直腸癌診療指引

大腸直腸癌醫療團隊訂定

2007 年 11 月制訂　2012 年 07 月修訂

2008 年 08 月修訂　2013 年 05 月修訂

2009 年 06 月修訂　2014 年 10 月修訂

2010 年 07 月修訂　2015 年 10 月修訂

2011 年 07 月修訂　2016 年 01 月修訂

2017 年 06 月修訂

參考資料：

1. **NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Rectal Cancer version 1.2017**

2.全民健康保局醫療給付標準行政院衛生署一百零六年版

3. Physicians' Cancer Chemotherapy Drug Manual 2016

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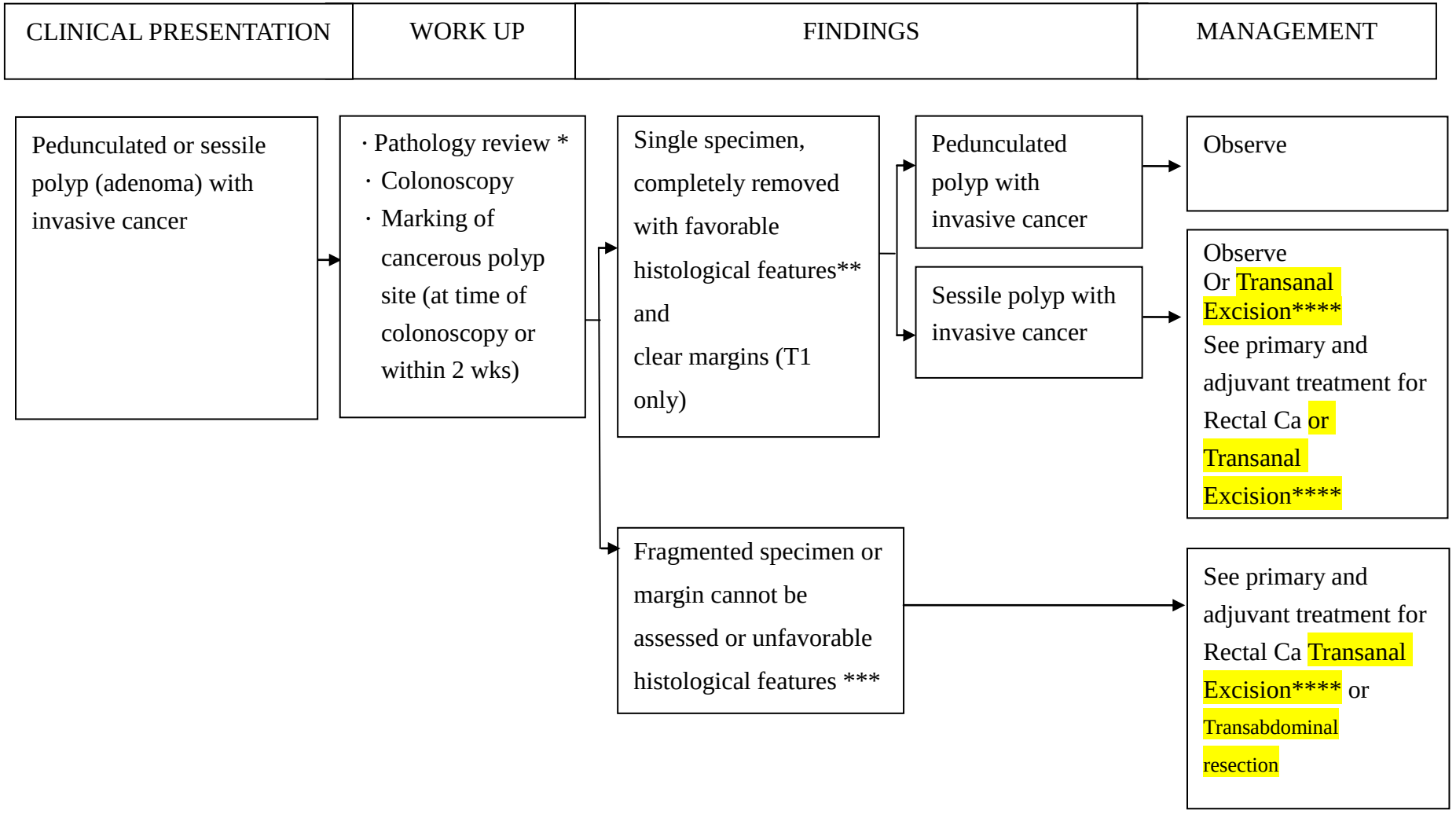
Malignant Polyp of Rectum Clinical Practice Guideline



201706（修訂）
直腸癌診療指引-1

* A malignant polyp is defined as one with cancer invading through the muscularis mucosae and into the submucosa (pT1). pTis is not considered to be a “malignant polyp.”

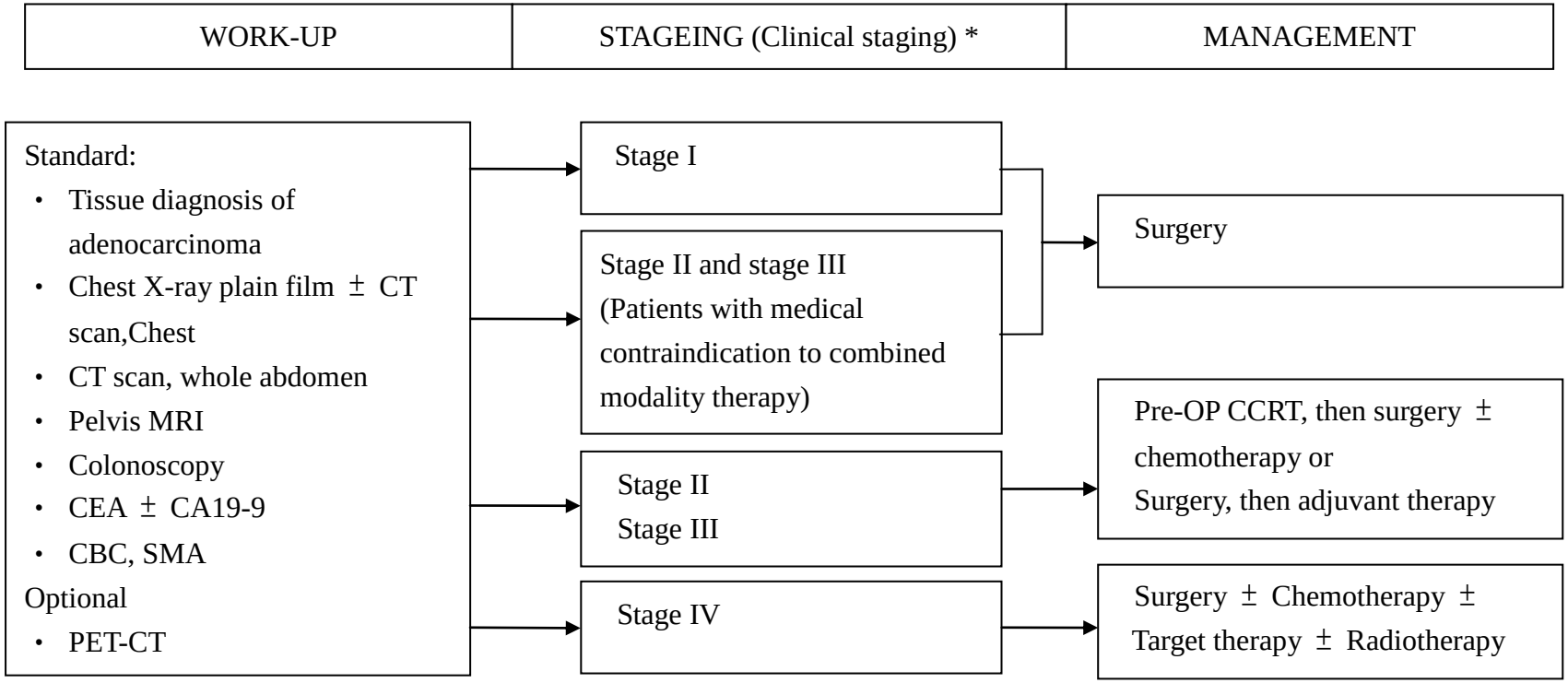
** Favorable histologic features grade 1 or 2, no angiolymphatic invasion, and negative margin of resection. There is no consensus as to the definition of what constitutes a positive margin of resection. A positive margin has been defined as: 1) tumor <1 mm from the transected margin, 2) tumor <2 mm from the transected margin, and 3) tumor cells present within the diathermy of the transected margin.[1-4]

*** Unfavorable histologic features grade 3 or 4, angiolymphatic invasion, or a “positive margin.” See above for definition of a positive margin.

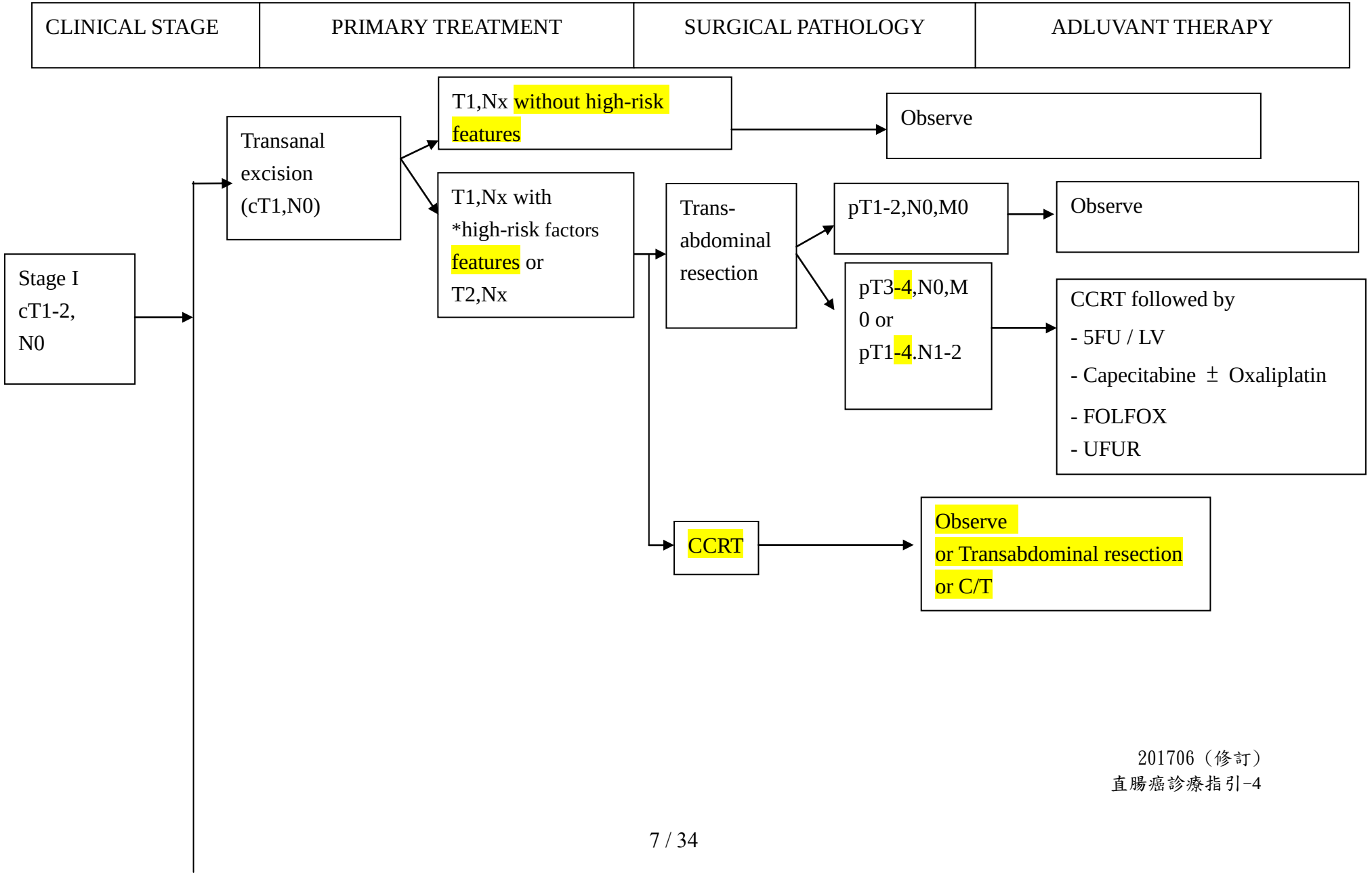
**** Transanal Excision:

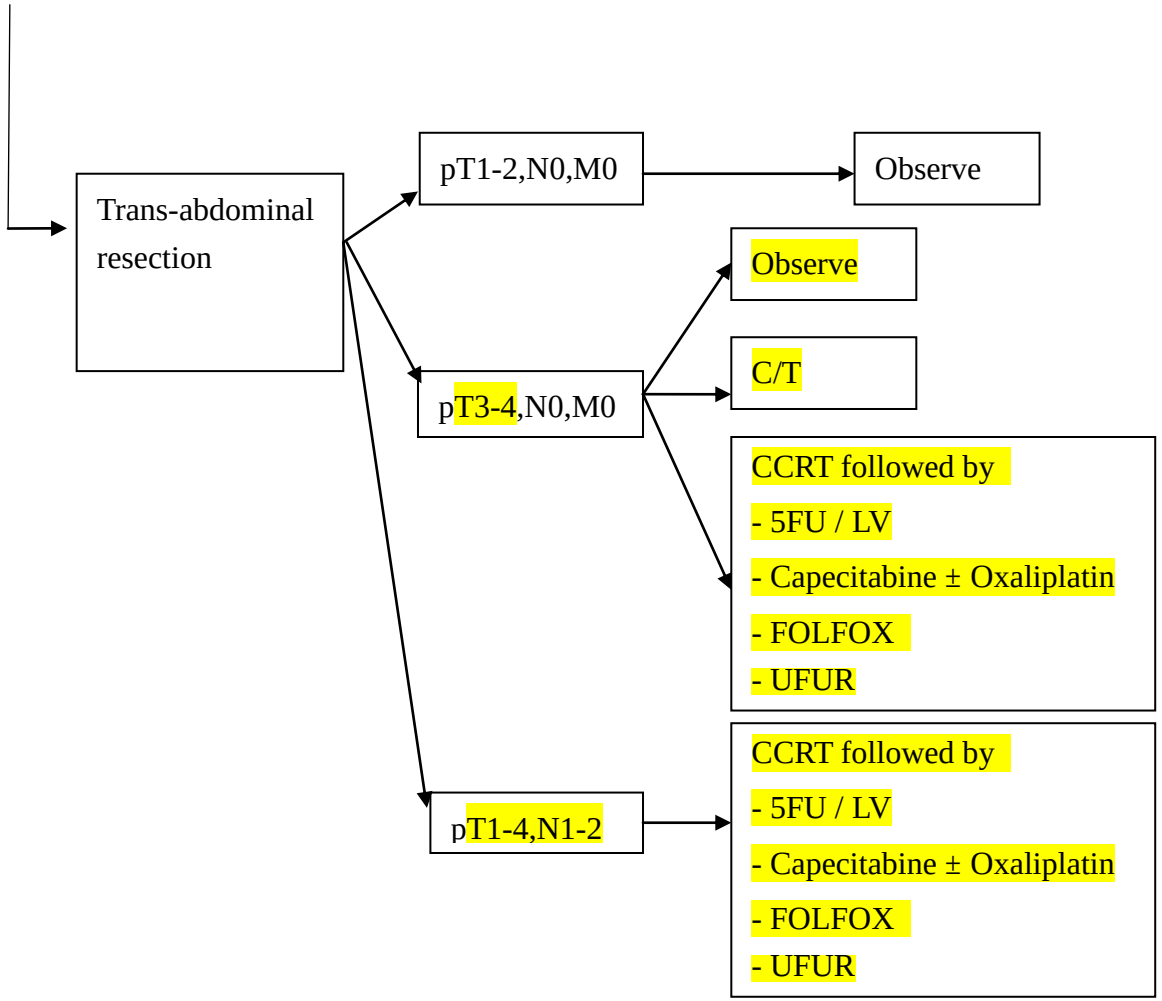
- <30% circumference of bowel
- <3 cm in size
- Margin clear (>3 mm)
- Mobile, nonfixed.
- Within 8 cm of anal verge
- T1 only
- Endoscopically removed polyp with cancer or indeterminate pathology
- No lymphovascular invasion or PNI
- Well to moderately differentiated
- No evidence of lymphadenopathy on pretreatment imaging

Initial management



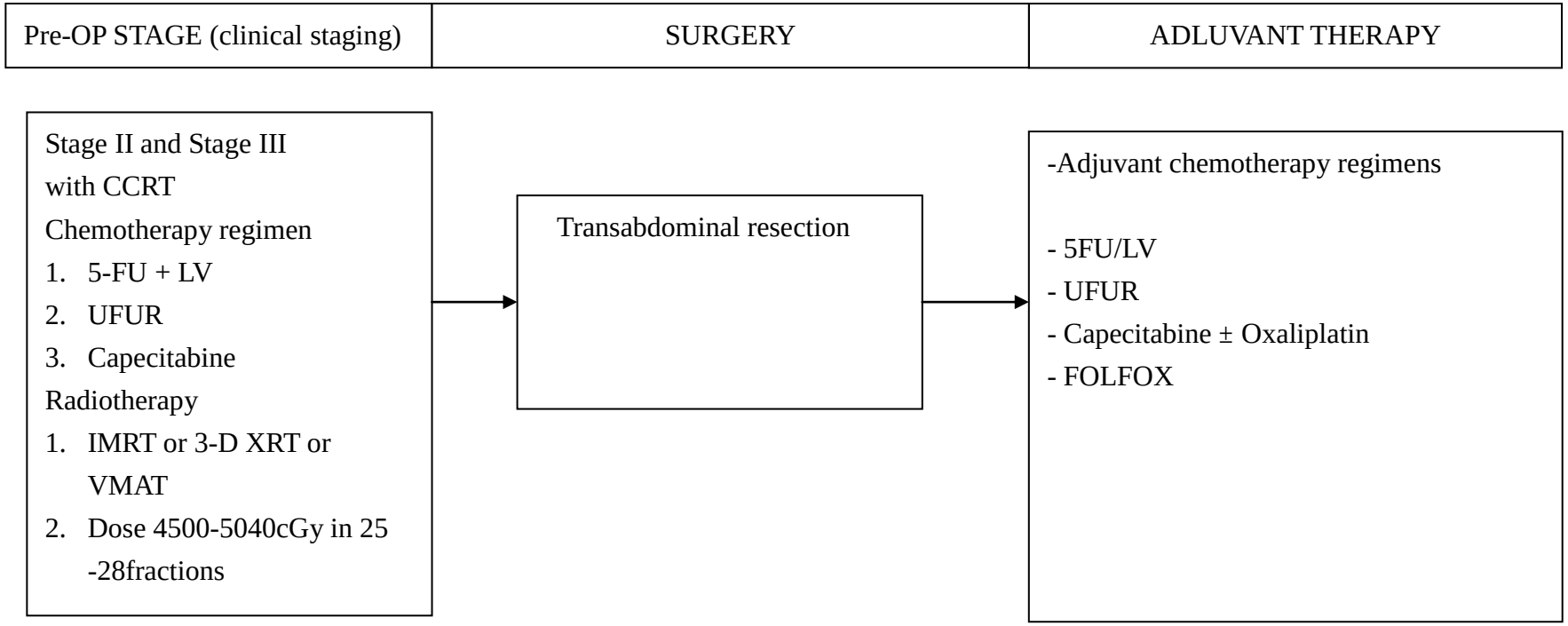
Post-operative management





* High-risk features include: poor differentiation, LVI, PNI, positive margins ,submucosal invasion

Post-operative management

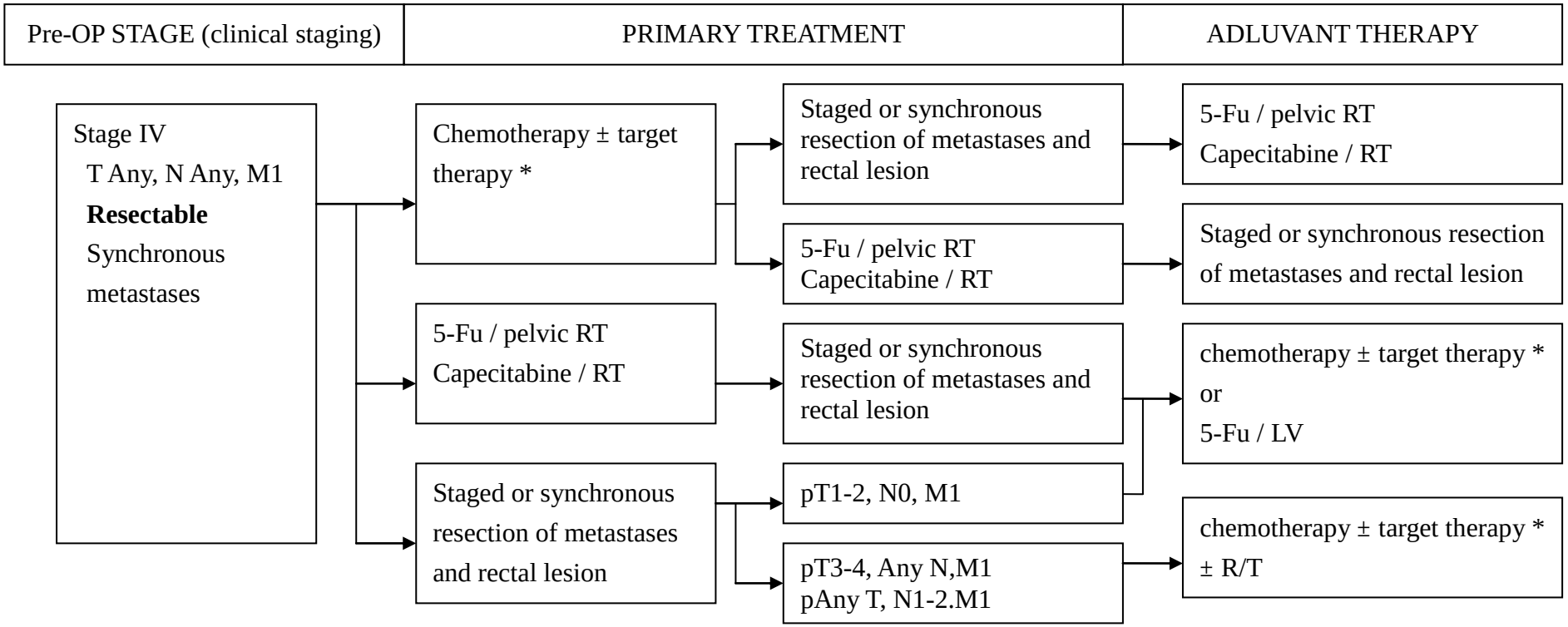


Post-operative management

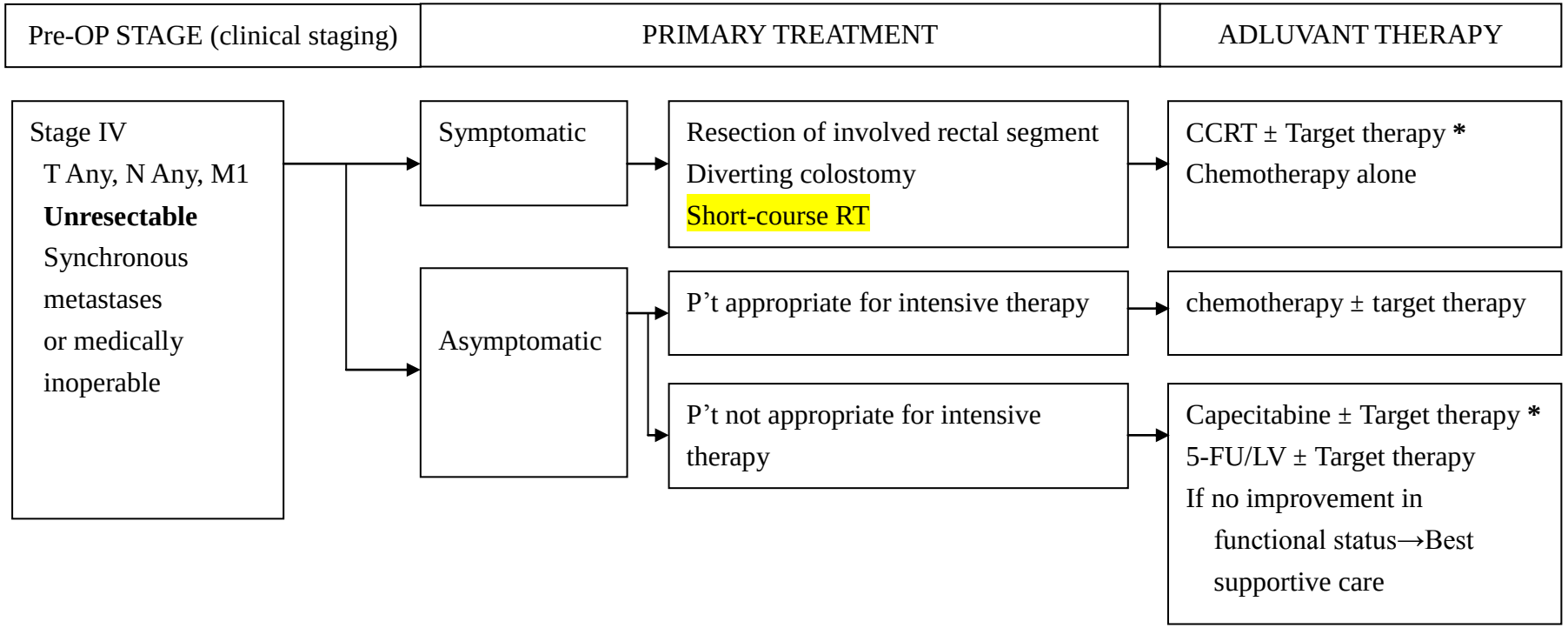
Pre-OP STAGE (clinical staging)	SURGERY	SURGICAL PATHOLOGY	ADJUVANT THERAPY
Stage II and stage III (Patients with medical contraindication to combined modality therapy)	Transabdominal resection	Stage I	- Observe
		Stage II	- CCRT followed by adjuvant Chemotherapy* - observe - adjuvant Chemotherapy
		Stage III	-CCRT followed by adjuvant Chemotherapy*

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

Post-operative management

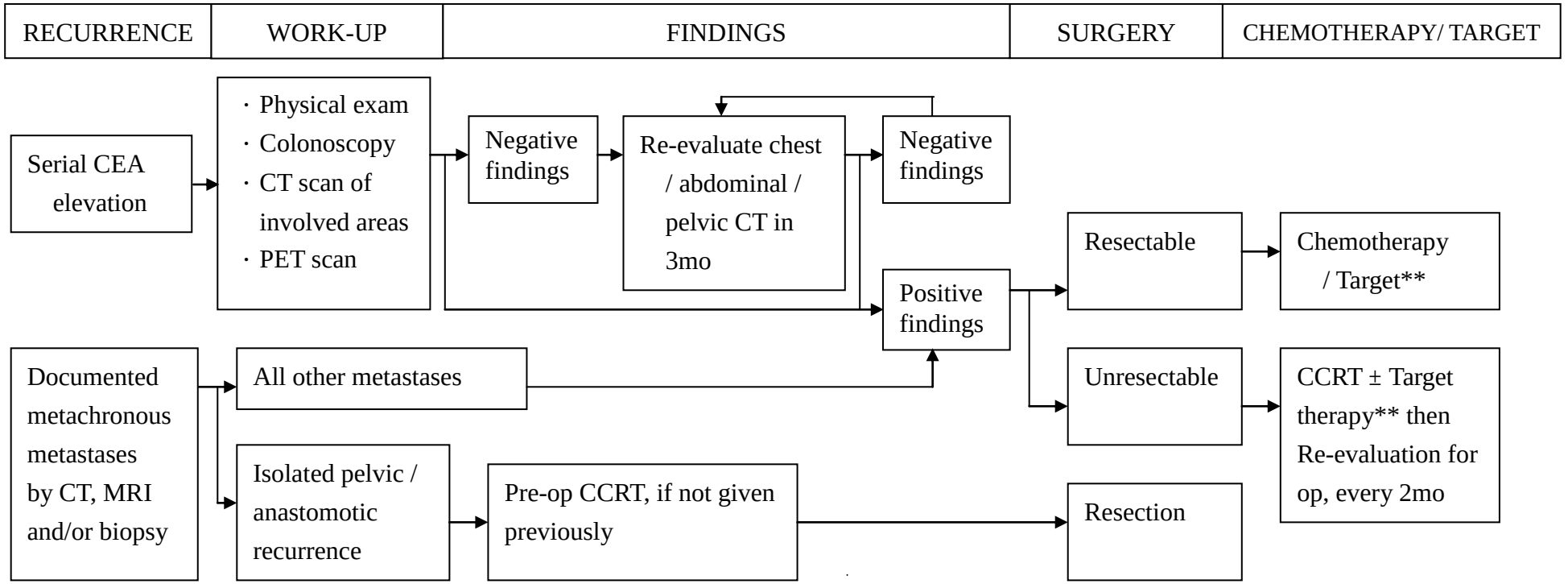


Post-operative management



* Target therapy: See page 11

Initial management for recurrence



** Target therapy: bevacizumab / Cetuximab (K-ras wild-type only):See page 12

**** Target therapy:**

Cetuximab(Erbitux)健保適應症：

(1) 與 FOLFIRI (Folinic acid/ 5- fluorouracil/irinotecan)或 FOLFOX (Folinic acid/ 5-fluorouracil /oxaliplatin) 合併使用於治療具表皮生長因子受體表現型 (EGFR expressing)，RAS 原生型之轉移性直腸結腸癌病患之第一線治療。

I.本藥品需經事前審查核准後使用，每次申請事前審查之療程以 18 週為限，再次申請必須提出客觀證據（如：影像學）證實無惡化，才可繼續使用。

II. 使用總療程以 36 週為上限。

III.本藥品不得與 bevacizumab 併用。

(2)與 irinotecan 合併使用，治療已接受過含 5-fluorouracil (5-FU)、irinotecan 及 oxaliplatin 二線以上之細胞毒性治療失敗、具有表皮生長因子受體(EGFR)表現型且 K-ras 基因沒有突變的轉移性直腸結腸癌的病患。

I. 本藥需經事前審查核准後使用，每次申請事前審查之療程以 9 週為限，再次申請必須提出客觀證據（如：影像學）證實無惡化，才可繼續使用。

II. 使用總療程以 18 週為上限

**** Target therapy:**

Bevacizumab (Avastin) 健保適應症：

(1)Bevacizumab 與含有 irinotecan/ 5-fluorouracil/ leucovorin 或 5-fluorouracil/ leucovorin 的化學療法合併使用，作為轉移性大腸或直腸癌患者的第一線治療。

(2)使用總療程以 36 週為上限。

(3)本藥須經事前審查核准後使用，每次申請事前審查之療程以 18 週為限，再次申請必須提出客觀證據（如：影像學）證實無惡化，才可繼續使用。

Panitumumab (Vectibix)健保適應症：

單獨使用治療已接受過含 5-fluorouracil(5-FU)、irinotecan 與 oxaliplatin 二線以上之細胞毒性治療失敗、具有表皮生長因子受體(EGF 表現型且 K-RAS 基因沒有突變的轉移性直腸結腸癌的病患。

Regorafenib (Stivarga) 健保適應症：

(1)用於治療先前曾接受下列療法的轉移性大腸直腸癌(mCRC)患者，療法包括fluoropyrimidine-、oxaliplatin-、irinotecan-為基礎的化療，和抗血管內皮生長因子(anti-VEGF)等療法；若K-ras為原生型(wild type)，則需接受過抗表皮生長因子受體(anti-EGFR)療法。

(2)須經事前審查核准後使用，每次申請事前審查之療程以8週為限，再次申請必須提出客觀證據（如：影像學）證實無惡化，才可繼續使用。

Monitoring / Surveillance

Time	Pre-CCRT	Post-CCRT	3M	6M	9M	1yr	3M	6M	9M	2yrs	6M	3yrs	6M	4yrs	6M	5yrs
Physical exam	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
CEA	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
CXR	O					O				O		O		O		O
Sono of liver				O				O			O		O		O	
Whole abdominal CT						O				O		O		O		O
Pelvis MRI	O	O														
Colonoscopy	O	O				O				O						O

PRINCIPLES OF ADJUVANT THERAPY

Postoperative Adjuvant Chemotherapy:

1. mFOLFOX 6

Oxalip<oxalipatin> 85mg/m² IV 2 hours, days 1

Leucovorin 400mg/m² IV 2 hours, days 1

5-Fluorouracil 400 mg/m² IV bolus, days 1

5-Fluorouracil 1200 mg/m² IV continuous infusion, days 1-2

Repeat every 2 week x 12 cycles

2. Capecitabine

850-1250 mg/m² PO twice daily, days 1-14

Repeat every 3 weeks x 8 cycles

3. CapeOx

Oxaliplatin 130 mg/ m² IV over 2 hours, day 1

Capecitabine 850-1000 mg/ m² twice daily PO for 14 days

Repeat every 3 weeks x 8 cycles

4. LV5FU2 (de Gramont regimen)

• 5-Fluorouracil: 400 mg/m 2 IV bolus, followed by 600 mg/m 2 IV continuous infusion for 22 hours on days 1 and 2

• Leucovorin: 200 mg/m 2 IV on days 1 and 2 as a 2-hour infusion before 5-fluorouracil

• Repeat cycle every 2 weeks for a total of 12 cycles

5.UFUR <Tegafur 100mg + Uracil 224mg >

350-500 mg/m² PO once daily

*Reference: see page 17

Dosing Schedules for Concurrent Chemotherapy/RT:

1. UFUR <Tegafur 100mg + Uracil 224mg >

350-500 mg/m²PO once daily

2.Capecitabine

825-1250 mg/m²PO twice daily, days 1-14

Repeat every 3 weeks

3. DeGramont (5-Fu x2 days)

Leucovorin 200mg/m²IV 2 hours, days 1-2

5-Fluorouracil 400 mg/m²IV bolus, days 1-2

5-Fluorouracil 600 mg/m²IV continuous infusion, days 1-2

Repeat every 2 weeks

***Reference: see page 18**

CHEMOTHERAPY FOR ADVANCED OR METASTATIC DISEASE - CHEMOTHERAPY REGIMENS

1. mFOLFOX 6

Oxalip<oxalipatin> 85mg/m²IV 2 hours, days 1

Leucovorin 400mg/m²IV 2 hours, days 1

5-Fluorouracil 400 mg/m²IV bolus, days 1

5-Fluorouracil 1200 mg/m²IV continuous infusion, days 1-2

Repeat every 2 week x 12 cycles

2. Cetuximab + FOLFOX

Oxaliplatin 85mg/m^2 IV over 2 hours, day 1

Leucovorin 400mg/m^2 IV over 2 hours, day 1

5-FU 400mg/m2 IV bolus on day 1, then 1200mg/m^2/day x 2 days (total 2400mg/m^2 over 46-48 hrs) IV continuous infusion

Repeat every 2 weeks

Cetuximab 400mg/m^2 IV over 2 hours first infusion, 250mg/m^2 IV over 60 minutes weekly

or Cetuximab 500mg/m^2 IV over 2 hours, day 1, every 2 weeks

Repeat every 2 weeks

3. CapeOx

Oxaliplatin 130 mg/ m²IV over 2 hours, day 1

Capecitabine 850-1000 mg/ m²twice daily PO for 14 days

Repeat every 3 weeks x 8 cycles

4. CapeOX+ Bevacizumab

Oxaliplatin 130mg/m^2 IV over 2 hours, day 1

Capecitabine 850-1000mg/m^2 PO twice daily for 14 days

Bevacizumab 7.5 mg/kg IV , day 1

Repeat every 3 weeks

5.FOLFIRI

Irinotecan 180 mg/m2 IV over 30–90 minutes, day 1

Leucovorin* 400 mg/m2 IV infusion to match duration of irinotecan infusion, day 1

5-FU 400 mg/m2 IV bolus day 1, then 1200 mg/m2/day x 2 days (total 2400 mg/m2 over 46–48 hours)† continuous infusion

Repeat every 2 weeks

6. **FOLFIRI+ Bevacizumab**

Irinotecan 180 mg/m2 IV over 30–90 minutes, day 1

Leucovorin* 400 mg/m2 IV infusion to match duration of irinotecan infusion, day 1

5-FU 400 mg/m2 IV bolus day 1, then 1200 mg/m2/day x 2 days (total 2400 mg/m2 over 46–48 hours)† IV continuous infusion

Bevacizumab 5 mg/kg IV, day 1

Repeat every 2 weeks

7. FOLFIRI+Cetuximab

Irinotecan 180mg/m^2 IV over30-90 minutes, day 1

Leucovorin 400mg/m^2 IV infusion to match duration of irinotecan infusion day 1

5-FU 400mg/m^2 IV bolus on day 1, then 1200mg/m^2/day x 2 days (total 2400mg/m^2 over 46-48 hrs) IV continuous infusion

Repeat every 2 weeks

Cetuximab 400mg/m^2 IV over 2 hours first infusion, 250mg/m^2 IV over 60 minutes weekly

or Cetuximab 500mg/m^2 IV over 2 hours, day 1, every 2 weeks

Repeat every 2 weeks

8. FOLFIRI + ziv-aflibercept

Irinotecan 180 mg/ m^2 IV over 30-90 minutes , day 1

Leucovorin 400mg/m^2 IV ,day 1

5-Fu 400mg/m2 IV bolus day 1,then 1200mg/m2/day x2 days , continuous infusion.

Ziv-aflibercept 4mg/kg IV

Repeat every 2 weeks.

* Irinotecan 健保適應症: 限轉移性大腸直腸癌之第一線治療藥物

(1)與 5-FU 及 folinic acid 合併，使用於未曾接受過化學治療之患者。

(2)單獨使用於曾接受 5-FU 療程治療無效之患者。

9. Capecitabine

850-1250 mg/m^2 PO twice daily, days 1-14

Repeat every 3 weeks

10. IROX

Oxaliplatin 85mg/m^2 IV over 2 hours, followed by irinotecan 200mg/m^2

over 30~90 minutes every 3 weeks

11. FOLFOXIRI

Irinotecan 165mg/m^2 IV day 1,

oxaliplatin 85mg/m^2 day 1,leucovorin 400 mg/m^2 day 1,

fluorouracil 1600mg/m^2/day x 2 days (total 3200mg/m^2 over 48 hours) continuous infusion starting on day 1.

Repeat every 2 weeks

12. Irinotecan

Irinotecan 125mg/m^2 IV over 30~90 minutes, day1 and day 8

Repeat every 3 weeks

or Irinotecan 180mg/m^2 IV over 30~90 minutes, day1

Repeat every 2 weeks

or Irinotecan 300~350mg/m^2 IV over 30~90 minutes, day1

Repeat every 3 weeks

13. Regorafenib

Regorafenib 160mg PO daily days 1-21

Repeat every 28 days

14. UFUR <Tegafur 100mg + Uracil 224mg >

350-500 mg/m^2 PO once daily

15. panitumumab*(KRAS/NRAS WT only)*

FOLFOX4 + Panitumumab (for patients with wild-type KRAS)

Panitumumab (Vectibix) 6 mg/kg iv over 60 min q2w

Leucovorin 200 mg/m2 iv over 2 hrs before 5-FU, d1 and 2

5-FU 400 mg/m2 iv bolus and then 600 mg/m2 iv over 22 hrs, d 1 and d2

Oxaliplatin (Eloxatin) 85 mg/m2 iv d1

Q2w until progressive disease

16. mFOLFOX + Bevacizumab

• Oxaliplatin: 85 mg/m 2 IV on day 1

• 5-Fluorouracil: 400 mg/m 2 IV bolus on day 1, followed by 2400 mg/m 2 IV continuous infusion for 46 hours

• Leucovorin: 400 mg/m 2 IV on day 1 as a 2-hour infusion, before 5-fluorouracil

• Bevacizumab: 5 mg/kg IV on day1 every 2 weeks

• Repeat cycle every 2 weeks

References(ADJUVANT THERAPY)

1. mFOLFOX 6

- [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.

-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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12177775.

-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.

2. Capecitabine

Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. N Engl J Med 2005;352(26):2696-2704.

3. CapeOx

- Schmoll HJ, Cartwright T, Tabernero J, et al. Phase III trial of capecitabine plus oxaliplatin as adjuvant therapy for stage III colon cancer: a planned safety analysis in 1,864 patients. J Clin Oncol 2007;25:102-109.

-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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21383294.

4. LV5FU2 (de Gramont regimen)

Wolmark N et al. A phase III trial comparing FULV to FULV + oxaliplatin in stage II or III carcinoma of the colon: survival results of NSABP protocol C-07. 2008 ASCO annual meeting. LBA4005 (link to the abstract).

References(Dosing Schedules for Concurrent Chemotherapy/RT)

1. UFUR

Journal of Clinical Oncology Volume 24, Number 13, May 1, 2005.

Int.J. Raditiona Oncology Biol.Phys., Vol.79, No. 1,pp.102-110, 2008.

Langenbeck's Arch Surg(2002)386;575-581.

British Journal of Cancer(2007)96, 1170-1177.

Journal of Clinical Oncology Volume 22, Number 15, August 1, 2004.

Int.J. Raditiona Oncology Biol.Phys., Vol.45, No. 3,pp.629-634, 1999.

Annals of Oncology Advance Access published April 1, 2008/10/14 Jpn Clin Oncol 2006;36(4)237-244.

J Gastrointest Surg. 2011 Dec;15(12):2239-45.

T.Kato,Y.Ohashi,et al.Efficacy of oral UFT as adjuvant chemotherapy to curative resection of colorectal cancar:multicenter prospective randomized trial.Original Article2002;386:575-581.

R. Scalamogna,S Brugnatelli,et al.UFT as maintenance therapy in patients with advanced colorectal cancer responsive to the FOLFOX4 regimen.Oncology 2007;72:267-273.

2. Capecitabine

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.

3. DeGramont

de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French Intergroup study. *J Clin Oncol* 1997; 15:808-815

References(ADVANCED OR METASTATIC DISEASE)

1. mFOLFOX 6

1Andre 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.

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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12177775.

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.

2. Cetuximab + FOLFOX

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.Available at:http://www.ncbi.nlm.nih.gov/pubmed/12177775.

3. CapeOx

deGramont A, Figer A, Seymour M, et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced rectal cancer. J Clin Oncol 2000;18:2938-2947.

4. CapeOX+ Bevacizumab

deGramont A, Figer A, Seymour M, et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced rectal cancer. J Clin Oncol 2000;18:2938-2947.

saltz LB, Clarke S, Diaz-Rubio E, et al. Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: a randomized phase III study. J Clin Oncol 2008;26:2013-2019. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18421054.

5.FOLFIRI

Andre T, Louvet C, Maindrault-Goebel F, et al. CPT-11(irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. Eur J Cancer 1999;35(9):1343-7.

References(ADVANCED OR METASTATIC DISEASE)

6. FOLFIRI+ Bevacizumab

Andre T, Louvet C, Maindrault-Goebel F, et al. CPT-11(irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. Eur J Cancer 1999;35(9):1343-7.

Fuchs CS, Marshall J, Mitchell E, et al. Randomized,controlled trial of irinotecan plus infusional, bolus, or oral fluoropyrimidines in first-line treatment of metastatic colorectal cancer: results from the BICC-C Study. J Clin Oncol 2007;25:4779-4786. Available at:http://www.ncbi.nlm.nih.gov/pubmed/17947725.

7. FOLFIRI+Cetuximab

Andre T, Louvet C, Maindrault-Goebel F, et al. CPT-11(irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. Eur J Cancer 1999;35(9):1343-7.

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 randomized, open-label, phase 3 trial.Lancet Oncol 2014. Available: http://www.ncbi.nlm.nih.gov/pubmed/25088940.

8. FOLFIRI + ziv-aflibercept

Andre T, Louvet C, Maindrault-Goebel F, et al. CPT-11(irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. Eur J Cancer 1999;35(9):1343-7.

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. Available at:http://www.ncbi.nlm.nih.gov/pubmed/22949147.

9. Capecitabine

Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. N Engl J Med 2005;352(26):2696-2704.

References(ADVANCED OR METASTATIC DISEASE)

10. IROX

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.

11. FOLFOXIRI

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.

12. Irinotecan

Loupakis F, Cremolini C, Masi G, et al. FOLFOXIRI plus

bevacizumab (bev) versus FOLFIRI plus bev as first-line treatment of metastatic colorectal cancer (MCRC): results of the phase III randomized TRIBE trial. J Clin Oncol 2013;31(Suppl 4): Abstract 336.

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.

13. Regorafenib

Van Custem 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.

14. UFUR

Journal of Clinical Oncology Volume 24, Number 13, May 1, 2005.

Int.J. Raditiona Oncology Biol.Phys., Vol.79, No. 1,pp.102-110, 2008.

Langenbeck's Arch Surg(2002)386;575-581.

British Journal of Cancer(2007)96, 1170-1177.

Journal of Clinical Oncology Volume 22, Number 15, August 1, 2004.

Int.J. Raditiona Oncology Biol.Phys., Vol.45, No. 3,pp.629-634, 1999.

Annals of Oncology Advance Access published April 1, 2008/10/14 Jpn Clin Oncol 2006;36(4)237-244.
J Gastrointest Surg. 2011 Dec;15(12):2239-45.
T.Kato,Y.Ohashi,et al.Efficacy of oral UFT as adjuvant chemotherapy to curative resection of colorectal cancar:multicenter prospective randomized trial.Original Article2002;386:575-581.
R. Scalamogna,S Brugnatelli,et al.UFT as maintenance therapy in patients with advanced colorectal cancer responsive to the FOLFOX4 regimen.Oncology 2007;72:267-273.
15. **panitumumab**
Van Custem 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.
16. mFOLFOX + Bevacizumab
Douillard JY, Oliner KS, Siena S, et al. Panitumumab – FOLFOX4 treatment and RAS mutations in colorectal cancer. N Engl J Med 2013;369:1023-34.

Principles of Radiation Therapy

一、 放射治療的適應症（直腸癌）

（一）若屬於 T2，只進行局部切除(local excision)應考慮輔助性合併化學放射治療(post-operative adjuvant CCRT)。

（二）第 II 及 III 期並可局部切除可進行手術前進行合併化學放射治療（pre-operative CCRT)，或在手術後進行輔助性合併化學放射治療（post-operative adjuvant CCRT)。

（三）第 III 期（T4 或局部無法切除)可考慮同步化學放射治療（CCRT)。

（四）第 IV 期: 針對轉移部位(如骨骼、腦等部位)施行緩解性放射治療

(五)手術中放射線治療(Intraoperative radiation therapy)可適用於考慮手術切除後邊緣非常接近或陽性、患者屬於 T4 及復發性癌症。

二、 放射治療技術

(一) 定位與照野設計

1. 採用舒適之仰臥姿勢，視狀況考慮施用固定器，若腹部凸出者，考慮以俯臥姿勢，並使用腹式板(belly board)。

2. 以電腦斷層進行定位，勾劃出腫瘤體積 (gross tumor volume, GTV) 和計劃靶區體積(planning target volume, PTV)的位置。

3. 採用三度空間順形技術(3-D conformal technique)或強度調控放射治療 (intensity modulated radiation therapy)，臨床腫瘤體積(clinical tumor volume, CTV)應包括 GTV 外加 2 公分邊界及骨盆淋巴區域 (包括 presacral, pelvic mesentery, internal iliac nodes)

4. 進行局部劑量追加時，照野應包括原始 GTV 外加 1-2 公分和薦骨前區。

5. PTV 為 CTV 外加 5 – 10mm

Principles of Radiation Therapy

(二) 劑量給予：

1. 建議療程應以標準分次進行(每日一次、每週 5-6 次)。

2. 若手術前放射治療，劑量應為 45.0 – 50.4 Gy / 25 – 28 分次

3.若手術中放射治療(Intraoperative radiation therapy)，劑量應為 12.0-20.0Gy

4. 若手術後放射治療，首先給予劑量應為 45.0 – 50.4 Gy / 25 – 28 分次後，及後進行局部劑量追加，再給予劑量應為 5.4 – 9.0 Gy / 3 – 5 分次

5. 三度空間順形放射治療 (3-D conformal radiotherapy)方式給予每次 1.8 Gy，總劑量為 45.0 – 50.4 Gy / 25 – 28 分次。

(三) 劑量限制 (dose constrain)：

1. 小腸：45 Gy – 50 Gy

2. 股骨頭：42 Gy

3. 膀胱：65 Gy

4. 直腸：60 Gy

參考資料:

1. NCCN clinical practice guideline in oncology-Colorectal cancer (V.1.2015)
2. 國家衛生研究院大腸直腸癌診斷與治療之共識(八十七年十月出版)
3. 亞東紀念醫院直腸癌放射治療標準政策與執行規範(2010-06-22 版)

STAGE CATEGORY DEFINITIONS	
PRIMARY TUMOR (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria*
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into pericolorectal tissues
T4a	Tumor penetrates to the surface of the visceral peritoneum**
T4b	Tumor directly invades or is adherent to other organs or structures^,**
*Note: Tis includes cancer cells confined within the glandular basement membrane (intraepithelial) or mucosal lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa. ^Note: Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retro-peritoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (i.e., respectively, a tumor on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix or vagina). **Tumor that is adherent to other organs or structures, grossly, is classified cT4b.However, if no tumor is present in the adhesion, microscopically, the classificationshould be pT1-4a depending on the anatomical depth of wall invasion. The V andL classifications should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN site-specific factor should be used for perineural invasion.	

REGIONAL LYMPH NODES (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 3 regional lymph nodes
N1a	Metastasis in 1 regional lymph node
N1b	Metastasis in 2-3 regional lymph nodes
N1c	Tumor deposit(s) in the subserosa, mesentery, or non-peritonealized pericolic or perirectal tissues without regional nodal metastasis
N2	Metastasis in 4 or more regional lymph nodes
N2a	Metastasis in 4 to 6 regional lymph nodes
N2b	Metastasis in 7 or more regional lymph nodes

Note: A satellite peritumoral nodule in the pericolorectal adipose tissue of a primary carcinoma without histologic evidence of residual lymph node in the nodule may represent discontinuous spread, venous invasion with extravascular spread (V1/2) or a totally replaced lymph node (N1/2). Replaced nodes should be counted separately as positive nodes in the N category, whereas discontinuous spread or venous invasion should be classified and counted in the Site-Specific Factor category Tumor Deposits (TD).

DISTANT METASTASIS (M)	
M0	No distant metastasis (no pathologic M0; use clinical M to complete stage group)
M1	Distant metastasis
M1a	Metastasis confined to one organ or site (e.g., liver, lung, ovary, non-regional node).
M1b	Metastases in more than one organ/site or the peritoneum.

ANATOMIC STAGE • P ROGNOSTIC GROUPS					
GROUP	T	N	M	Dukes*	MAC*
0	Tis	N0	M0	-	-
I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
IIA	T3	N0	M0	B	B2
IIB	T4a	N0	M0	B	B2
IIC	T4b	N0	M0	B	B3
IIIA	T1-T2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3-T4a	N1/N1c	M0	C	C2
	T2-T3	N2a	M0	C	C1/C2
	T1-T2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3-T4a	N2b	M0	C	C2
	T4b	N1-N2	M0	C	C3
IVA	Any T	Any N	M1a	-	-
IVB	Any T	Any N	M1b	-	-
*Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (Any TN1 M0 and Any T N2 M0). MAC is the modified Astler-Coller classification.					
Stage unknown					