

大腸癌診療指引

大腸直腸癌醫療團隊修訂

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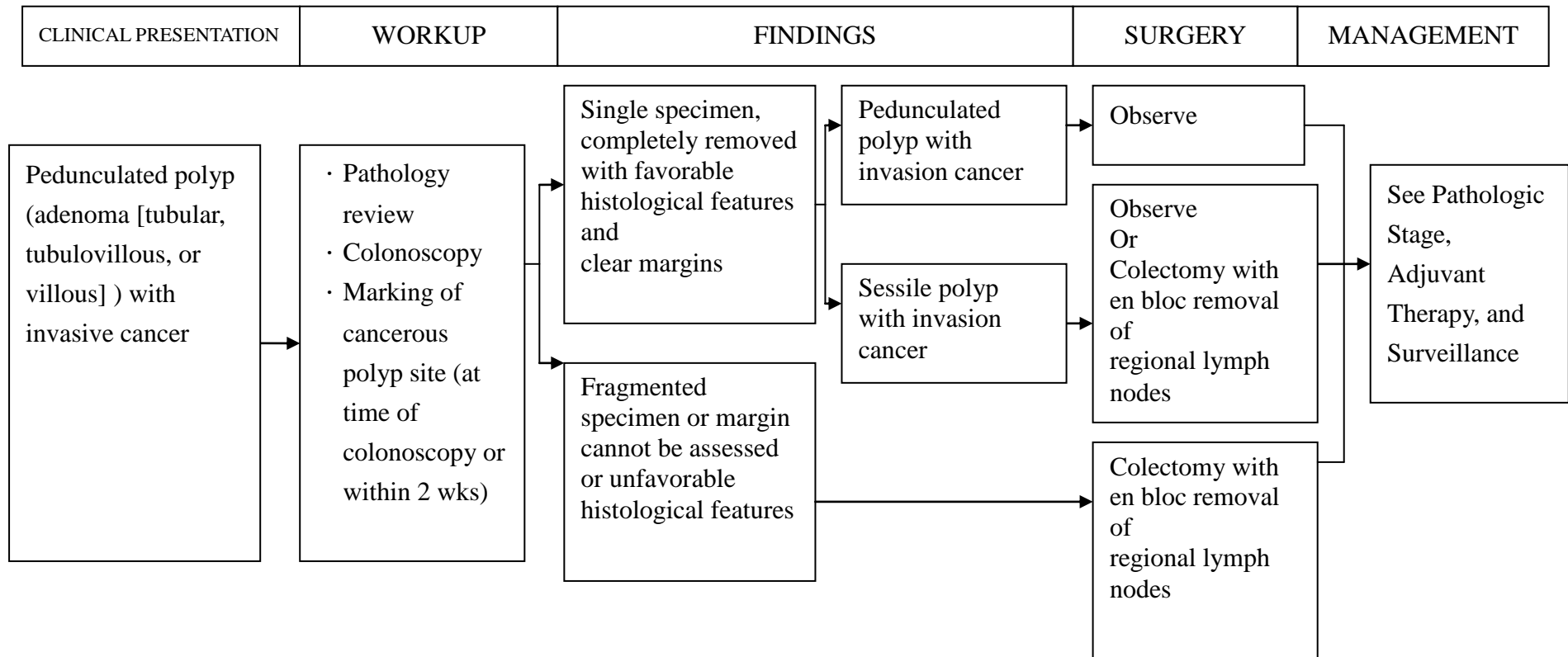
參考資料：

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2. 全民健康保局醫療給付標準行政院衛生署一百零三年版
3. Physicians' Cancer Chemotherapy Drug Manual 2010

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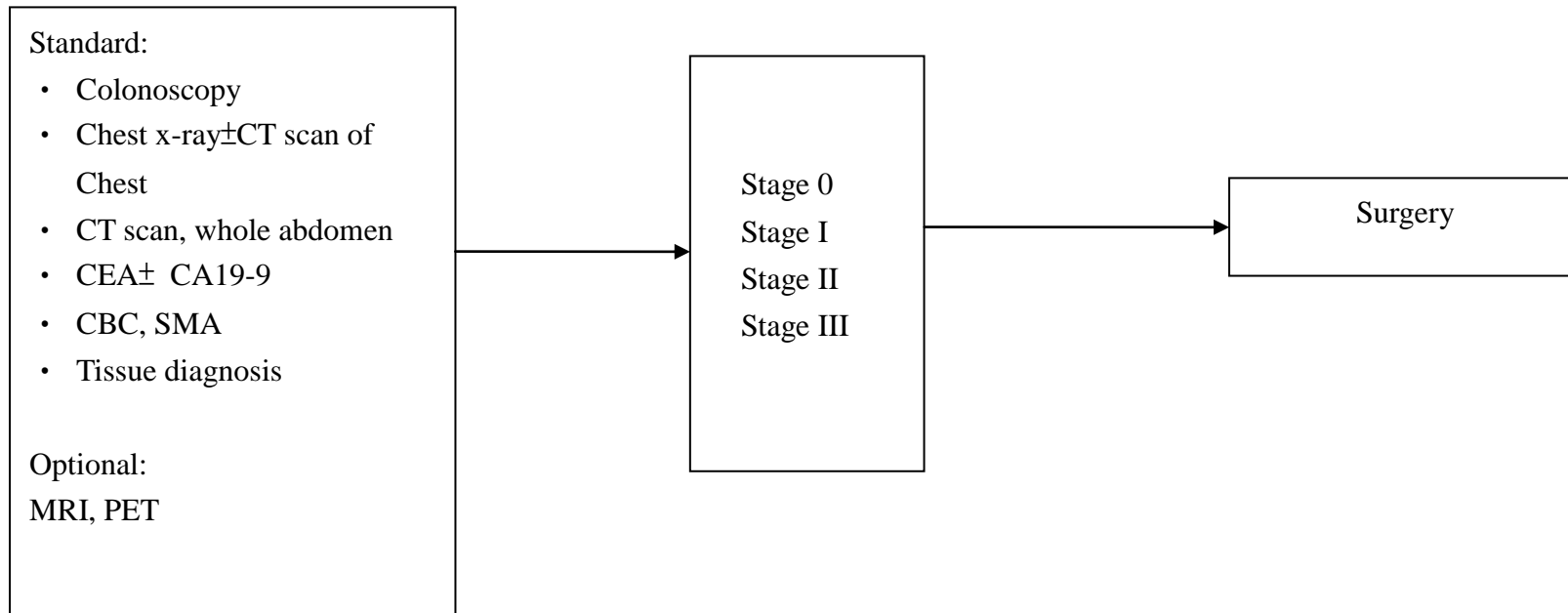
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Malignant Polyp of Colon



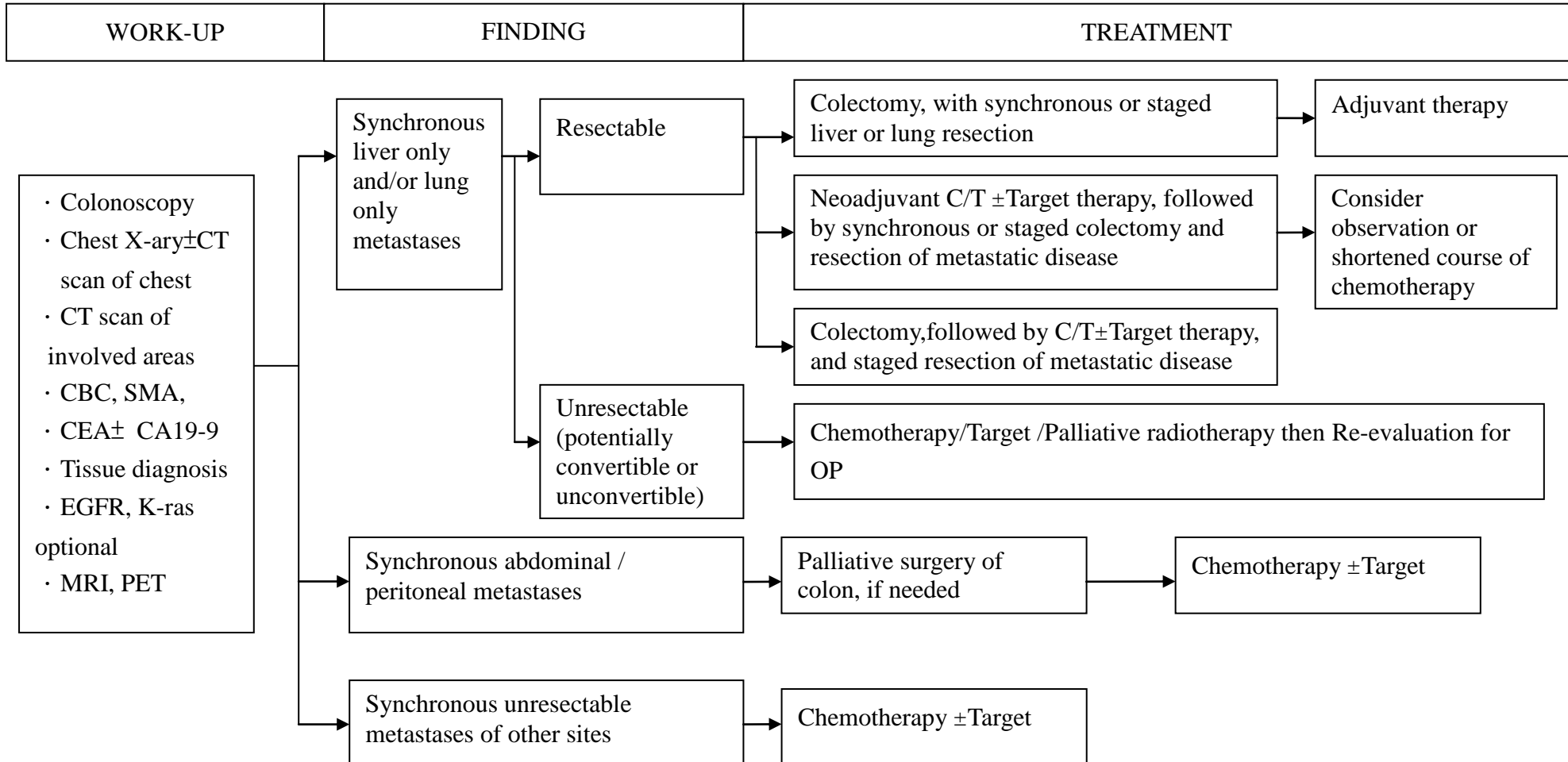
Initial management for stage 0, I, II, III disease

WORK-UP	STAGE *	INITIAL THERAPY
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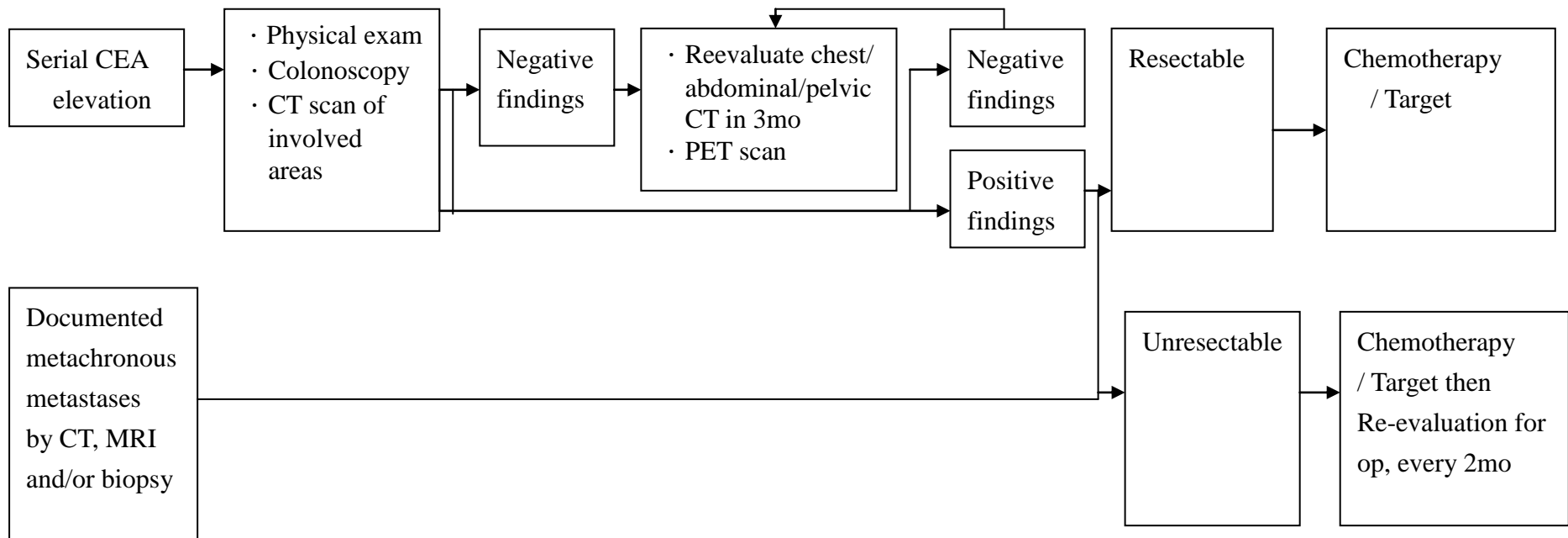
* Colon cancer 之分期依 7th AJCC staging.

Initial management for stage IV disease



Initial management for recurrence

RECURRENCE	WORK-UP	FINDING	SURGERY	CHEMOTHERAPY/TARGET
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PATHOLOGIC STAGE	ADJUVANT THERAPY
Stage 0 / stage I	None
Stage II A (Without risk factors*)	None/ UFUR/Capecitabine
Stage II A (With risk factors *) Stage II B Stage II C ***	5FU/LV/ UFUR/ FOLFOX./ Capecitabine
Stage III***	5FU/LV / FOLFOX / UFUR / Capecitabine / CapeOx / FLOX
Stage IV	Salvage / palliative chemotherapy / Target therapy ** /Palliative radiotherapy***

* risk factor: poor differentiation, LVI, PNI, perforation, obstruction, < 12 lymph nodes examined, positive margins

**See page 6

***放射治療的適應症(大腸癌): (1)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。

(2)Stage IV: 針對轉移部位(如骨骼、腦等部位)施行緩解性放射治療 (3)對於 T4 合併侵犯其他固定的器官,可考慮 RT (4) 手術後病理檢驗結果證實沒有淋巴轉移,但在原發腫瘤切除邊緣接近或侵犯,而且能夠明確勾畫出此位置。

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 fractions
3. 若手術後放射治療,首先給予劑量應為 45.0 – 50.4 Gy / 25 – 28 fractions to whole pelvis 後,進行局部劑量追加 (tumor bed),再給予劑量 5.4 – 9.0 Gy / 3 – 5 fractions

**** Target therapy:**

Cetuximab(Erbitux) (K-ras wild-type only)健保適應症：

(1)與 FOLFIRI(Folinic acid/5-fluorouracil/irinotecan)合併使用於治療具表皮生長因子受體表現型(EGFR expressing)，K-ras 基因沒有突變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 12 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 24 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

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 24 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 12 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。

Follow-up

Time	Pre-Treatment	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
CEA	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		O
Colonoscopy	O				O				O						O

Principles of Adjuvant therapy -Chemotherapy Regimens

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

350-500 mg/m² PO once daily for 24 months

*健保適應症:直腸癌、結腸癌第Ⅱ、Ⅲ期患者之術後輔助性治療，且使用期限不得超過2年

2.Capecitabine*

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

Repeat every 3 weeks x 8 cycles

*健保適應症:第三期結腸癌患者手術後的輔助性療法，以八個療程為限

3.Capecitabine + Bevacizumab

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

Bevacizumab 7.5mg/kg IV,day 1

Repeat every 3 weeks

4.DeGramont (5-Fu x2 days)

Leucovorin 200mg/m² IV 2 hours, days 1-2

5-Fluorouracil 400 mg/m² IV bolus, days 1-2

5-Fluorouracil 600 mg/m² IV continuous infusion, days 1-2

Repeat every 2 weeks x 12 cycles

5. Bolus or infusional 5-FU/leucovorin (Roswell-Park regimen)

Leucovorin 500 mg/m² IV over 2 hours, days 1, 8, 15, 22, 29, and 36
5-Fluorouracil 500 mg/m² IV bolus 1 hour after start of leucovorin, days 1, 8, 15, 22, 29, 36

Repeat every 8 weeks for 3-4 cycles

6. CapeOx (Oxaliplatin+ Capecitabine)

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

7.CapeOX+ Bevacizumab

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

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

Bevacizumab 7.5 mg/kg IV , day 1

Repeat every 3 weeks

8.FLOX

Oxaliplatin 85 mg/m² IV administered on weeks 1, 3, and 5

5-Fluorouracil 500 mg/m² IV bolus weekly x 6

Leucovorin 500 mg/m² IV weekly x 6,

Repeat of each 8 week for total of 3 cycle for 3 cycles

9.FOLFOX4

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

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 x 12 cycles

10. 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

11.FOLFIRI + ziv-aflibercept

Irinotecan 180 mg/ m²IV over 30-90 minutes , day 1

Leucovorin 400mg/m²IV ,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。

12.Regorafenib

Regorafenib 160mg PO daily days 1-21

Repeat every 28 days

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

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5. XELOX

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6. FLOX

-Kuebler JP, Wieand HS, O'Connell MJ, et al. Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07. *J Clin Oncol* 2007;25:2198-2204.

7. mFOLFOX 6

Cassidy J, Clarke S, Diaz Rubio E, et al. Randomized phase III study of capecitabine plus oxaliplatin compared with fluorouracil/folinic acid plus oxaliplatin as first-line therapy for metastatic colorectal cancer. *J Clin Oncol* 2008;26:2006-12.

Reference

11. FOLFIRI + ziv-aflibercept

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>

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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 [^] ,**
<p>*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.</p> <p>[^]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).</p> <p>**Tumor that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumor is present in the adhesion, microscopically, the classification should be pT1-4a depending on the anatomical depth of wall invasion. The V and L 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.</p>	

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
<p>Note: A satellite peritumoral nodule in the pericorectal 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).</p>	

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					