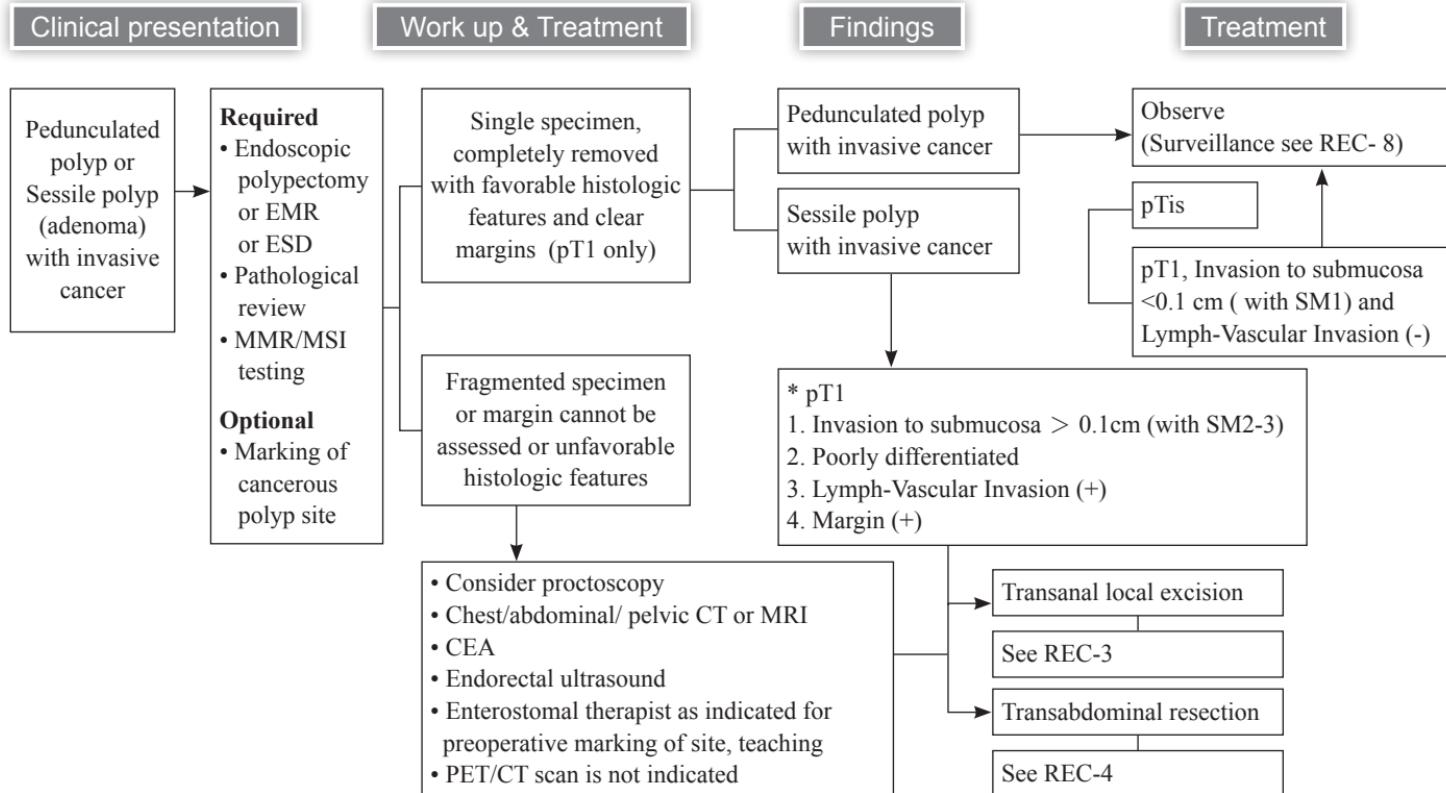


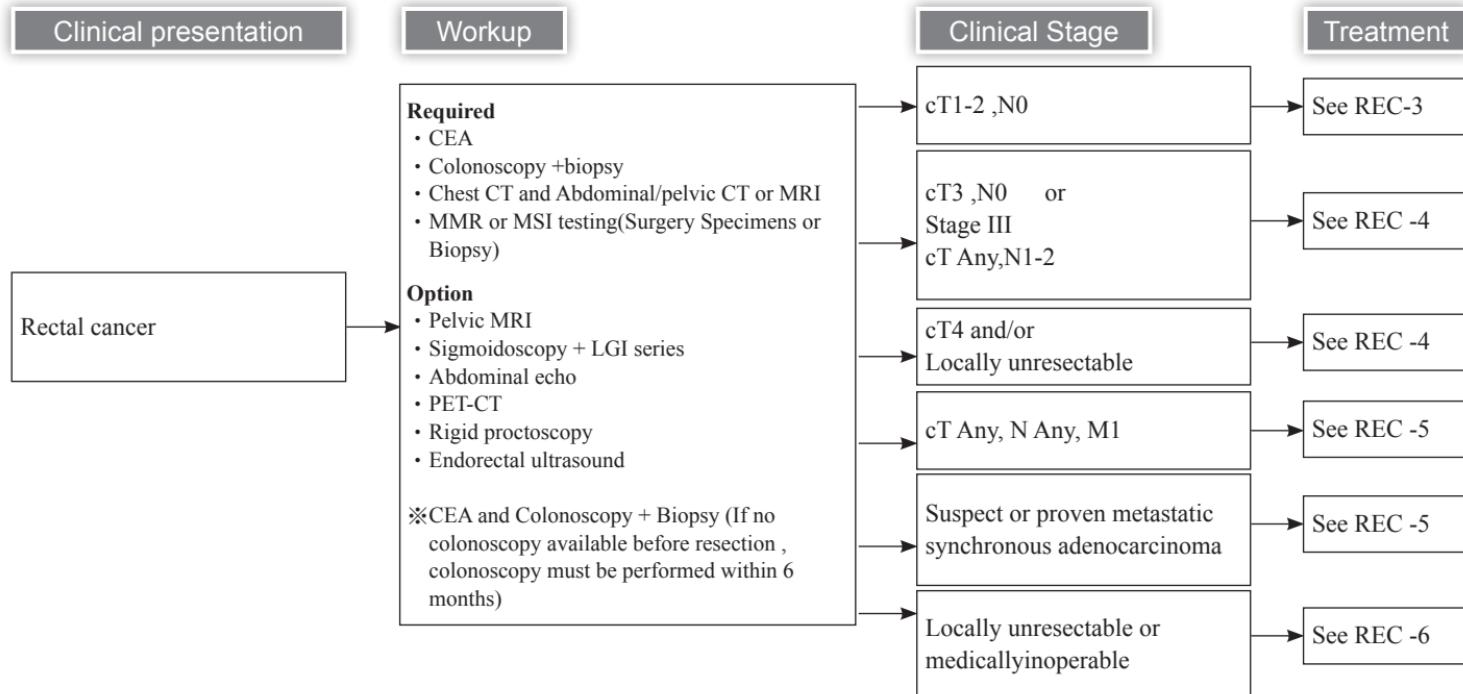


Colorectal Cancer

《 REC-1 》

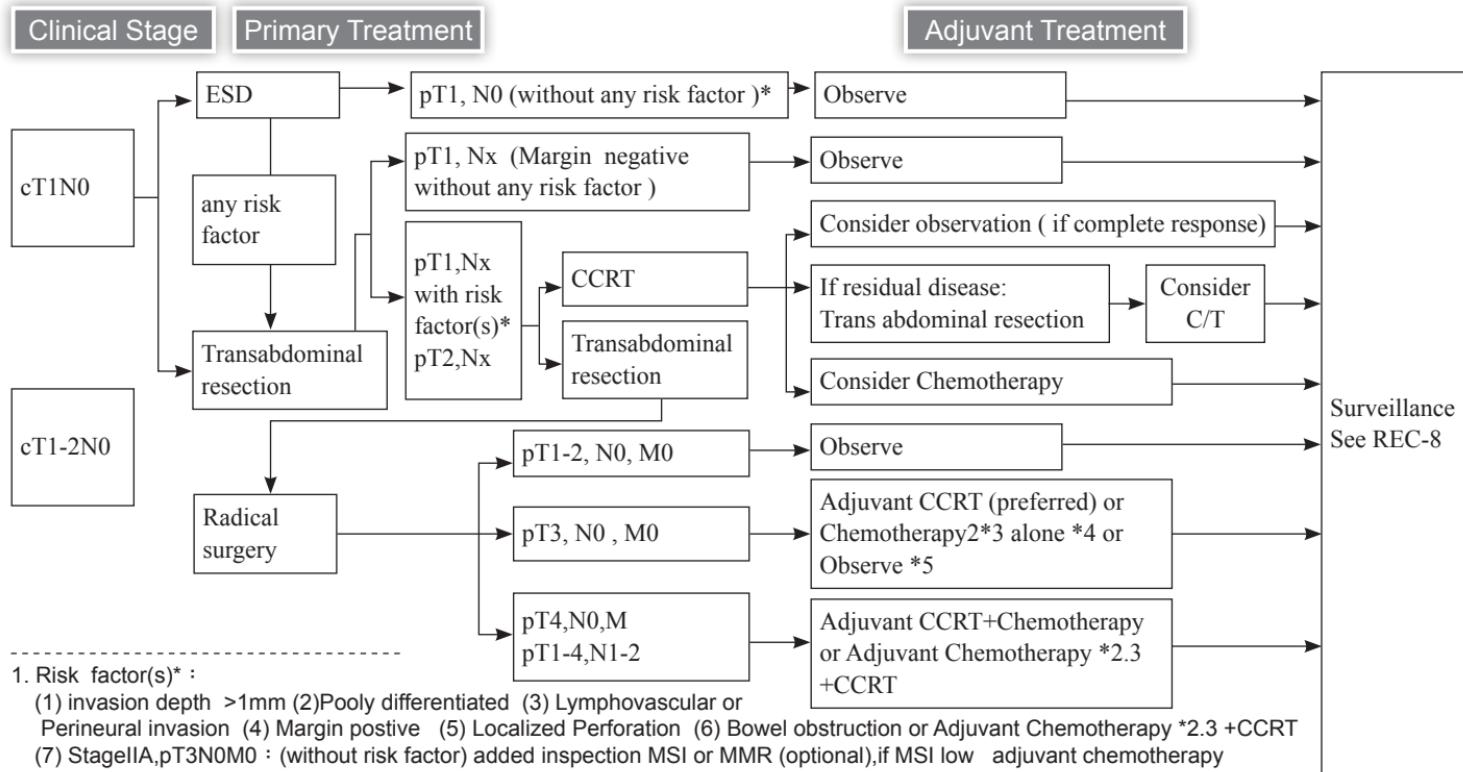


« REC-2 »



Definition of rectal cancer:

The distance from the lower edge of the lesion to the anus within 15 cm is the definition of rectal cancer. Lower third rectal cancer is 0-7 cm from anal verge. Middle third rectal cancer is 7.1-11cm from anal verge. Upper third rectal cancer is 11.1-15 cm from anal verge. For patients with locally advanced middle third and lower third rectal cancers, and age between 18-75 years old, neoadjuvant concurrent chemo-radiotherapy was recommended.



1. Risk factor(s)* :

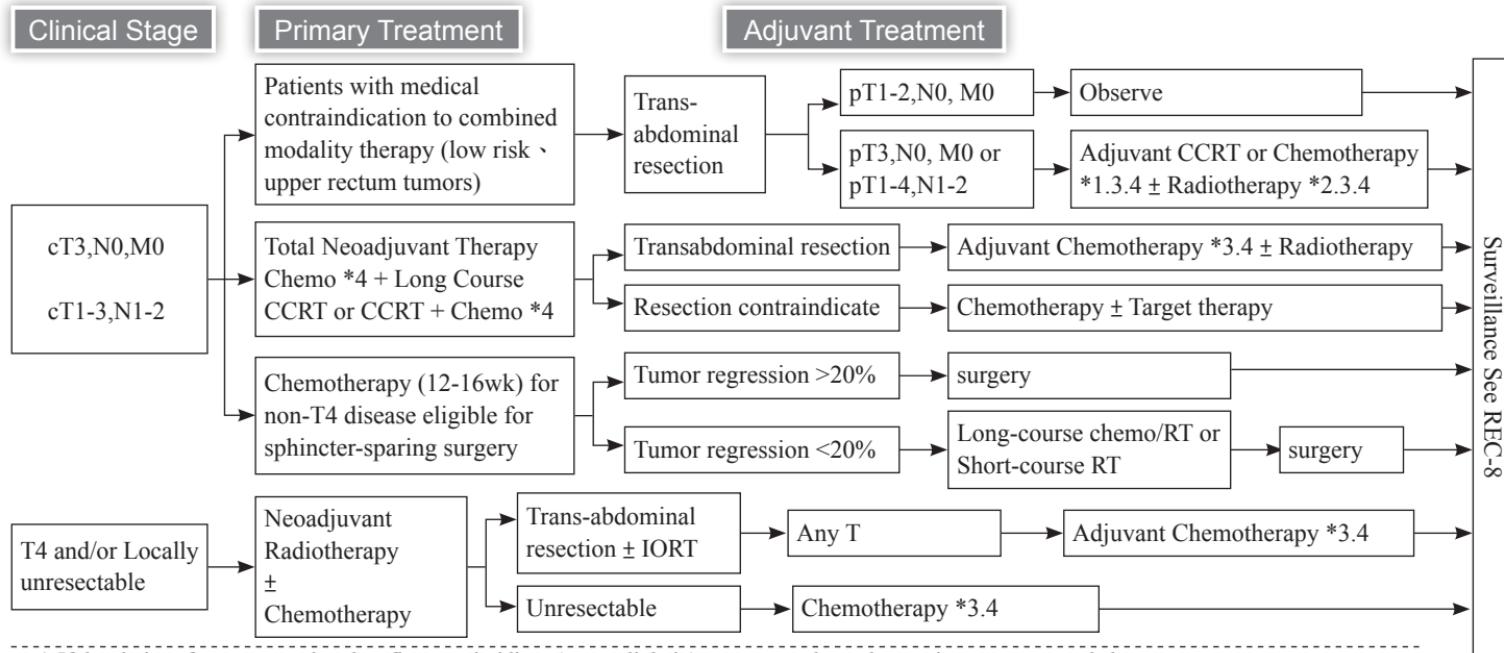
- (1) invasion depth >1mm (2) poorly differentiated (3) Lymphovascular or Perineural invasion (4) Margin positive (5) Localized Perforation (6) Bowel obstruction or Adjuvant Chemotherapy *2.3 +CCRT (7) Stage IIA, pT3N0M0 : (without risk factor) added inspection MSI or MMR (optional), if MSI low adjuvant chemotherapy

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

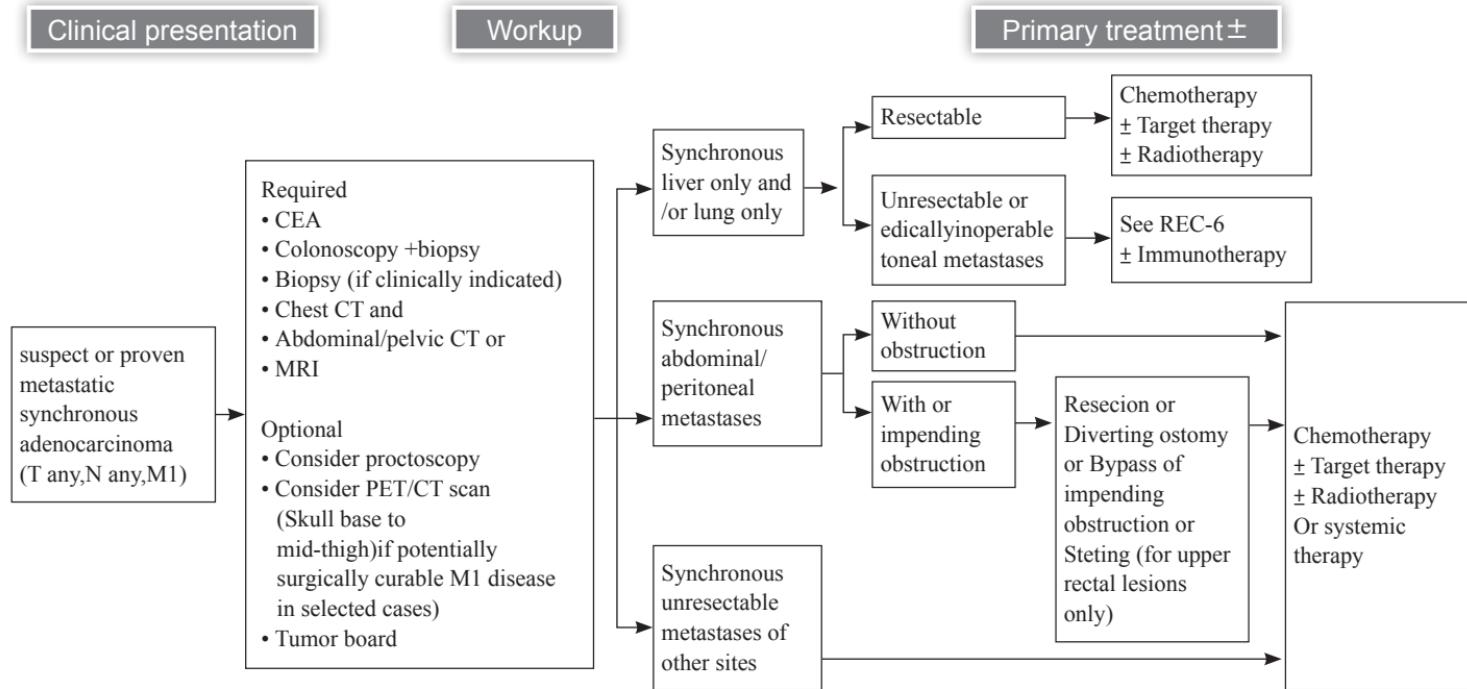
3. Only for R0 resection

4. Observe : only for upper rectum , G1/G2 , LVS(-), R0 resection & mesorectum invasion <2mm

《 REC-4 》

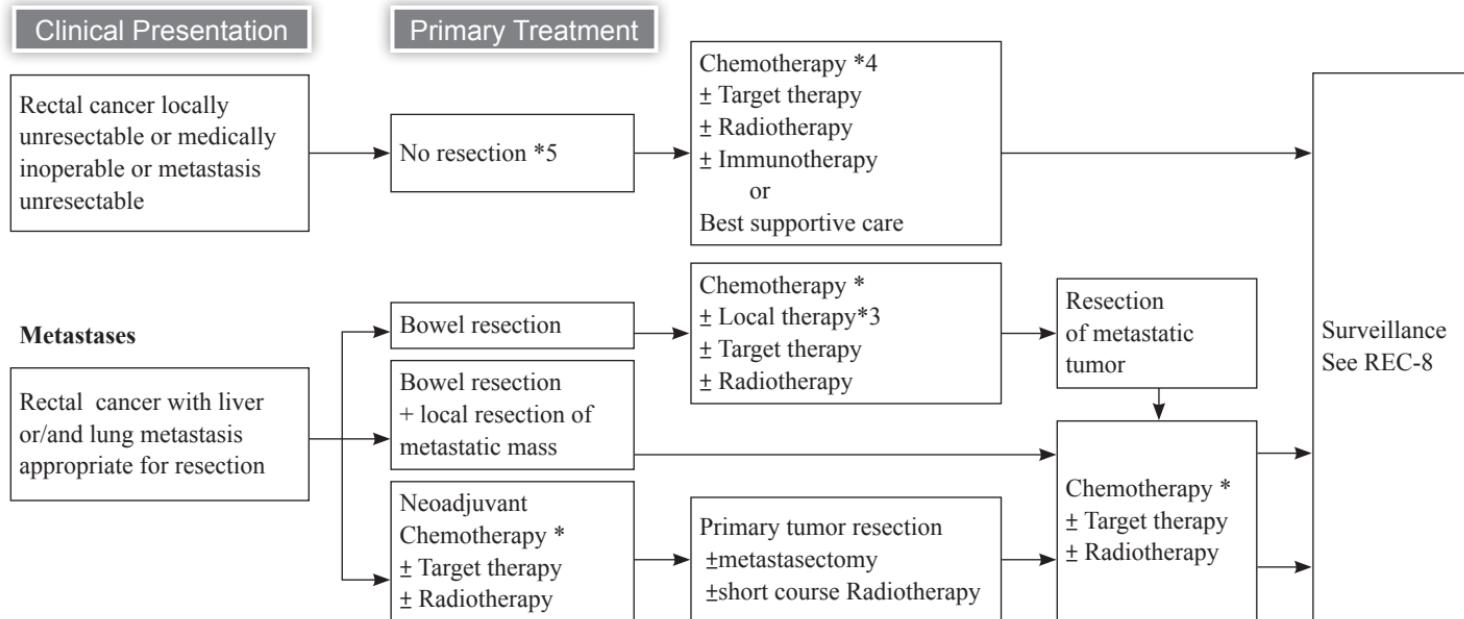


- * 1. If the choice of agents are other than fluoropyrimidines (eg, oxaliplatin) concurrent chemotherapy is not recommended.
- * 2. For patients with proximal T3, N0 disease with clear margins and favorable prognostic features, the incremental benefit of RT is limited. Chemotherapy alone is considered.
- * 3. For patients who are under 70 years old of age and ECOG: 0-2 points, we suggested standard combination chemotherapy.
- * 4. Post CCRT and before surgery maintenance add oral chemotherapy with 5-Fluorouracil base (optional)
- * 5. Surveillance recommendations include DRE, proctoscopy every 3-4 months for 2 years, then every 6 months for a total of 5 years. MRI rectum is recommended every 6 months for at least 3 years to monitor for extraluminal local recurrence.(considered)
- * 6. dMMR, MSI-H:checkpoint inhibitor immunotherapy.(considered)
- * 7. Consider PIK3CA testing for stage II-III. If PIK3CA mutation, add aspirin 100-162 mg PO daily for 3 years following surgery.



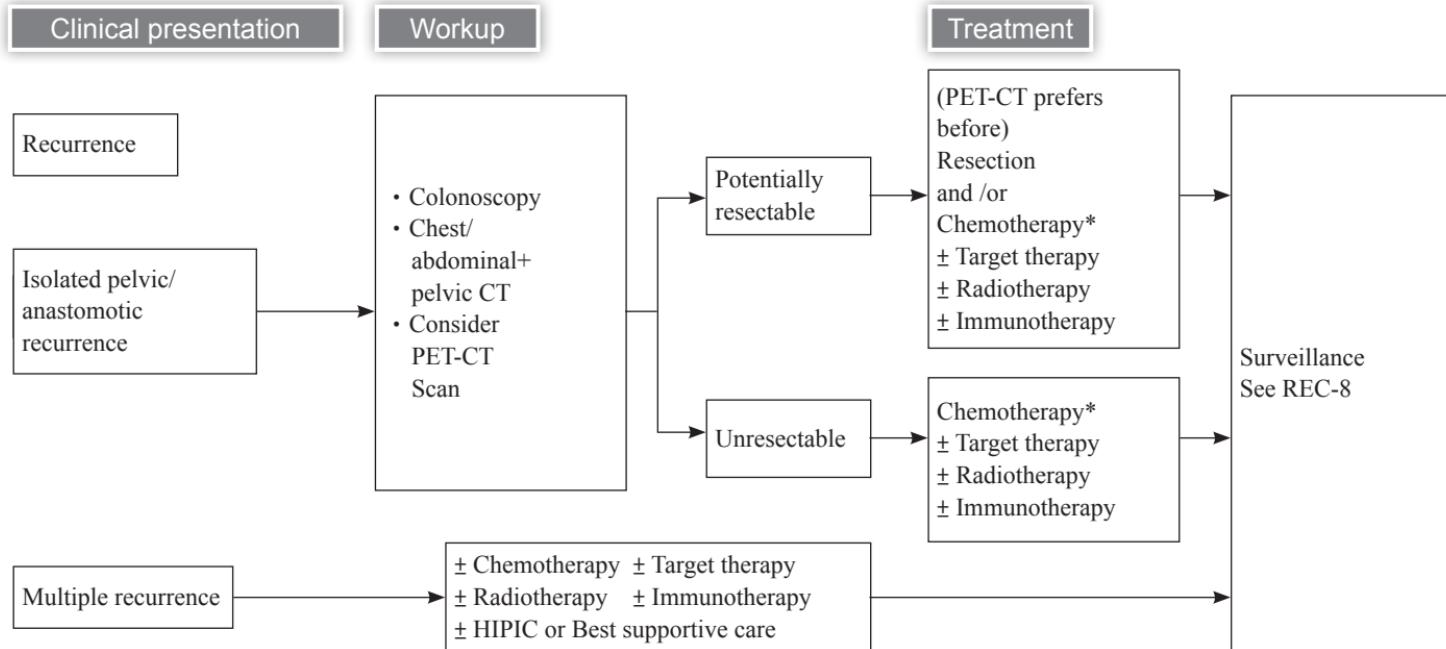
- * 1. Determination of tumor gene status for KRAS, NRAS and BRAF mutations and HER2, POLE /POLD1, RET 和 NTRK amplifications (individually or as part of tissue- or blood-based next generation sequencing [NGS panel]) (optional).
- * 2. For patients who are under 70 years old of age and ECOG: 0-2 points, we suggested standard combination chemotherapy.
- * 3. Consider resection only if imminent risk of obstruction, significant bleeding, perforation, or other significant tumor-related symptoms.

《 REC-6 》



- * 1. Determination of tumor gene status for KRAS.NRAS and BRAF mutations and HER2, POLE /POLD1,RET 和 NTRK amplifications (individually or as part of tissue- or blood-based).
- * 2. For patients who are under 70 years old of age and ECOG: 0-2 points, we suggested standard combination chemotherapy.
- * 3. For non-progressive primary tumor, resection is preferred over locally ablative procedures (eg, image-guided ablation or stereotactic body radiation therapy (SBRT). However, these local techniques can be considered for liver or lung oligometastases.
- * 4. Hepatic artery infusion ± systemic 5-FU/leucovorin (category 2B) is also an option at institutions with experience in both the surgical and medical oncologic aspects of this procedure.
- * 5. If obstruction or perforation occurs, colostomy or palliative surgery could be considered.

《REC-7》



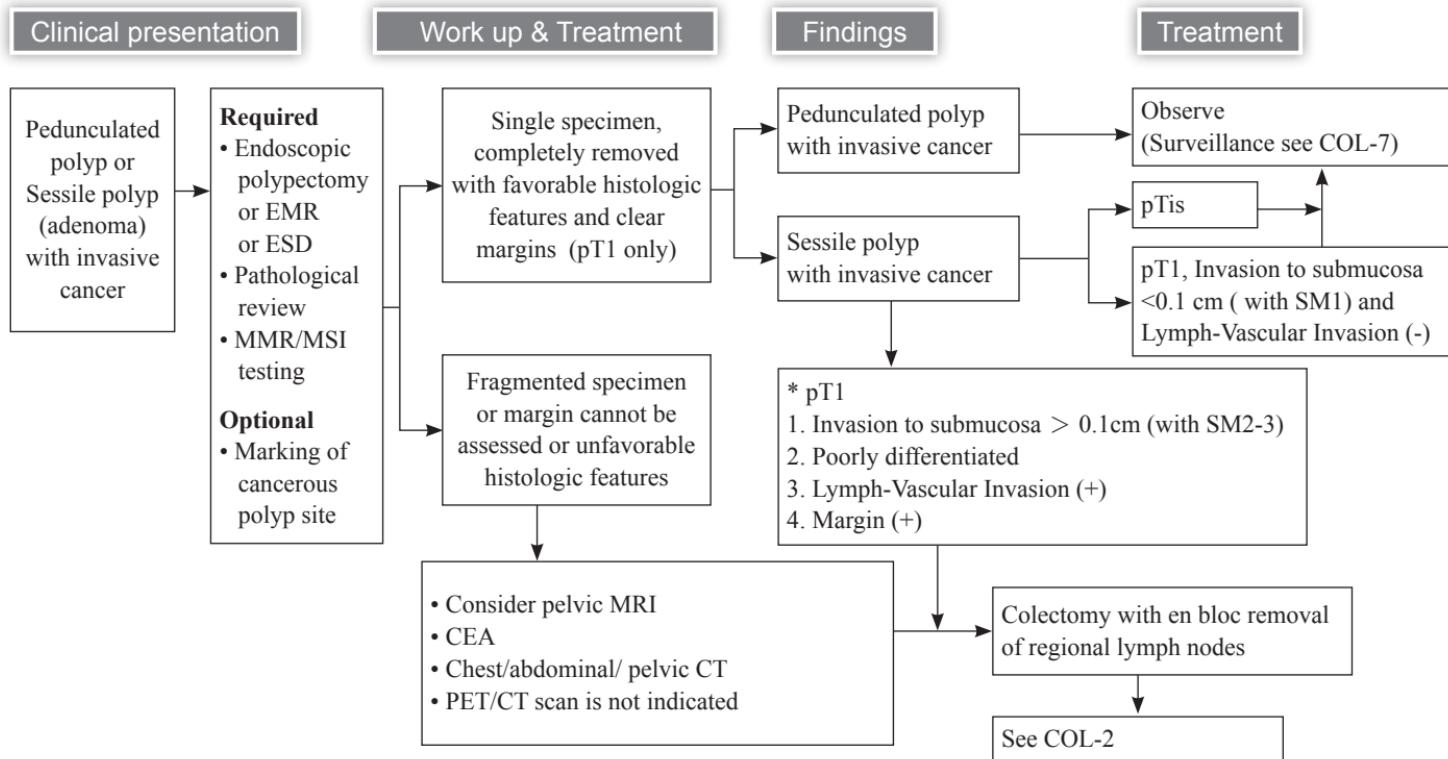
1. Determination of tumor gene status for KRAS, NRAS and BRAF mutations and HER2, POLE /POLD1, RET 和 NTRK amplifications (individually or as part of tissue- or blood-based next-generation sequencing [NGS panel]) (optional).
2. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy
3. Colorectal cancer is not only associated with peritoneal metastasis of liver and lung metastasis, and ECOG:0-1, heart, lung, kidney function normal, → Complete cytoreductive surgery and/or HIPEC (Hyperthermic Intraperitoneal Chemotherapy) or PIPAC (optional).

《 REC-8 (Surveillance) 》

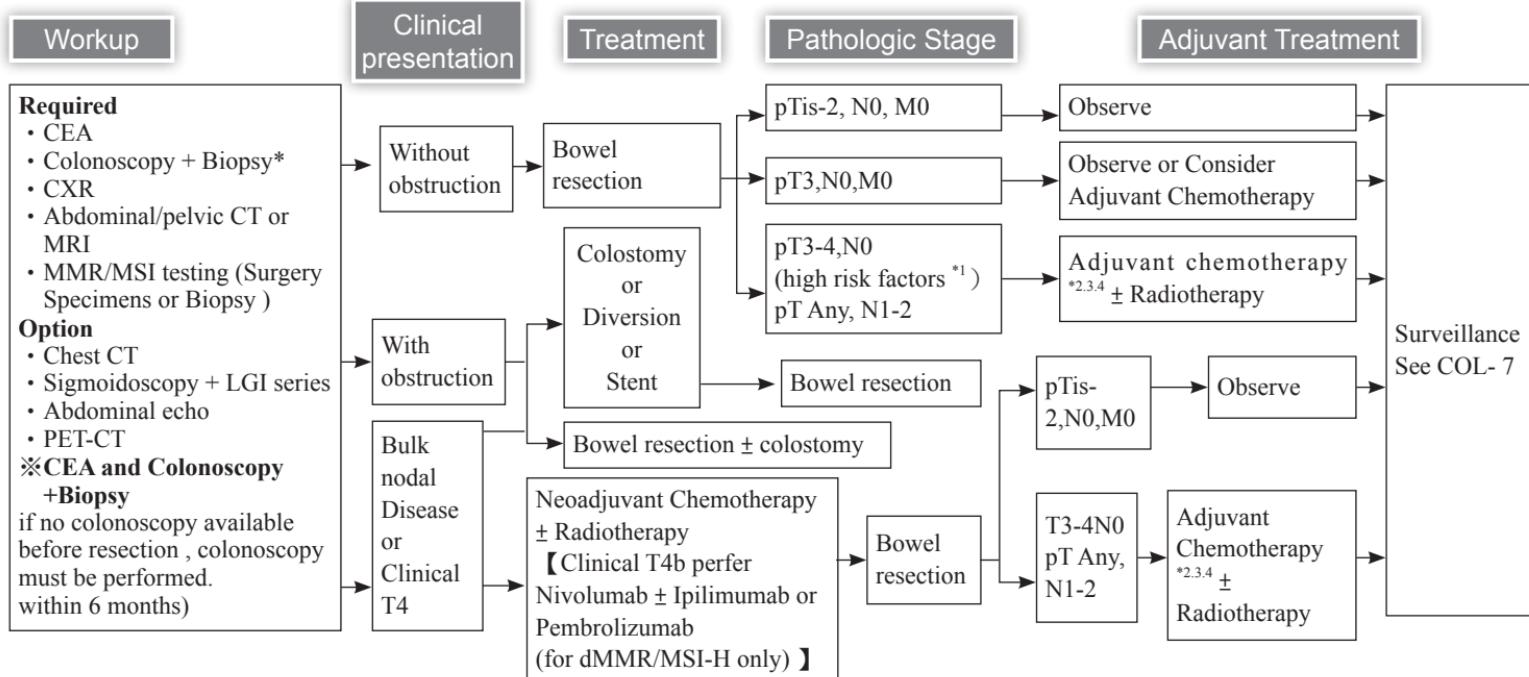
Follow up Program for Rectal Cancer Patients (at least 5 years)

CEA	After the first month, every three to six months,in first two years. once every six months thereafter. (1) Stage II,III: every 6–12 months for a total of 5 y
Chest /Abdomen + pelvic CT	(2) Stage IV: every 3–6 mo x 2 y, then every 6–12 mo for a total of 5 y.
Colonoscopy or Barium enema + Sigmoidoscopy	At least once in the first year, then once every other year. 1. Those who didn't have whole colonoscopy before preoperative obstructive lesions should do the whole colonoscopy 3-6 months after operation. 2. If advanced adenoma, repeat in every 1 year. 3. If no advanced adenoma, repeat in every 3 years, then every 5 years.
Rigid proctoscopy (optional)	every 3-4 months for 2 years, then every 6 months for a total of 5 years.
Abdomen sono (optional)	six months.
PET-CT scan (optional)	Clinical evaluation is required when needed.

《COL-1》



« COL-2 »

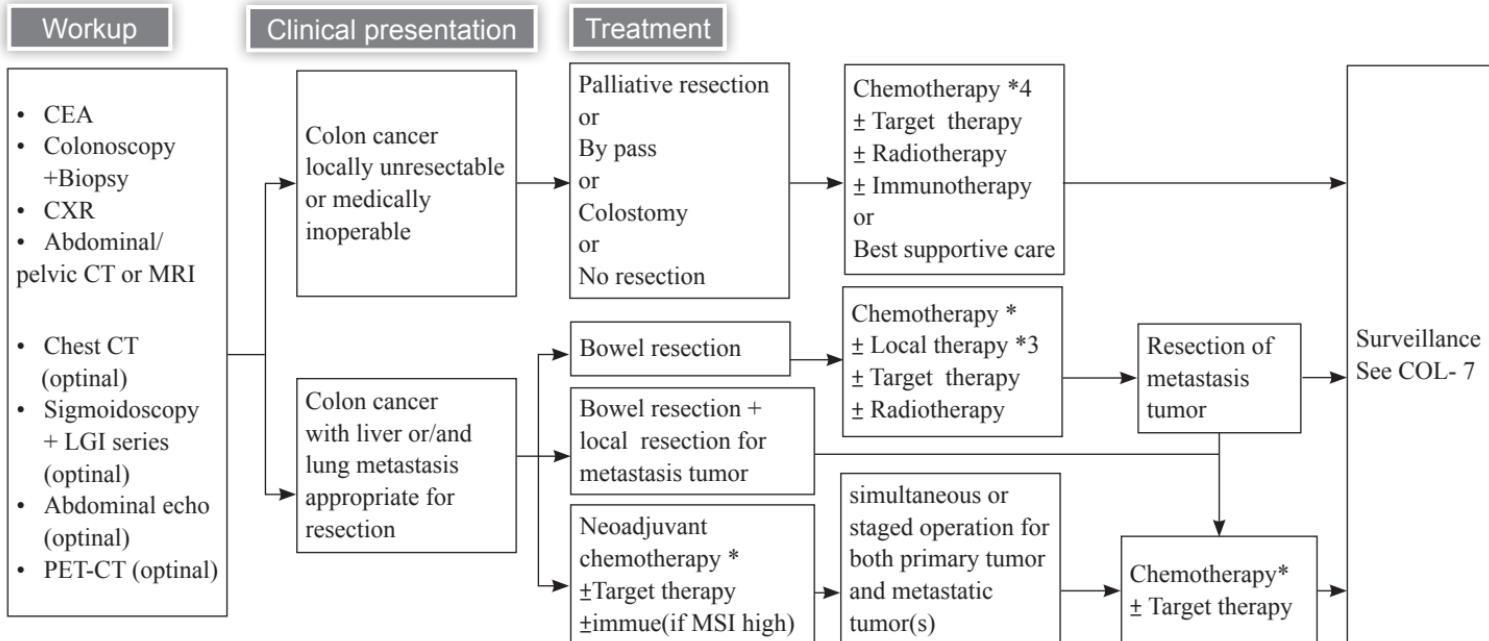


* 1. High risk factors : (1) Poorly differentiated (2) Lymphatic/vascular/perineural invasion 3) <12 lymph nodes examined (4) Localized Perforation (5) Bowel obstruction (6) Close, indeterminate or positive margins (7) StageIIA,pT3N0M0 : (without risk factor) added inspection MSI or MMR (optional),if MSI low → adjuvant Chemotherapy

* 2. A survival benefit has not been demonstrated for the addition of oxaliplatin to 5-FU/leucovorin in stage II colon cancer. Tournigand C, André T, Bonneterain F, et al. Adjuvant therapy with fluorouracil and oxaliplatin in stage II and elderly patients (between ages 70 and 75 years) with colon cancer: subgroup analyses of the Multicenter International Study of Oxaliplatin, Fluorouracil, and Leucovorin in the Adjuvant Treatment of Colon Cancer trial. J Clin Oncol 2012; published online ahead of print on August 20, 2012.

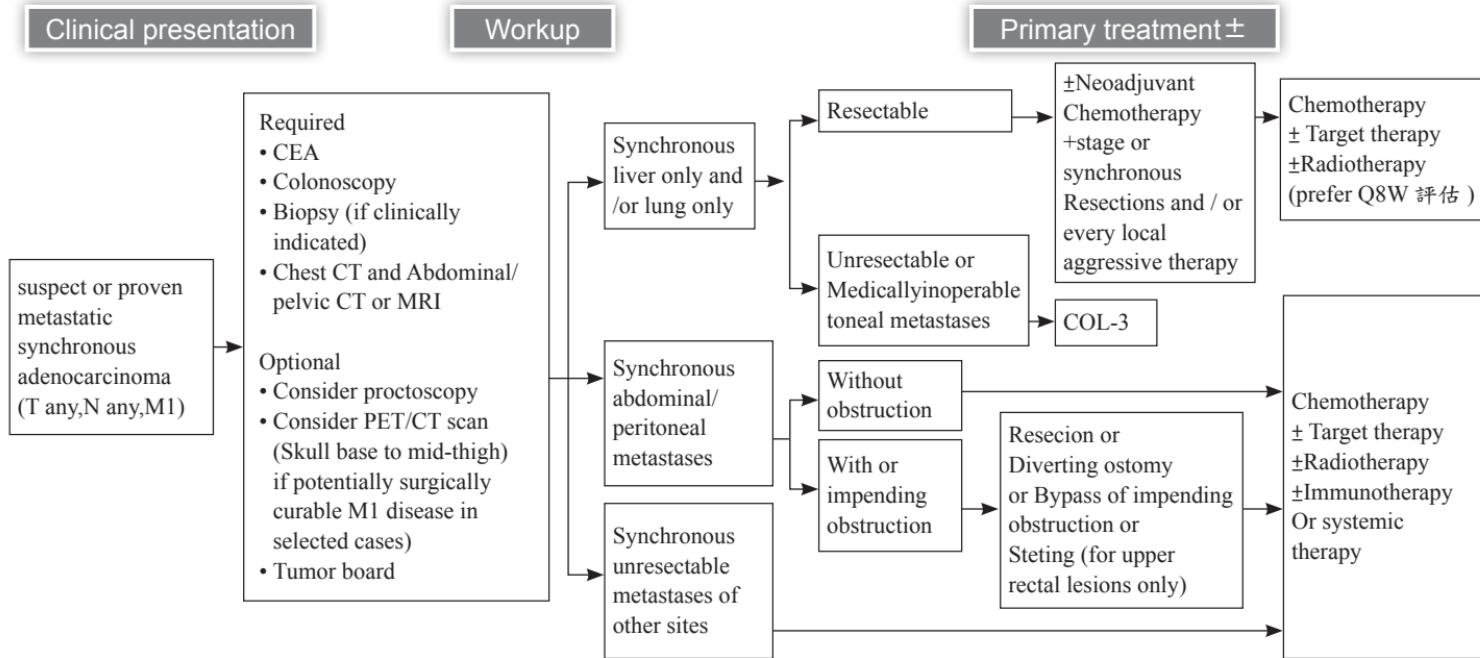
* 3. For patients who are under 70 years old of age and ECOG: 0-2 points, we suggested standard combination chemotherapy.

* 4. Consider PIK3CA testing for stage II-III. If PIK3CA mutation, add aspirin 100-162 mg PO daily for 3 years.



1. Determination of tumor gene status for KRAS, NRAS and BRAF mutations and HER2, POLE /POLD1, RET 和 NTRK amplifications (individually or as part of next-generation sequencing [NGS panel]) (optional)
2. For patients who are under 70 years old of age and ECOG: 0-2 points, suggested standard combination chemotherapy
3. For non-progressive primary tumor, resection is preferred over locally ablative procedures (eg, image-guided ablation or stereotactic body radiation therapy (SBRT)). However, these local techniques can be considered for liver or lung oligometastases.²²
4. Hepatic artery infusion ± systemic 5-FU/leucovorin (category 2B) is also an option at institutions with experience in both the surgical and medical oncologic aspects of this procedure.

《 COL-4 》



1. Determination of tumor gene status for KRAS, NRAS and BRAF mutations and HER2, POLE /POLD1, RET 和 NTRK amplifications (individually or as part of tissue or blood-based next-generation sequencing [NGS panel]) (optional)
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. Colorectal cancer is not only associated with peritoneal metastasis of liver and lung metastasis, and ECOG: 0-1, heart, lung, kidney function normal, → Complete cytoreductive surgery and/or HIPEC (Hyperthermic Intraperitoneal Chemotherapy) or PIPAC (optional).

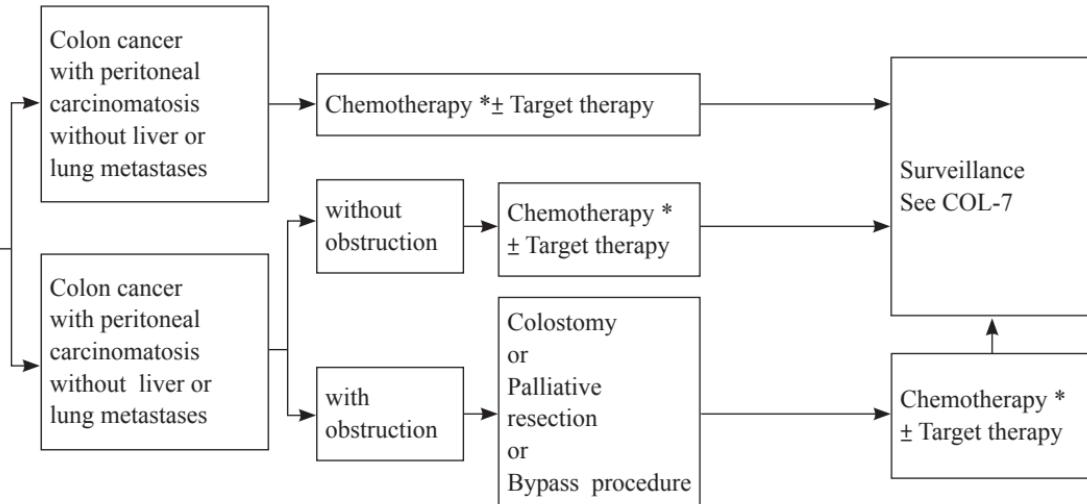
Workup

Clinical presentation

Treatment

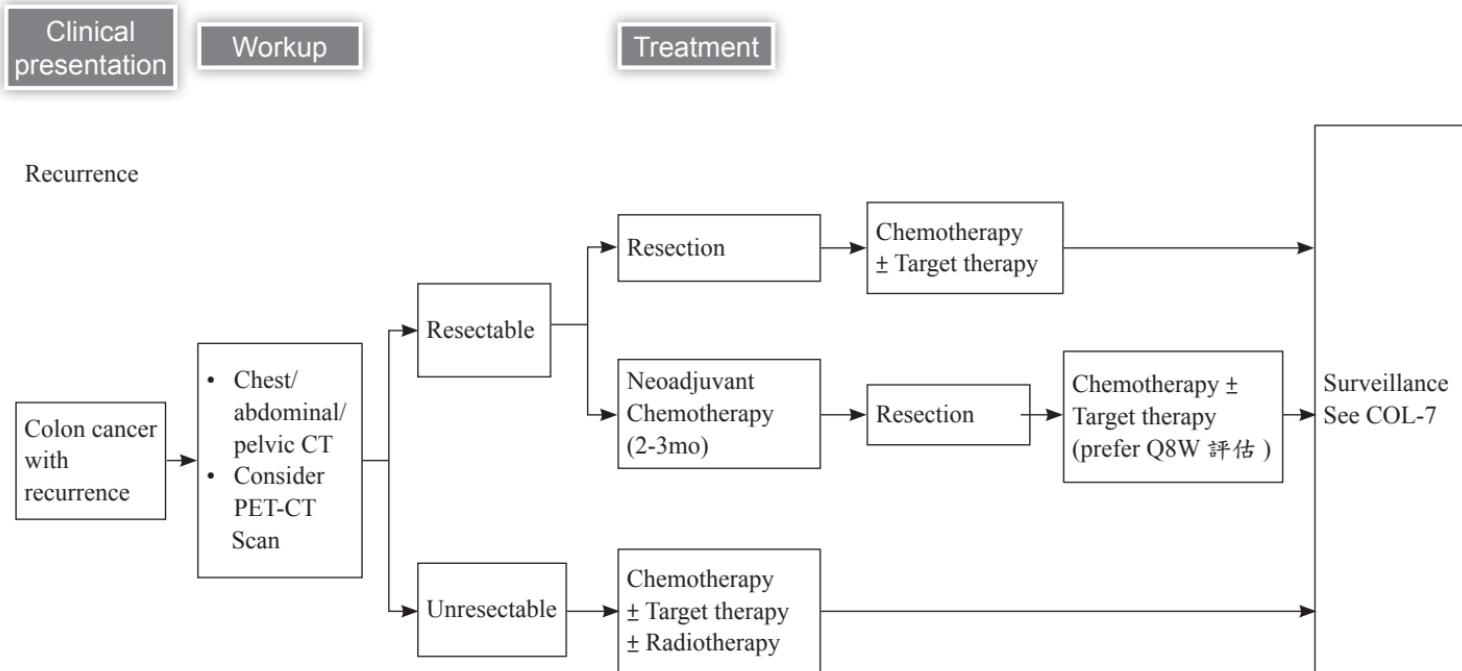
Metastases

- CEA
- Colonoscopy +Biopsy
- CXR
- Abdominal/pelvic CT or MRI
- KRAS gene status
- Chest CT (optional)
- Sigmoidoscopy + LGI series (optional)
- Abdominal echo (optional)
- PET-CT (optional)
- Needle biopsy, if clinically indicated
- Multidisciplinary team evaluation, including a surgeon experienced in the resection of hepatobiliary and lung metastases



1. Determination of tumor gene status for KRAS.NRAS and BRAF mutations and HER2, POLE /POLD1,RET 和 NTRK amplifications (individually or as part of tissue- or blood-based next-generation sequencing [NGS panel]) (optional)
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. Colorectal cancer is not only associated with peritoneal metastasis of liver and lung metastasis, and ECOG:0-1, heart, lung, kidney function normal, → Complete cytoreductive surgery and/or HIPEC (Hyperthermic Intraperitoneal Chemotherapy) or PIPAC (optional).

《COL-6》



1. Determination of tumor gene status for KRAS.NRAS and BRAF mutations and HER2 , POLE /POLD1,RET 和 NTRK amplifications (individually or as part of tissue- or blood-based next-generation sequencing [NGS panel]) (optional)
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

《COL-7 (Surveillance)》

Follow up Program for Rectal Cancer Patients (at least 5 years)

CEA After the first month, every three to six months,in first two years. once every six months thereafter.

(1) Stage II,III: every 6–12 months for a total of 5 y.

Chest /Abdomen + pelvic CT
 (2) Stage IV: every 3–6 months x 2 y, then every 6–12 mo for a total of 5 y.

Colonoscopy or Barium enema + Sigmoidoscopy At least once in the first year, then once every other year.
 1.Those who didn't had whole colonoscopy before preoperative obstructive lesions should do the whole colonoscopy 3-6 months after operation.
 2.If advanced adenoma, repeat in every 1 year.
 3.If no advanced adenoma, repeat in every 3 year , then every 5 years.

Abdomen sono (optional) six months.

PET-CT scan (optional) Clinical evaluation is required when needed.

《 Reference 》

1. NCCN Clinical Practice in Oncology: Rectal Cancer Version 3.2025— August 26, 2025.
2. NCCN Clinical Practice in Oncology: Colon Cancer Version 4.2025 —June 27, 2025.
3. Colorectal Cancer- From Prevention to Patient Care .Published in print edition February , 2012.
4. Japanese Society for Cancer of the Colon and Rectum. JSCCR Guidelines 2016 for the Treatment of Colorectal Cancer. 金原出版株式會社 , ISBN978-4-307-20361-6.
5. Recommendations and consensus on the treatment of peritoneal metastases of colorectal origin: a systematic review of national and international guidelines. *Colorectal Dis.* 2017 Mar;19(3):224-236.doi:10.1111/codi.13593. <https://www.ncbi.nlm.nih.gov/pubmed/28008728>
6. 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.
7. André, Corrado Boni, Lamia Mounedji-Boudiaf, Matilde Navarro, Josep Tabernero, Tamas Hickish, Clare Topham, Marta Zaninelli, Philip Clingan, John Bridgewater, Isabelle Tabah-Fisch, Aimery de Gramont, for the Multicenter International Studyof 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.
8. 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.
9. 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.

10. 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.
11. Barry C. Lemmersky, 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*.124 2006;24(13): 2059-2064.
12. Daniel G. Haller, Josep Tabernero, 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
13. E Bajetta, M Di Bartolomeo, R Buzzoni, et al. Uracil/ftorafur/Leucovorin combined with irinotecan(TEGAFIRI) or oxaliplatin(TEGAFOX) as
14. first-line treatment for metastatic colorectal cancer patients: results of randomised phase II study. *British Journal of Cancer* 96:439-444, 2007

Principle of Radiation Therapy for Colorectal Cancer

1. Radiotherapy targets :

- (1) Rectal tumor / Low sigmoid colon tumor and/or gross tumors
- (2) Involved pelvic lymphadenopathy
- (3) High risk pelvic / inguinal lymphatic basin drainage area

2. Dose prescriptions :

- (1) Pre-operative radiotherapy
 - * Conventional course : 45-50.4 Gy in 25-28 fractions, fraction size 1.8-2.0 Gy.
 - * Short course : 25 Gy in 5 fractions, fraction size 5 Gy.
- (2) Post-operative radiotherapy
 - * 45-50.4 Gy in 25-28 fractions, fraction size 1.8-2.0 Gy
- (3) Radiotherapy for unresectable lesions
 - * 54-60.4 Gy in 30-33 fractions, fraction size 1.8-2.0 Gy

3. RT technique :

Conformal radiotherapy techniques, such as 3DCRT, IMRT, VMAT, and tomotherapy, are preferred. Optional image guidance during radiotherapy with cone beam CT or orthogonal X-ray films can be considered.

4. Reference :

1. NCCN clinical practice guidelines in oncology-Rectal cancer. version 4.2025.
2. Roels S et al. Definition and delineation of the clinical target volume for rectal cancer. Int J Oncol Biol Phys 2006; 65: 1129–1142
3. Sauer R 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: 1926-1935.

4. Bahadoer RR et al. Short-course radiotherapy followed by chemotherapy before total mesorectal excision versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomized, open-label, phase 3 trial. Lancet Oncol 2021; 22:29-42