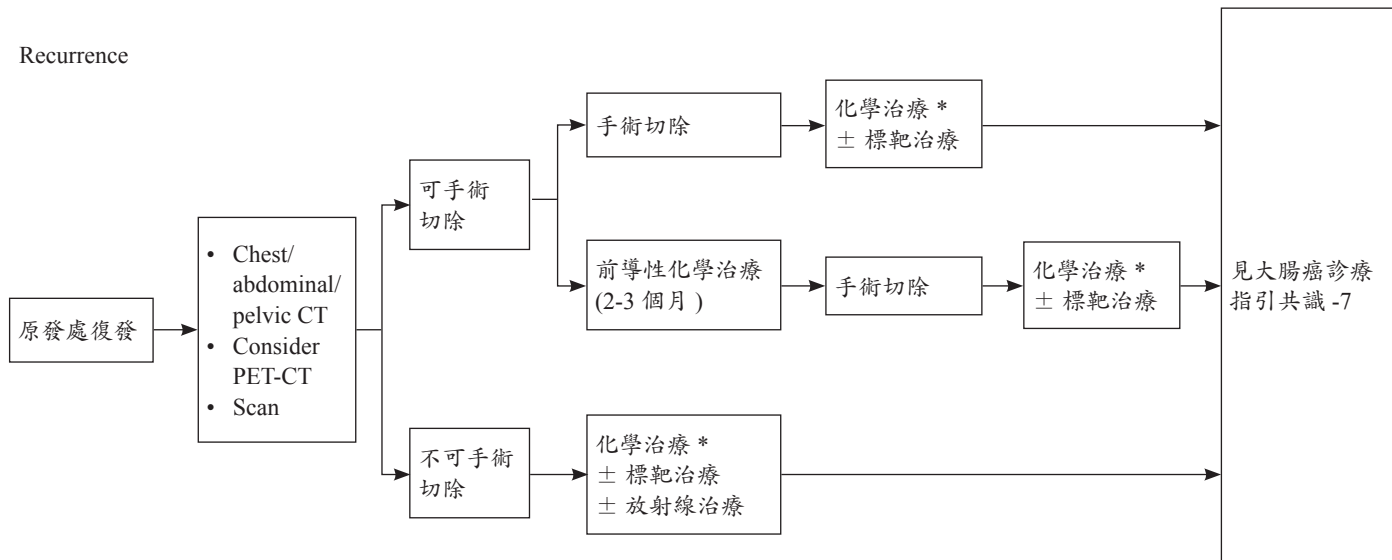
1. Stage IV 化學治療前加驗 RAS Mutation or BRAF,NGS (其餘 Stage Optional, optional 項目包括 :B-RAF,MSI,MMR)
2. If d-MMR,MSI-H consider Immunotherapy
3. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy
4. 大腸癌僅腹膜轉移未合併肝肺轉移,且 ECOG:0-1,心臟、肺、腎功能正常者,→ 癌細胞減積手術 ± 腹腔內溫熱化學治療(選擇性)。

診斷

評估

處置

Recurrence



1. Stage IV 化學治療前加驗 RAS Mutation or B-RAF (其餘 Stage Optional, optional 項目包括 :B-RAF、MSI、MMR)。
2. If d-MMR,MSI-H consider Immunotherapy
3. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy

## 《大腸癌診療指引共識 -6》

Follow up Program for Rectal Cancer Patients ( at least 5 years )	
CEA	術後第一個月，兩年內每 3-6 個月一次，以後每 6 個月一次。
Chest /Abdomen + pelvic CT	(1) stage II,III：每 6-12 個月一次。
	(2) Stage IV patients：兩年內每 3-6 個月一次，以後每 6-12 個月一次
Colonoscopy or Barium enema + Sigmoidoscopy	第一年一次，之後每隔一年一次。 1. 術前為阻塞型病灶，未全程做完大腸鏡檢者，術後 3-6 個月內即應再施檢一次。 2. 若為 advanced adenoma，追蹤 1 年。 3. 若非為 advance adenoma，追蹤 3 年而後追蹤 5 年。
Abdomen sono ( 選擇性 )	每半年一次
PET-CT scan ( 選擇性 )	臨床評估需要時。

## 《大腸直腸癌抗癌藥物治療指引》

### Adjuvant Therapy of Colon Cancer

#### mFOLFOX6

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	12	1-3
Leucovorin	400	1	Q2W	12	
5-FU	400	1	Q2W	12	
5-FU	1200*	1-2	Q2W	12	

\* Continuous infusion for 24 hours

#### FOLFOX4

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	12	8
Leucovorin	200	1	Q2W	12	
5-FU	400	1	Q2W	12	
5-FU	600*	1-2	Q2W	12	

\* Continuous infusion for 24 hours

#### FOLFOX7

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W		11
Leucovorin	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

\* Continuous infusion for 24 hours

### Capecitabine

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Capecitabine	1250 PO BID	1-14	Q3W	8	4

### CapeOx

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	1	Q3W	8	5
Capecitabine	1000 PO BID	1-14	Q3W	8	

### 5-FU+LV

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Leucovorin	500	1, 8, 15, 22, 29, 36	Q8W	4	6
5-FU	500	1, 8, 15, 22, 29, 36	Q8W	4	

### sLV5FU2

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Leucovorin	400	1	Q2W	12	7
5-FU	400	1	Q2W	12	
5-FU	1200*	1-2	Q2W	12	

\* Continuous infusion for 24 hours

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
UFUR	300-350/day PO	1-28	Q4W	6	9
± Leucovorin	50-150 mg PO QD	1-28	Q4W	6	

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

## Neoadjuvant Therapy of Colon Cancer

同 1<sup>st</sup> 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. 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. *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, Taernero 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, Maindault-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, 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.
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.

## Adjuvant Therapy of Rectal Cancer

### Chemotherapy

#### mFOLFOX6

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	12	1-3
Leucovorin	400	1	Q2W	12	
5-FU	400	1	Q2W	12	
5-FU	1200*	1-2	Q2W	12	

\* Continuous infusion for 24 hours

#### sLV5FU2

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Leucovorin	400	1	Q2W	12	4, 13
5-FU	400	1	Q2W	12	
5-FU	1200*	1-2	Q2W	12	

\* Continuous infusion for 24 hours

#### Capecitabine

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Capecitabine	1250 PO BID	1-14	Q3W	8	5



### CapeOx

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	1	Q3W	8	6, 7
Capecitabine	1000 PO BID	1-14	Q3W	8	

### 5-FU+LV

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Leucovorin	500	1, 8, 15, 22, 29, 36	Q8W	4	8
5-FU	500	1, 8, 15, 22, 29, 36	Q8W	4	

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
UFUR	300-350/day PO	1-28	Q4W	6	14

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
TS-1	40-60mg PO BID	1-28	Q42D	4	15

### Chemotherapy + RT

#### XRT + continuous infusion 5-FU

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
5-FU	225	1-5 or 1-7	Q4W	During XRT	9

#### XRT + 5-FU/LV

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
5-FU	400	1-4	Q4W	During week 1, 5	10
Leucovorin	20	1-4	Q4W	of XRT	

### XRT + Capecitabine

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Capecitabine	825 PO BID	1-5	QW	5	11, 12

### XRT + mFOLFOX6

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1			16
Leucovorin	400	1			
5-FU	400	1			
5-FU	1200*	1-2			

\* Continuous infusion for 24 hours

## Neoadjuvant Therapy of Rectal Cancer

### FOLFOX

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	6	16
Leucovorin	400	1	Q2W	6	
5-FU	400	1	Q2W	6	
5-FU	1200*	1-2	Q2W	6	

\* Continuous infusion for 24 hours

### CapeOx

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	1	Q3W	4	17
Capecitabine	1000 PO BID	1-14	Q3W	4	

## 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, Taberero 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.

## Chemotherapy for Advanced or Metastatic Colon and Rectal Cancer

### First-line therapy

#### mFOLFOX6 or mFOLFOX7

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	8-12	1, 2, 3, 28
Leucovorin	400	1	Q2W	8-12	
5-FU (optional)	400	1	Q2W	8-12	
5-FU	1200*	1-2	Q2W	8-12	

\* Continuous infusion for 24 hours

#### FOLFOX + Bevacizumab

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Bevacizumab	5 mg/kg	1	Q2W		4
Oxaliplatin	85	1	Q2W		
Leucovorin	400	1	Q2W		
5-FU (optional)	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

\* Continuous infusion for 24 hours

**FOLFOX + Panitumumab (KRAS/NRAS WT gene only)**

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Panitumumab	6 mg/kg	1	Q2W		5
Oxaliplatin	85	1	Q2W		
Leucovorin	400	1	Q2W		
5-FU (optional)	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

\* Continuous infusion for 24 hours

**FOLFOX + Cetuximab (KRAS/NRAS WT gene only)**

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	500 (400 → 250)	1	Q2W (QW)		6
Oxaliplatin	85	1	Q2W		
Leucovorin	400	1	Q2W		
5-FU (optional)	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

\* Continuous infusion for 24 hours

**Xelox**

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	Max 12	34
Capecitabine	1000 PO BID	1-7	Q2W	Max 12	

**CapeOx**

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	1	Q3W	Max 16	7
Capecitabine	1000 PO BID	1-14	Q3W	Max 16	

### CapeOx + Bevacizumab

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Bevacizumab	7.5 mg/kg	1	Q3W	Max 16	7
Oxaliplatin	130	1	Q3W	Max 16	
Capecitabine	1000 PO BID	1-14	Q3W	Max 16	

### FOLFIRI

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Irinotecan	180	1	Q2W		8, 9
Leucovorin	400	1	Q2W		
5-FU (optional)	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

\* Continuous infusion for 24 hours

### FOLFIRI + Cetuximab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	500 (400 → 250)	1	Q2W (QW)		11, 12
Irinotecan	180	1	Q2W		
Leucovorin	400	1	Q2W		
5-FU (optional)	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

\* Continuous infusion for 24 hours

**FOLFIRI + Panitumumab (KRAS/NRAS WT gene only)**

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Panitumumab	6 mg/kg	1	Q2W		13
Irinotecan	180	1	Q2W		
Leucovorin	400	1	Q2W		
5-FU (optional)	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

\* Continuous infusion for 24 hours

**Capecitabine**

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Capecitabine	1000 (825-1250) PO BID	1-14	Q3W		16

**Capecitabine + Bevacizumab**

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Bevacizumab	7.5 mg/kg	1	Q3W		16
Capecitabine	1000 (825-1250) PO BID	1-14	Q3W		

**FOLFOXIRI ± Bevacizumab**

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
± Bevacizumab	5 mg/kg	1	Q2W		21, 22
Oxaliplatin	85	1	Q2W		
Irinotecan	165	1	Q2W		
Leucovorin	400	1	Q2W		
5-FU	1600*	1-2	Q2W		

\* Continuous infusion for 24 hours



### Cetuximab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	500 (400 → 250)	1	Q2W (QW)		12, 25

### Panitumumab (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Panitumumab	6 mg/kg	1	Q2W		26

### Pembrolizumab (MSI-H)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Pembrolizumab	2 mg/kg	1	Q3W		29

### Nivolumab (MSI-H)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Nivolumab	3 mg/kg	1	Q2W		31

### Nivolumab (MSI-H)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Nivolumab	240 mg	1	Q2W		30

### Nivolumab + Ipilimumab (MSI-H)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Nivolumab	3 mg/kg	1	Q3W	4	33
Ipilimumab	1 mg/kg	1	Q3W		
Followed by Nivolumab	3 mg/kg or 240 mg	1	Q2W		

### Bolus or Infusional 5FU/Leucovorin

#### Roswell Park

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Leucovorin	500	1, 8, 15, 22, 29, 36	Q8W		17
5-FU	500	1, 8, 15, 22, 29, 36	Q8W		

### Simplified biweekly infusional 5-FU/LV (sLV5FU2)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Leucovorin	400	1	Q2W		8
5-FU	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

### Weekly

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Leucovorin	20	1	QW		18
5-FU	500	1	QW		

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Leucovorin	500	1	QW		19
5-FU	2600*	1	QW		

\* Continuous infusion for 24 hours

## Second-line and other therapy ★

### FOLFIRI + Ziv-aflibercept

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Ziv-aflibercept	4 mg/kg	1	Q2W		14
Irinotecan	180	1	Q2W		
Leucovorin	400	1	Q2W		
5-FU (optional)	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

\* Continuous infusion for 24 hours

### FOLFIRI + Ramucirumab

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Ramucirumab	8 mg/kg	1	Q2W		15
Irinotecan	180	1	Q2W		
Leucovorin	400	1	Q2W		
5-FU (optional)	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

\* Continuous infusion for 24 hours

## IROX

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q3W		20
Irinotecan	200	1	Q3W		

## Irinotecan

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Irinotecan	125 (180) (300-350)	1, 8 (1)	Q3W (Q2W)(Q3W)		23, 24

## Cetuximab + Irinotecan (KRAS/NRAS WT gene only)

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Cetuximab	500 (400 → 250)	1	Q2W (QW)		12, 25
Irinotecan	125 (180) (300-350)	1, 8 (1)	Q3W (Q2W)(Q3W)		

## Regorafenib

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
Regorafenib	160 mg PO	1-21	Q4W		27

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
UFUR	200mg PO BID/TID	1-28	Q4W		31

藥品名	劑量 mg/m <sup>2</sup>	給藥日	頻率	週期	參考文獻
TS-1	50-75mg PO BID	1-28	Q42D		32

## 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. 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. *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. Falcone A, Ricci S, Brunetti I, et al. Phase III Trial of Infusional Fluorouracil, Leucovorin, Oxaliplatin, and Irinotecan (FOLFOXIRI) 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.
  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, KRS, 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.



## 《直腸癌放射治療共識》

### 一、治療範圍

1. 直腸腫瘤 / 低位乙狀結腸腫瘤或腫瘤原發部位
2. 骨盆腔內淋巴轉移病灶
3. 骨盆腔高風險淋巴轉移範圍

### 二、治療劑量 / 次數

1. 總劑量：45~60 Gy
2. 分次劑量：1.8~2.0 Gy

### 三、治療方式：

使用強度調控放射治療技術，包含弧形及螺旋放射規畫，可考慮搭配影像導引治療，治療選擇可使用同步照射高與低危險部位的方式或先給予整個照射部位部份劑量照射後，再針對高危險部位加強劑量。

### 四、參考文獻：

1. NCCN clinical practice guidelines in oncology-Rectal cancer. version 1.2019.
2. RT Elective Clinical Target Volumes in Anorectal Cancer: An RTOG Consensus Panel Contouring Atlas. Myerson R , Garofalo M , Naqa Iel , et al.
3. S. Roels, et al. Definition and delineation of the clinical target volume for rectal cancer. Int J Oncol Biol Phys 2006; 65: 1129-1142
4. Sauer R, Liersch T, Merkel S, et al. Preoperatorative Versus postoperative Chemoradiotherapy for Locally Advanced Rectal Cancer: Results of the German CAO/ARO/AIO-94 Randomized Phase III Trial After a Median Follow-UP of 11 Years. J Clin Oncol 2012; 30: 1926-19335.

## 《參考文獻》

1. NCCN Clinical Practice in Oncology : Rectal Cancer V.1.2019.
2. NCCN Clinical Practice in Oncology : Colon Cancer V.2.2018
3. Andre T, Quinaux E, Louvet C, Colin P, Gamelin E, Bouche O, Achille E, Piedbois P, Tubiana-Mathieu N, Boutan-Laroze A, Flesch M, Lledo G, Raoul Y, Debrix I, Buyse M, de Gramont A. Phase III Study Comparing a Semimonthly With a Monthly Regimen of Fluorouracil and Leucovorin As Adjuvant Treatment for Stage II and III Colon Cancer Patients : Final Results of GERCOR C96.1. *L Clin Oncol* 25(24) : 3732-3738, 2007.
4. André, Corrado Boni, Lamia Mounedji-Boudiaf, Matilde Navarro, Josep Taberero, Tamas Hickish, Clare Topham, Marta Zaninelli, Philip Clingan, John Bridgewater, Isabelle Tabah-Fisch, Aimery de Gramont, for the Multicenter International Study of Oxaliplatin / 5-Fluorouracil / Leucovorin in the Adjuvant Treatment of Colon Cancer (MOSAIC) Investigators Oxaliplatin, Fluorouracil, and Leucovorin as Adjuvant Treatment for Colon Cancer. *NEJM* 350 (23) : 2343-2351, 2004.
5. Chris Twelves, Alfred Wong, Marek P. Nowacki, Markus Abt, Howard Burris, III, et al. Capecitabine as Adjuvant Treatment for Stage III Colon Cancer. *NEJM* 352(26) : 2696-2704, 2005.
6. Kato T, Ohashi Y, Nakazato H, Koika A, Saji S, Suzuki H, et al. Efficacy of oral UFT as adjuvant chemotherapy to curative resection of colorectal cancer : multicenter prospective randomized trial. *Langenbeck's Arch Surg* 2002; 386 : 575-81.
7. Akasu T, Moriya Y, Ohashi Y, Yoshida S, Shirao K, Kodaira S. Adjuvant chemotherapy with uraciltegafur for pathological stage III rectal cancer after excision with selective lateral pelvic lymphadenectomy : a multicenter randomized controlled trial. *Jpn J Clin Oncol* 2006; 36 : 237-44.
8. Barry C. Lembersky, H. Samuel Wieand, Nicholas J. Petrelli, Michael J. O'Connell, Linda H. Colangelo, Roy E. Smith, Thomas E. Seay, Jeffrey K. Giguere, M. Ernest Marshall, Andrew D. Jacobs, Lauren K. Colman, Atilla Soran, Greg Yothers, and Norman Wolmark. Oral Uracil and Tegafur Plus Leucovorin Compared With Intravenous Fluorouracil and Leucovorin in Stage II and III Carcinoma of the Colon : Results From National Surgical Adjuvant Breast and Bowel Project Protocol C-06. *Journal of Clinical Oncology*. 24(13) : 2059-2064.
9. Daniel G. Haller, Josep Taberero, Jean Maroun, et al. Capecitabine Plus Oxaliplatin Compared with Fluorouracil and Folinic Acid as Adjuvant Therapy for Stage III Colon Cancer. *Journal of Clinical Oncology* 29 : 1-9, 2011
10. E Bajetta, M Di Bartolomeo, R Buzzoni, et al. Uracil/ftorafur/Leucovorin combined with irinotecan (TEGAFIRI) or oxaliplatin (TEGAFOX) as
11. first-line treatment for metastatic colorectal cancer patients: results of randomised phase II study. *British Journal of Cancer* 96: 439-444, 2007