

高雄榮民總醫院

大腸癌診療指引

大腸直腸癌醫療團隊 制定

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Kaohsiung Veterans General Hospital
Colon Cancer Clinical Practice Guidelines

Colorectal Cancer Multidisciplinary Team

August 2025 *version 1*

Colon Cancer Clinical Practice Guidelines

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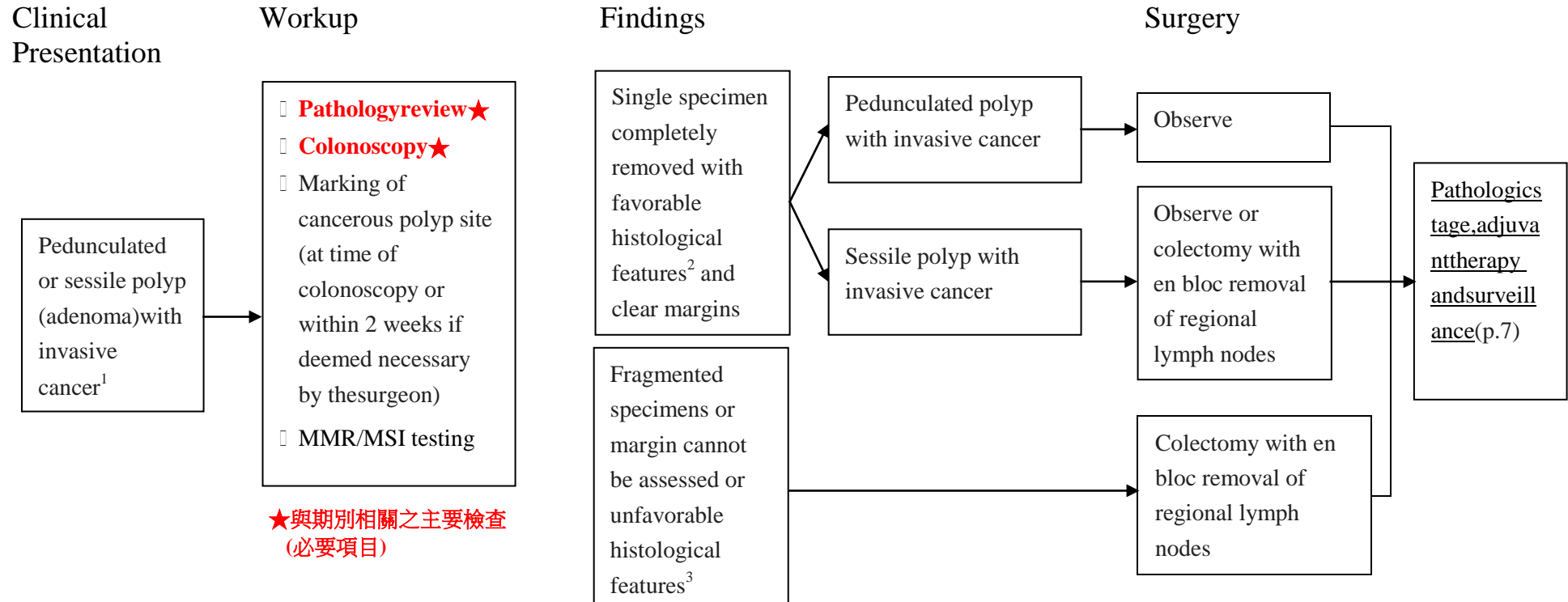
<Revision Summary>

Updates in Version 1 2023 of the VGHKS ColonCancer Clinical Practice Guidelines from Version 1 2022 include:

ESD may be an alternative option of local excision for early T disease or well responder after neo-adjuvant therapy and relatively contra-indicated to major surgery.

- PET/CT scan is considered if potentially surgical curable M1 disease in selected cases
- T3N0, high rectal tumour → transabd resection
- Colonic self-expandable stenting is available for selected cases in KSVGH

Malignant polyp

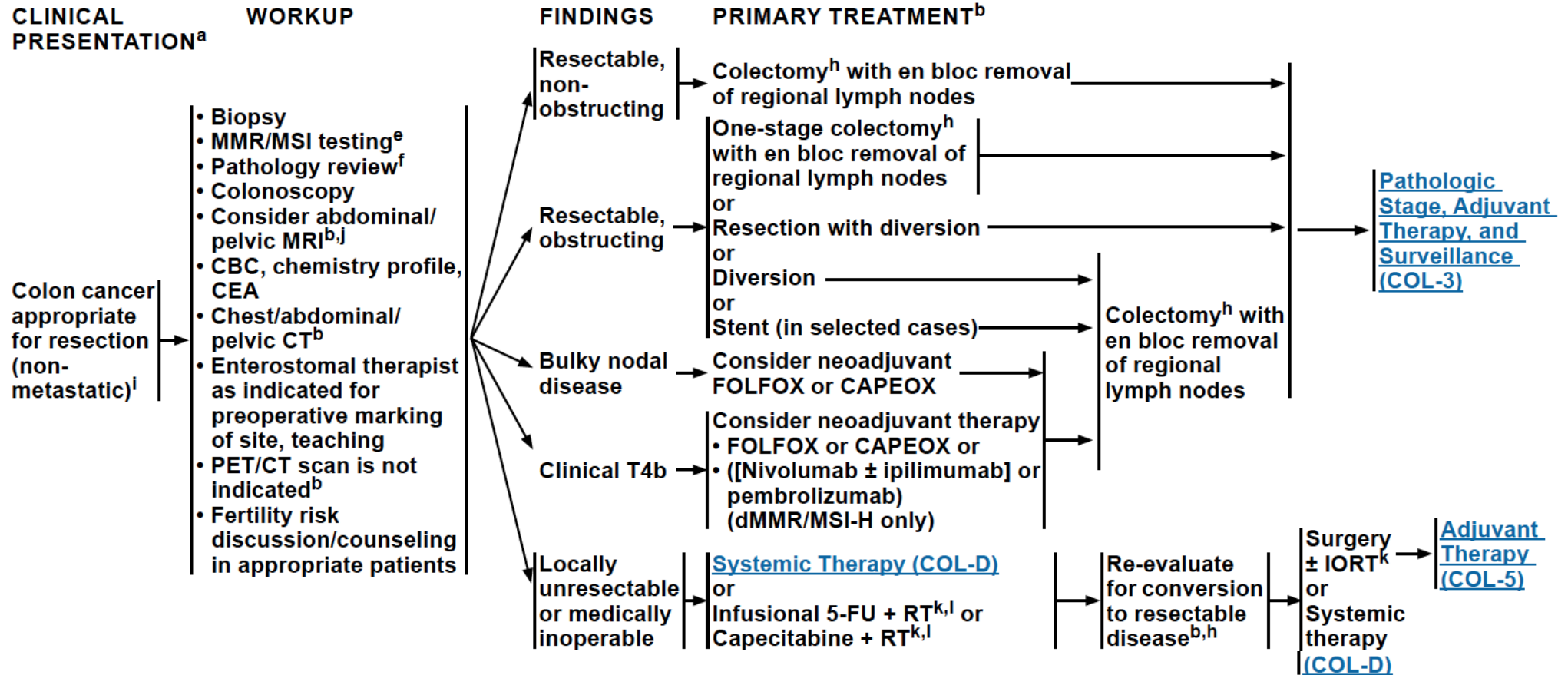


¹A malignant polyp is defined as one with cancer invading through the muscularis mucosae and into the submucosa (pT1). pTis is not considered a “malignant polyp”.

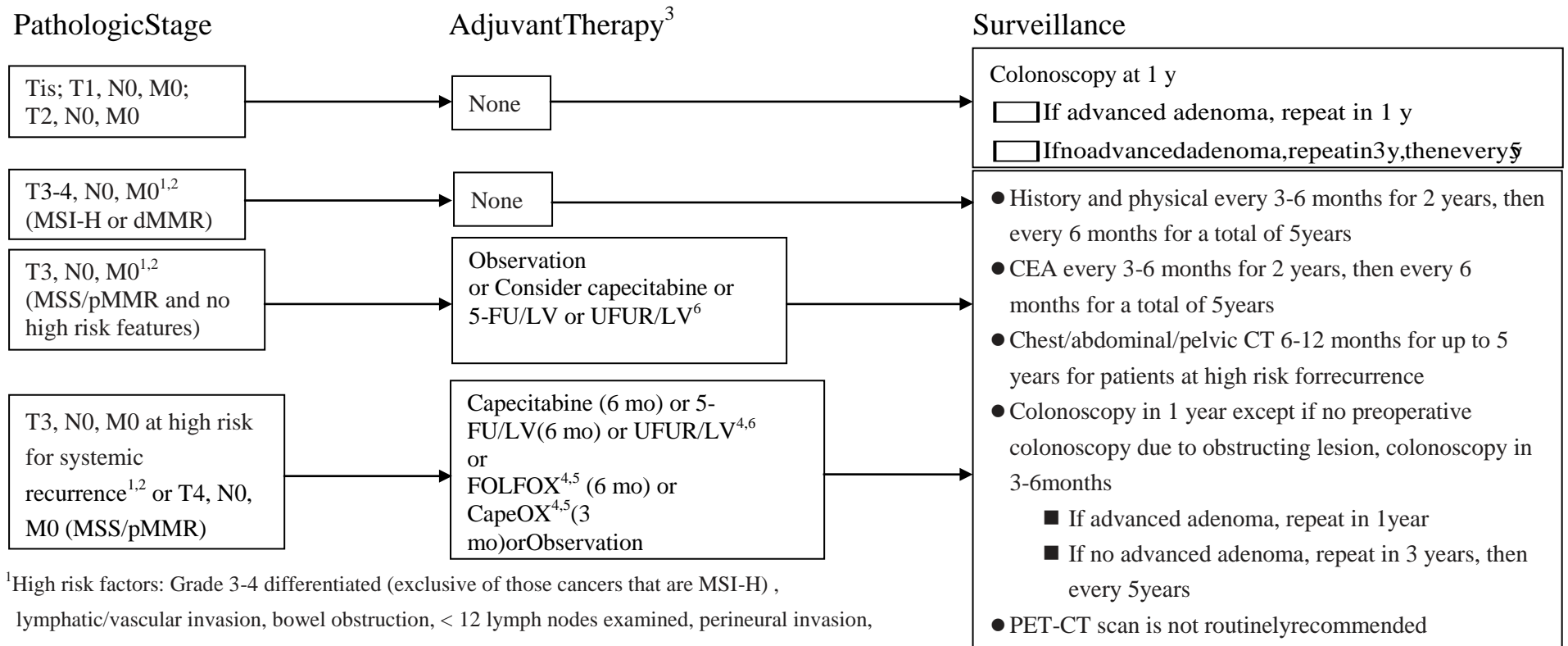
²Favorable histological features: Grade 1 & 2, no angiolymphatic invasion and negative margin of resection

³Unfavorable histological features: Grade 3 & 4, or angiolymphatic invasion, or a “positive” margin (tumour < 1mm from the transected margin)

Resectable primary colon cancer



Adjuvant therapy for stage I-II colon cancer



¹High risk factors: Grade 3-4 differentiated (exclusive of those cancers that are MSI-H), lymphatic/vascular invasion, bowel obstruction, < 12 lymph nodes examined, perineural invasion, localized perforation or close, indeterminate or positive margins. In high-risk stage II patients, there are no data that correlate risk features and selection of chemotherapy.

²Testing for mismatch repair proteins (MMR) should be considered for all patients <70 Y/O or with stage II disease. Stage II MSI-H patients may have a good prognosis and do no benefit from 5-FU adjuvant therapy.

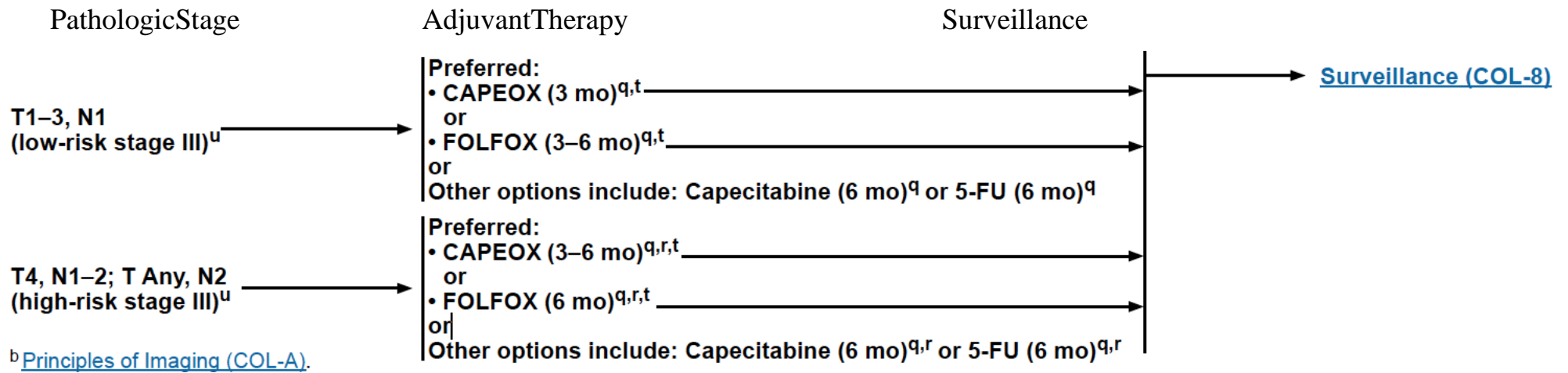
³Bevacizumab, cetuximab, panitumumab, or irinotecan should be not used in the adjuvant setting for stage II or III patients outside the setting of a clinical trial

⁴Consider RT for T4 with penetration to a fixed structure

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

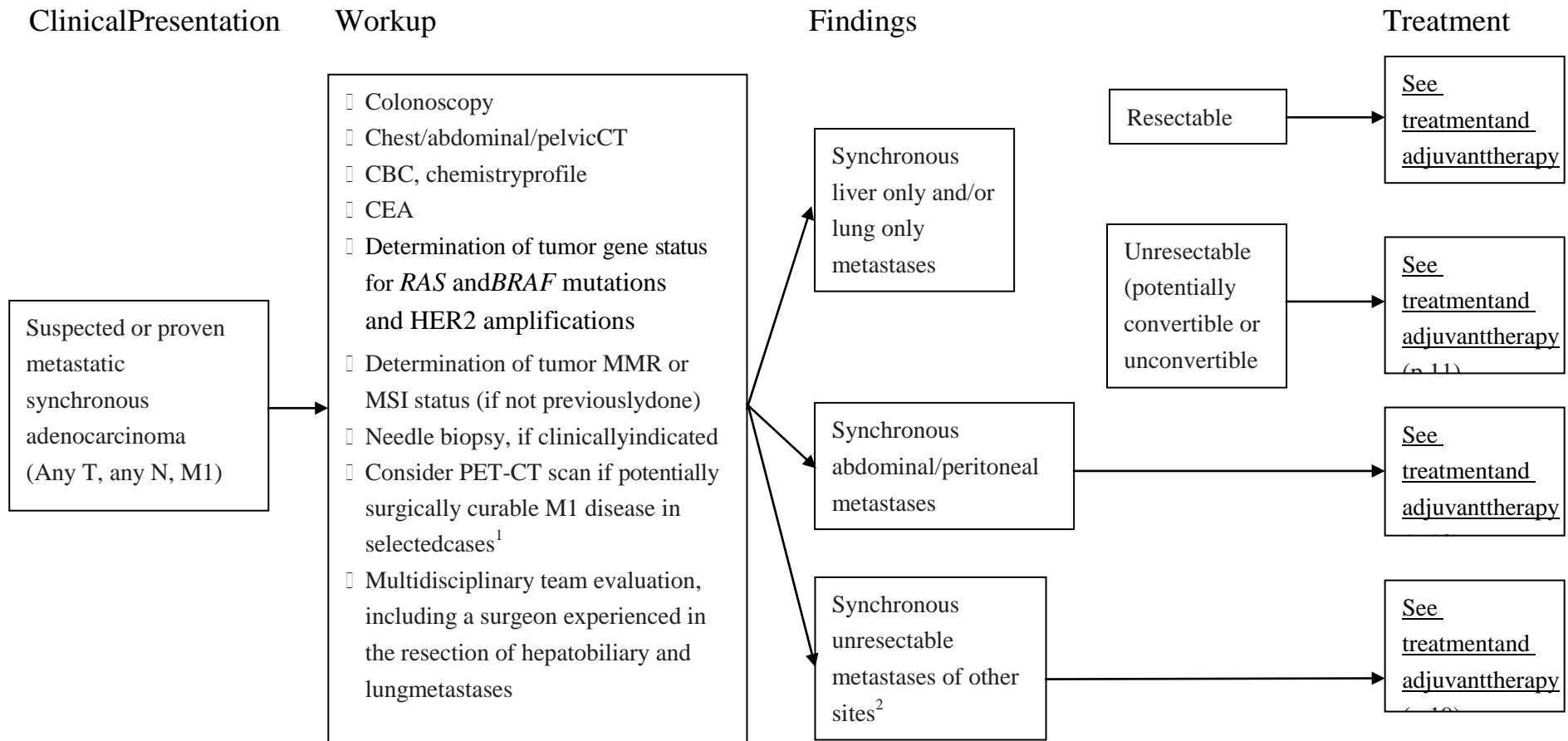
⁶Japanese regimen, also see [Chemotherapy Regimens](#)

Adjuvant therapy for stage III colon cancer



^b [Principles of Imaging \(COL-A\)](#).

Metastatic synchronous adenocarcinoma from large bowel



¹Moulton CA, Gu CS, Law CH, et al. Effect of PET before liver resection on surgical management for colorectal adenocarcinoma metastases: a randomized clinical trial. *JAMA* 2014;311:1863-1869.

²Consider colon resection only if imminent risk of obstruction or significant bleeding.

Resectable synchronous liver and/or lung metastases only

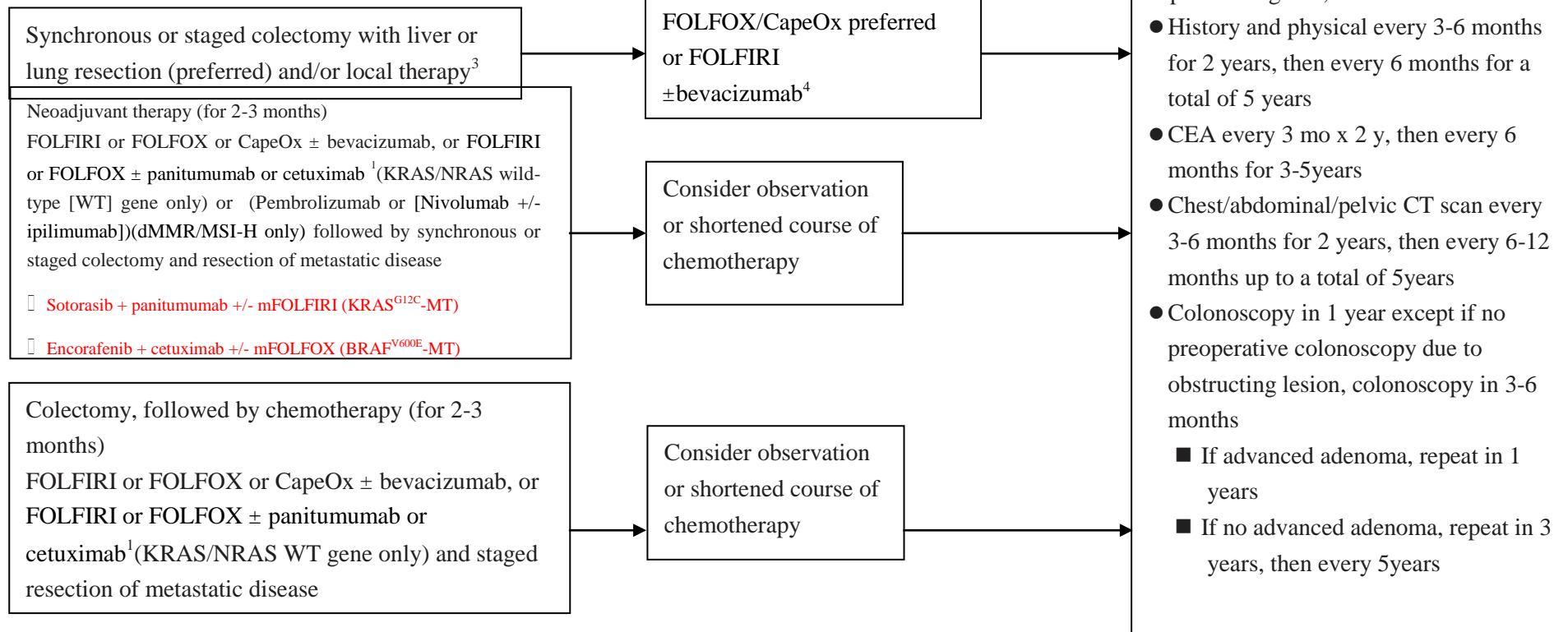
TREATMENT

Resectable synchronous liver and/or lung metastases only

ADJUVANT THERAPY

Resectable metastatic disease
6 months peri-OP treatment preferred²

SURVEILLANCE



¹There are conflicting data regarding the use of FOLFOX + cetuximab in patients who have potentially resectable liver metastases. ²Total duration of perioperative chemotherapy should not exceed 6 months. ³Resection is preferred over locally ablative procedures (eg, image-guided ablation or SBRT). However, these local techniques can be considered for liver oligometastases

⁴BMC Cancer. 2010 Oct 11;10:545. A randomized two arm phase III study in patients post radical resection of liver metastases of colorectal cancer to investigate bevacizumab in combination with capecitabine plus oxaliplatin (CAPOX) vs CAPOX alone as adjuvant treatment.

Unresectable synchronous liver and/or lung metastases only

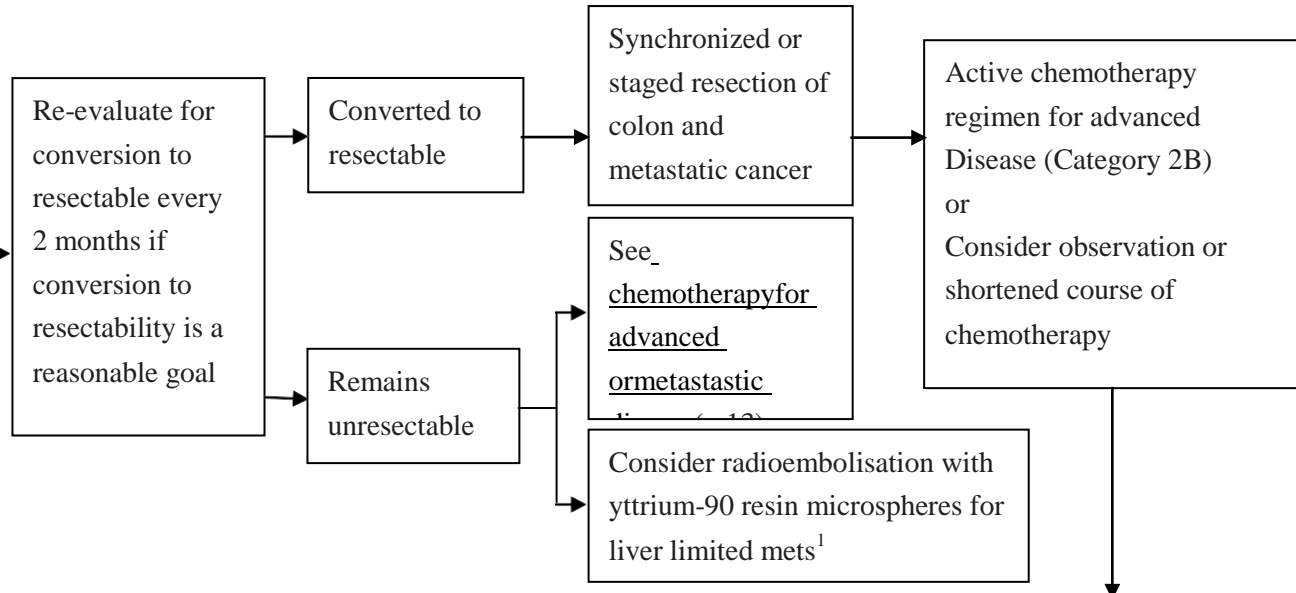
TREATMENT

Unresectable synchronous liver and/or lung metastases only

- ☐ Systemic therapy (FOLFIRI or FOLFOX or CapeOX ± bevacizumab, or FOLFIRI or FOLFOX or FOLFIRINOX ± panitumumab or cetuximab [KRAS /NRAS WT gene only] or, FOLFIRINOX ± bevacizumab)
- ☐ [Nivolumab +/- ipilimumab] or Pembrolizumab (preferred) (dMMR/MSI-H only)
- ☐ Sotorasib + panitumumab +/- mFOLFIRI (KRAS^{G12C}-MT)
- ☐ Encorafenib + cetuximab +/- mFOLFOX (BRAF^{V600E}-MT)
- ☐ Consider colon resection only if imminent risk of obstruction or significant bleeding

ADJUVANT THERAPY

6 months peri-OP treatment preferred



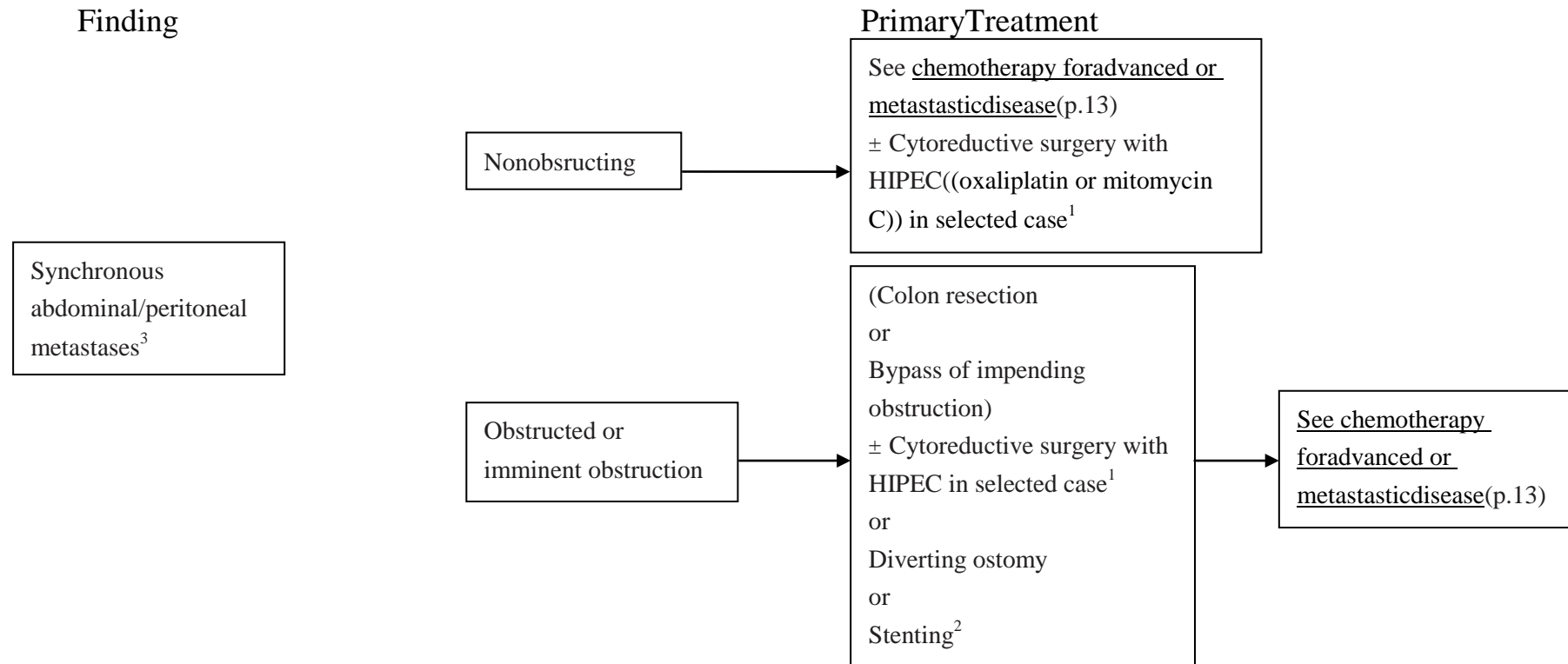
SURVEILLANCE

If patient stage IV, no evidence of disease (NED):

- History and physical every 3-6 months for 2 years, then every 6 months for a total of 5 years
- CEA every 3 months for 2 years, then every 6 months for 3-5 years
- Chest/abdominal/pelvic CT scan every 3-6 months for 2 years, then every 6-12 months up to a total of 5 years
- Colonoscopy in 1 year except if no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3-6 months
 - If advanced adenoma, repeat in 1 year
 - If no advanced adenoma, repeat in 3 years, then every 5 years

¹Not documented in NCCN guideline 2015 v2 but in ESMO guideline 2014 (evidence grade IVB). Also refer to reference [9]

Synchronous abdominal/peritoneal metastases

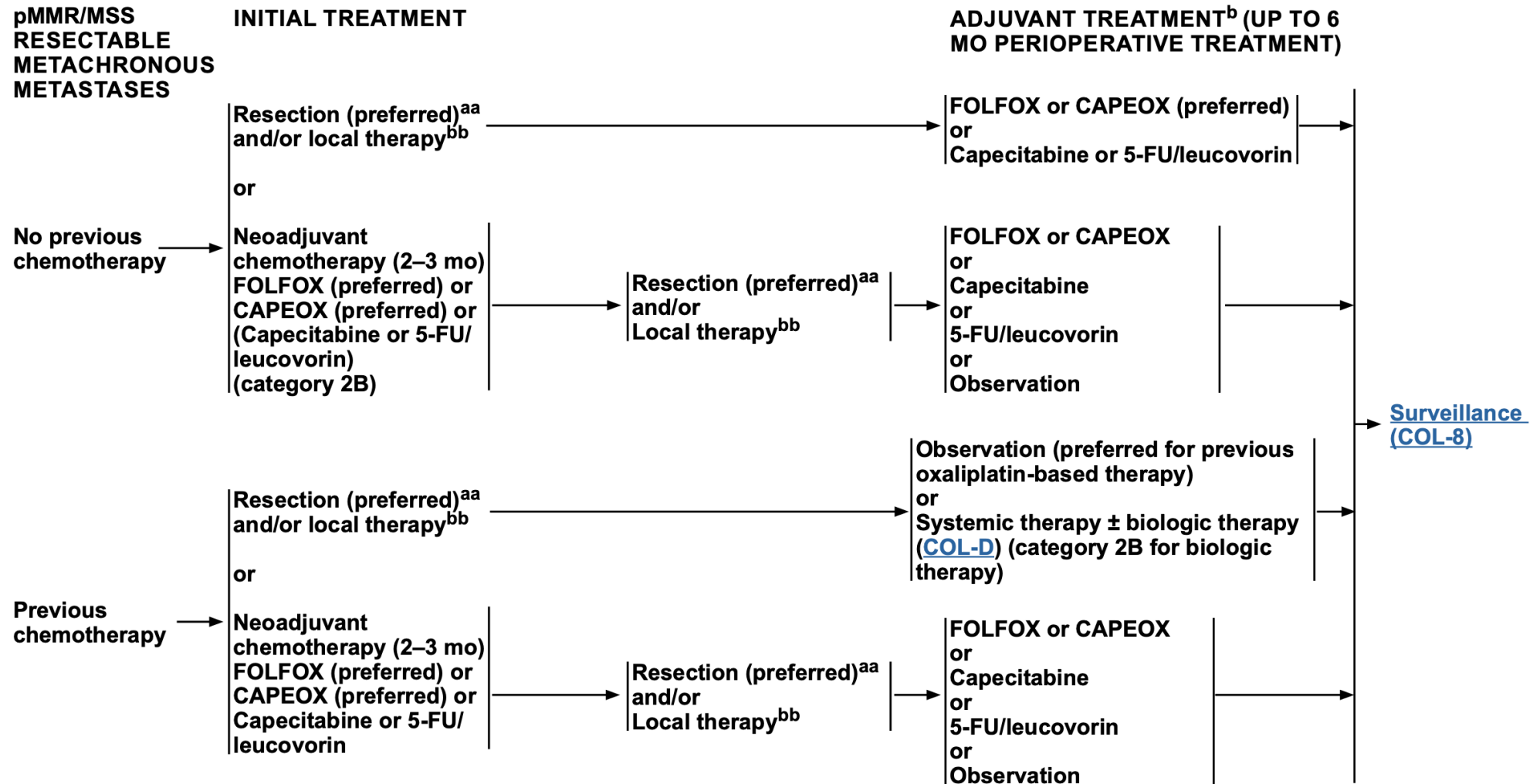


¹HIPEC = Hyperthermic Intraperitoneal Chemotherapy; Not documented in NCCN guideline 2015 v2 but in ESMO guideline 2014 (evidence grade IVB). Also refer to Reference [7], [8]

²Not available in VGHS now

³Aggressive cytoreductive debulking and/or intraperitoneal chemotherapy are not recommended outside the setting of a clinical trial. If R0 resection can be achieved, surgical resection of isolated peritoneal disease may be considered at experienced centers.

Chemotherapy for advanced or metastatic disease (1 of 4)

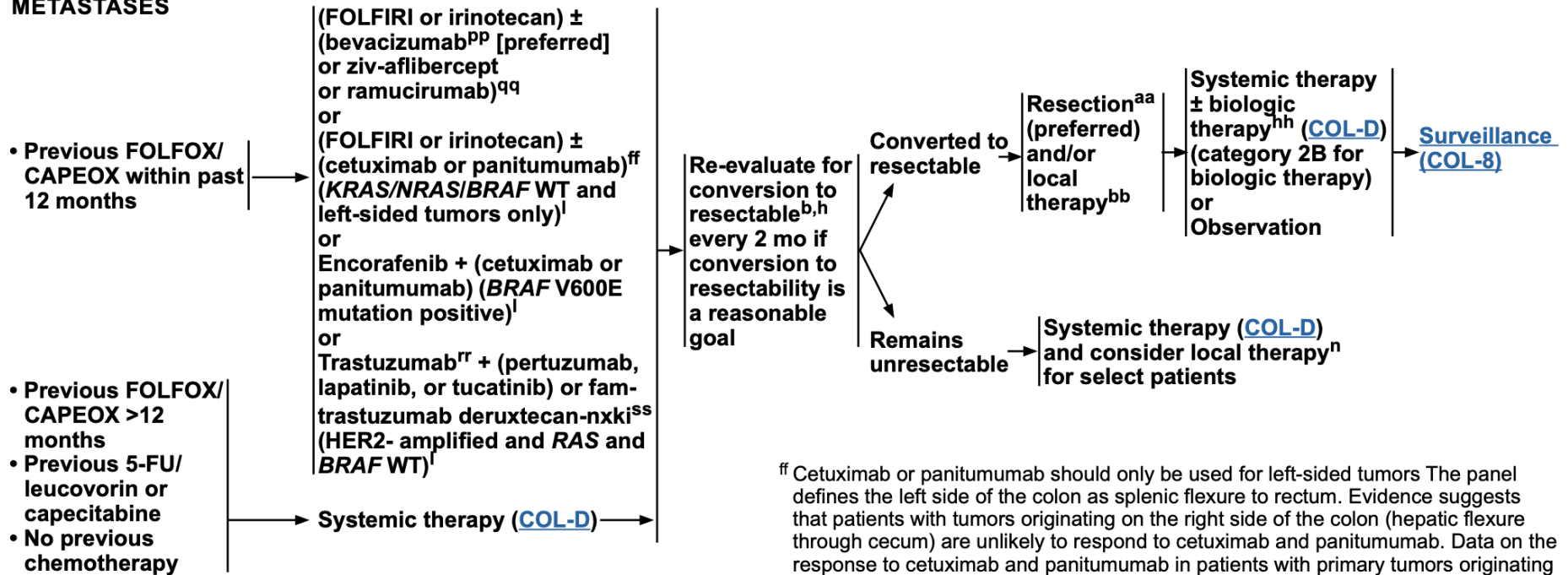


Chemotherapy for advanced or metastatic disease (1 of 4)

**pMMR/MSS
UNRESECTABLE
METACHRONOUS
METASTASES**

INITIAL TREATMENT^{oo}

**ADJUVANT TREATMENT^b
(UP TO 6 MO PERIOPERATIVE
TREATMENT)**



^b [Principles of Imaging \(COL-A\)](#).

^h [Principles of Surgery \(COL-C 2 of 3\)](#).

ⁿ [Principles of Radiation and Chemoradiation Therapy \(COL-E\)](#).

^l [Principles of Pathologic Review \(COL-B 4 of 8\)](#) - *KRAS*, *NRAS*, and *BRAF* Mutation Testing.

^{aa} 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.

^{bb} Resection is preferred over locally ablative procedures (eg, image-guided ablation or SBRT). However, these local techniques can be considered for liver or lung oligometastases ([COL-C](#) and [COL-E](#)).

^{ff} Cetuximab or panitumumab should only be used for left-sided tumors. The panel defines the left side of the colon as splenic flexure to rectum. Evidence suggests that patients with tumors originating on the right side of the colon (hepatic flexure through cecum) are unlikely to respond to cetuximab and panitumumab. Data on the response to cetuximab and panitumumab in patients with primary tumors originating in the transverse colon (hepatic flexure to splenic flexure) are lacking.

^{hh} Biologic therapy is only appropriate for continuation of favorable response from conversion therapy.

^{oo} For infection risk, monitoring, and prophylaxis recommendations for targeted therapies, see INF-A in the [NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections](#).

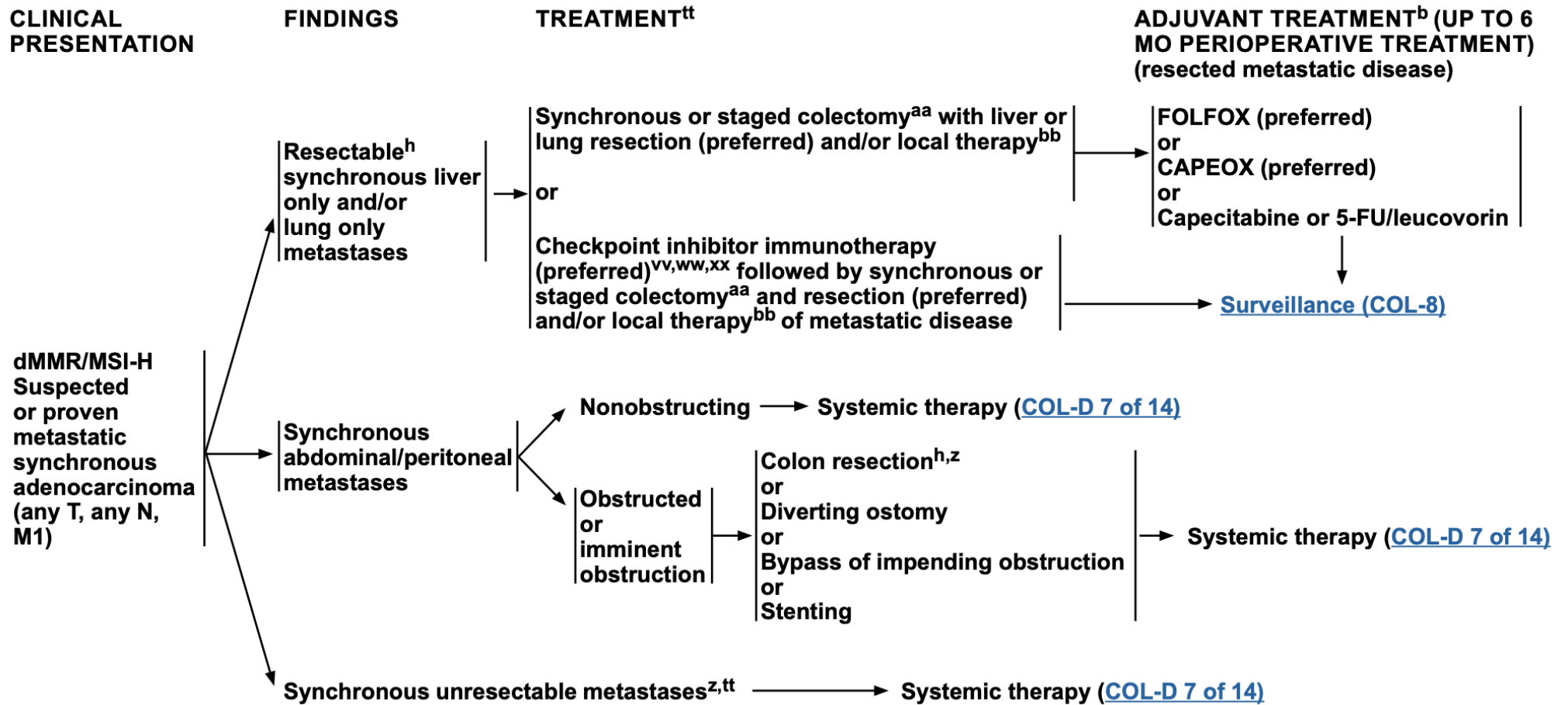
^{pp} An FDA-approved biosimilar is an appropriate substitute for bevacizumab.

^{qq} Bevacizumab is the preferred anti-angiogenic agent based on toxicity and/or cost.

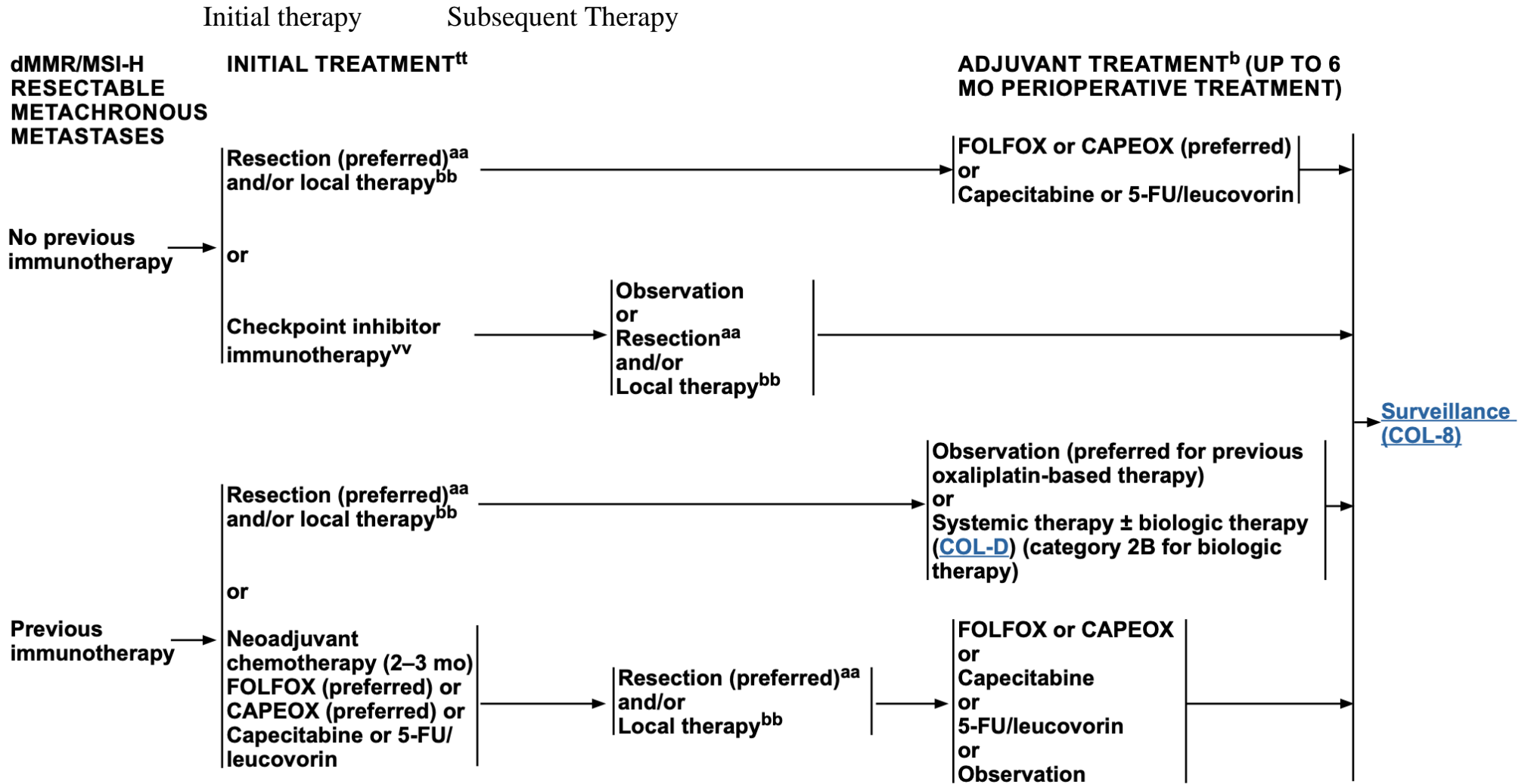
^{rr} An FDA-approved biosimilar is an appropriate substitute for trastuzumab.

^{ss} Some activity was seen after a previous HER2-targeted regimen. May not be indicated in patients with underlying lung issues due to lung toxicity (2.6% report of deaths from interstitial lung disease).

Chemotherapy for advanced or metastatic disease (1 of 4)

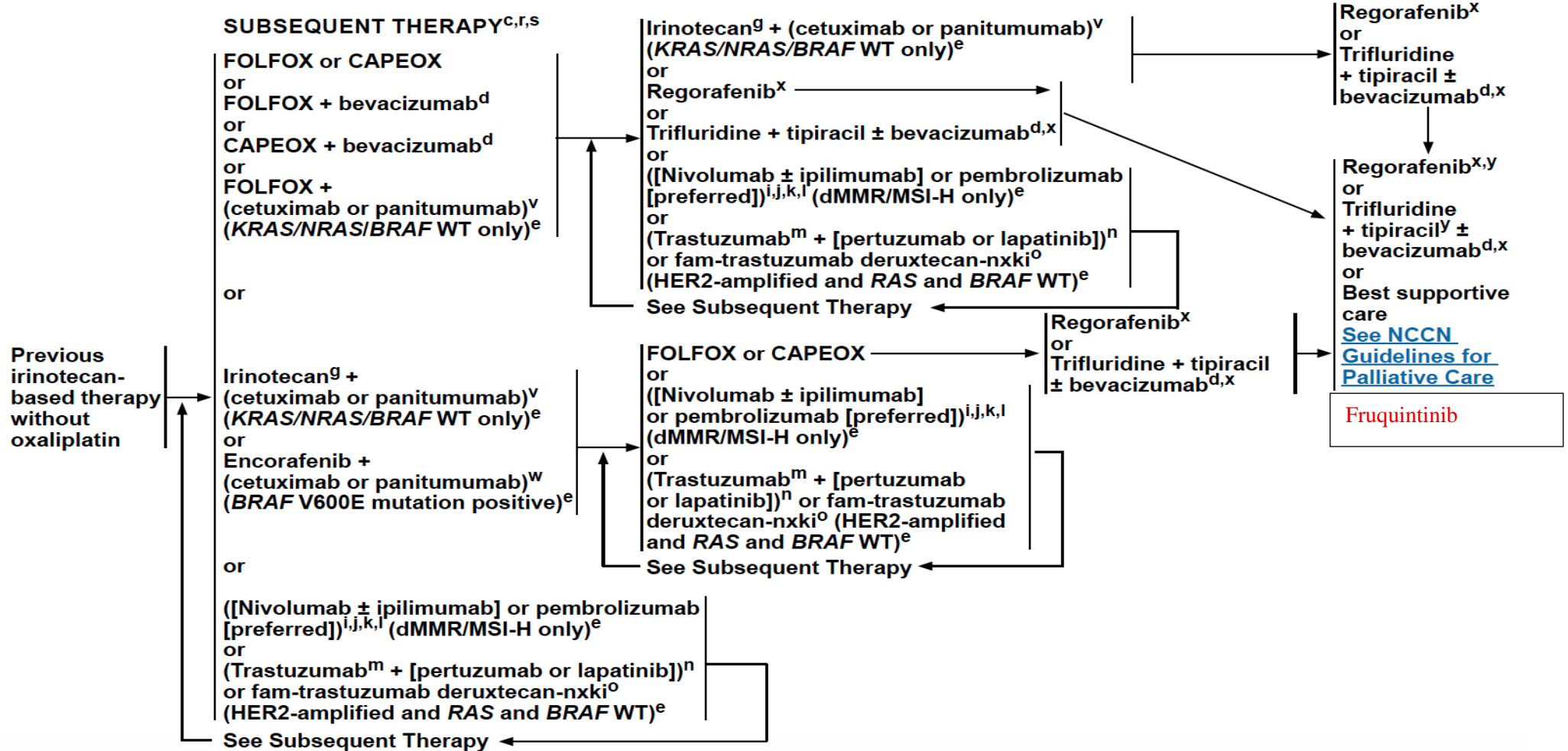


Chemotherapy for advanced or metastatic disease (2 of 4)



Chemotherapy for advanced or metastatic disease (3 of 4)

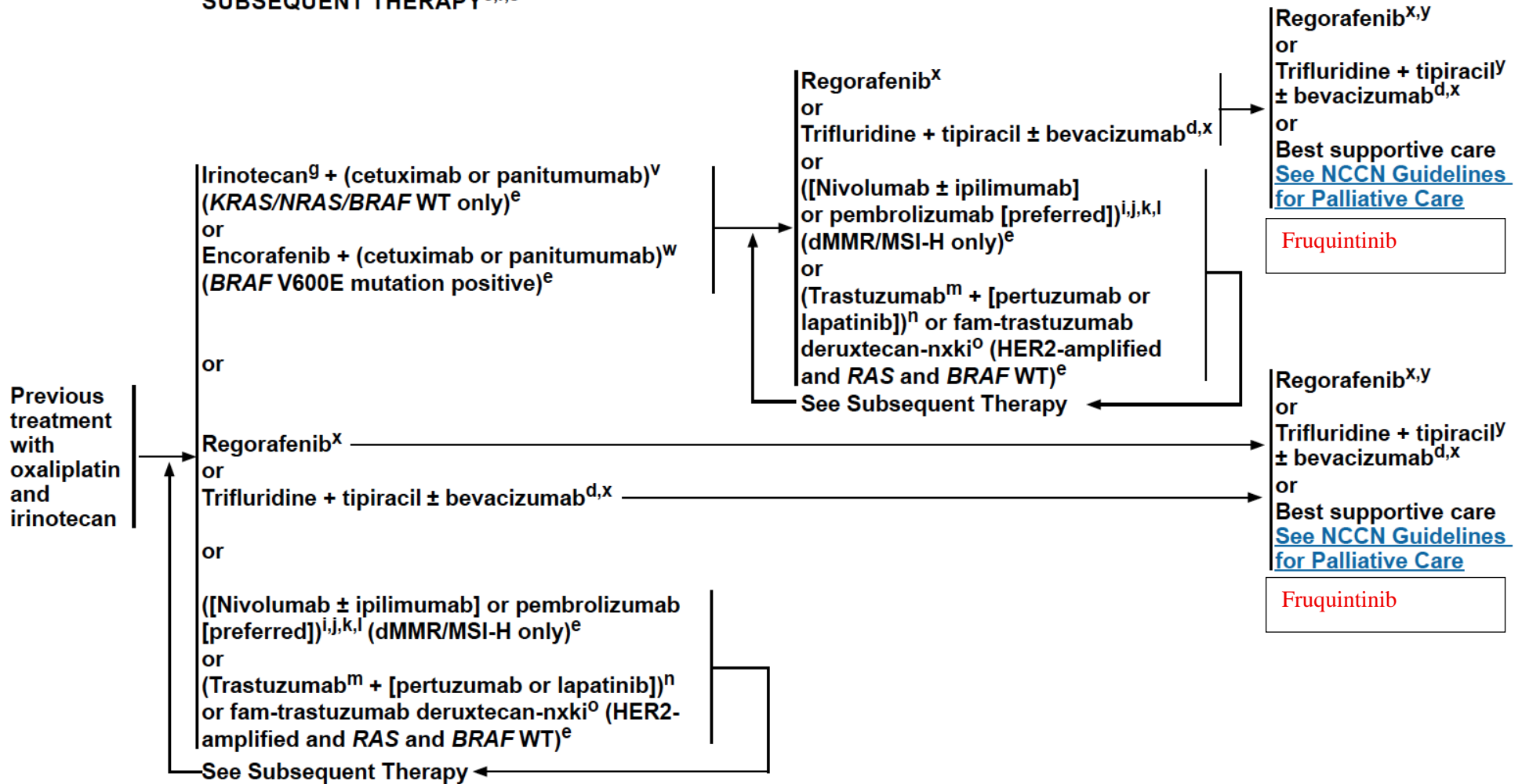
CONTINUUM OF CARE - SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE^{a,b,q}



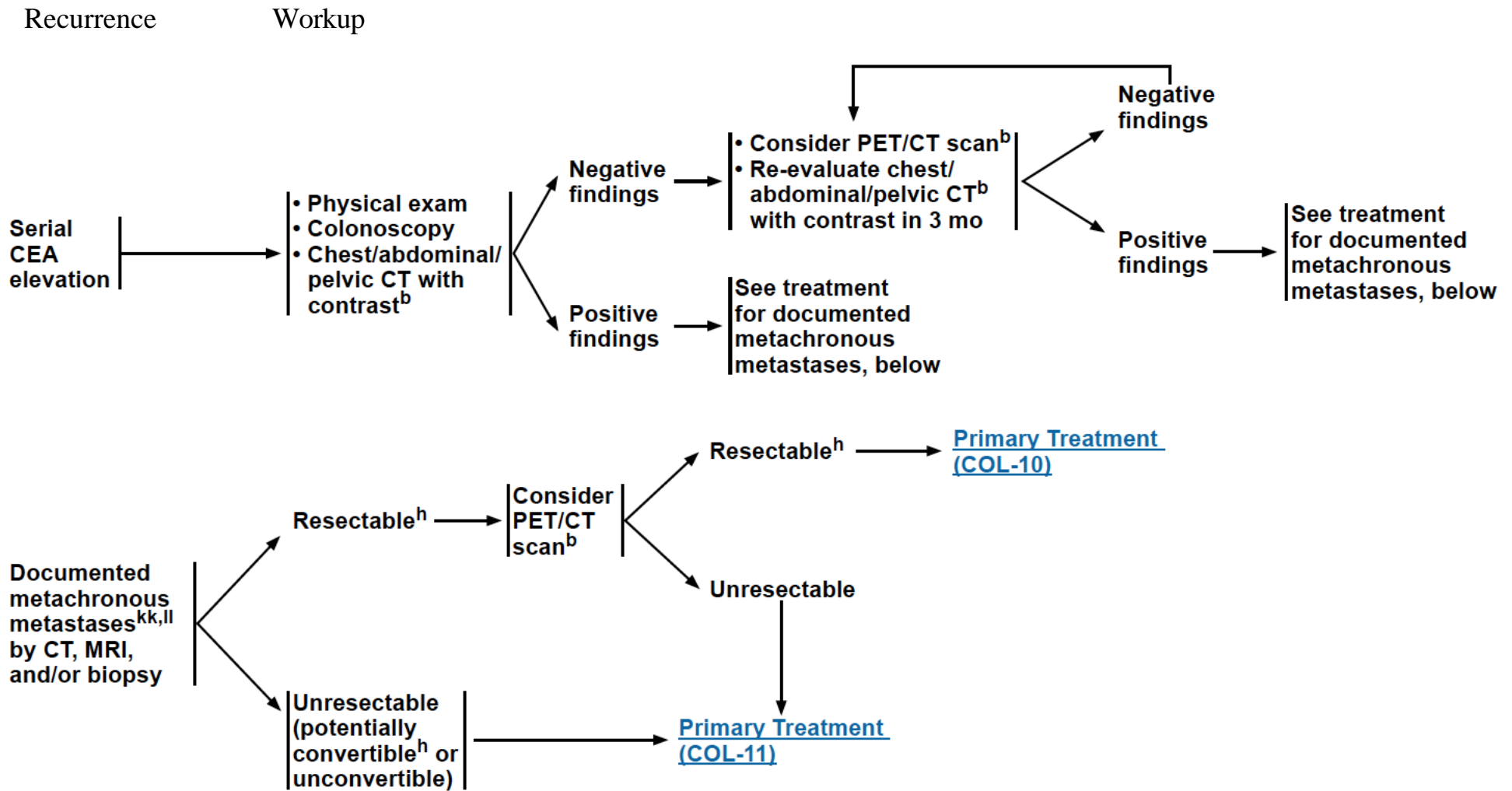
See footnotes on [COL-D \(7 of 13\)](#)

Chemotherapy for advanced or metastatic disease (4 of 4)

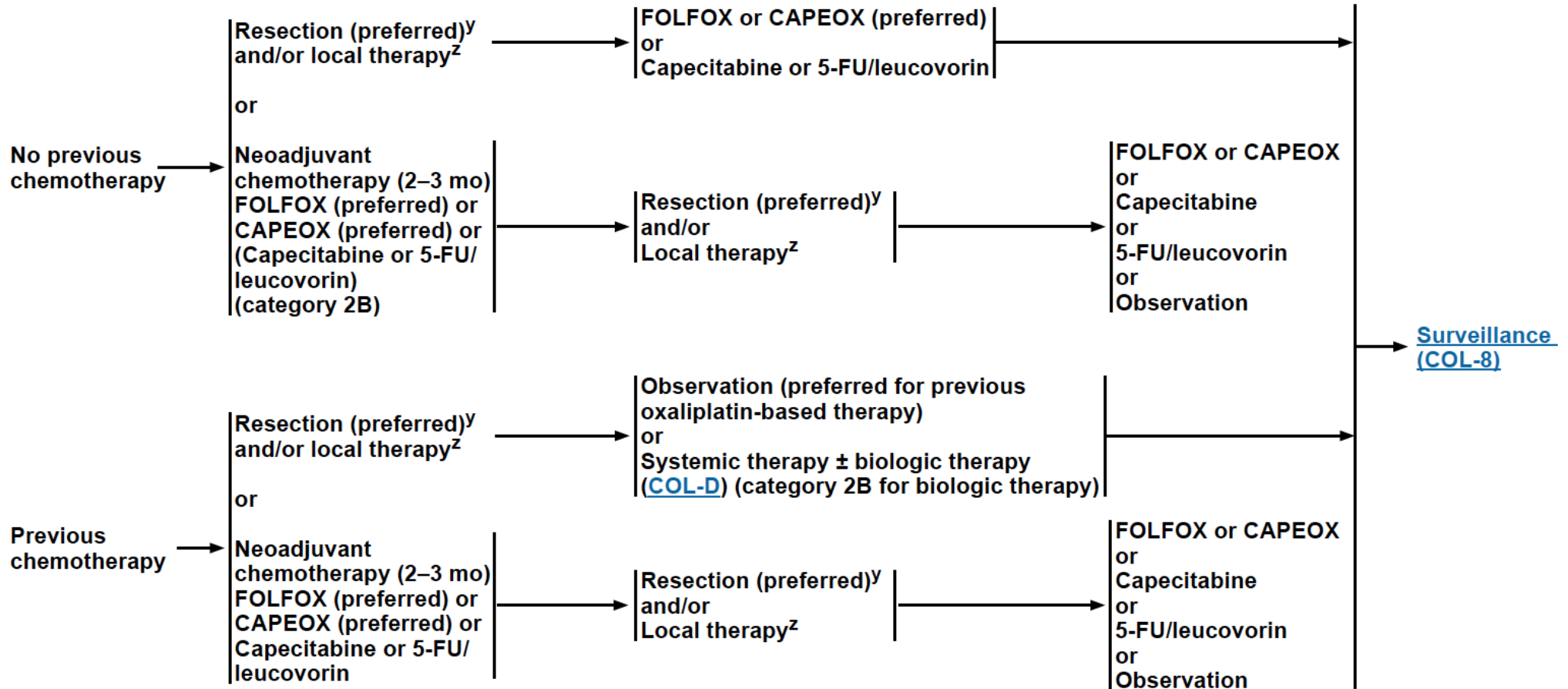
SUBSEQUENT THERAPY^{c,r,s}



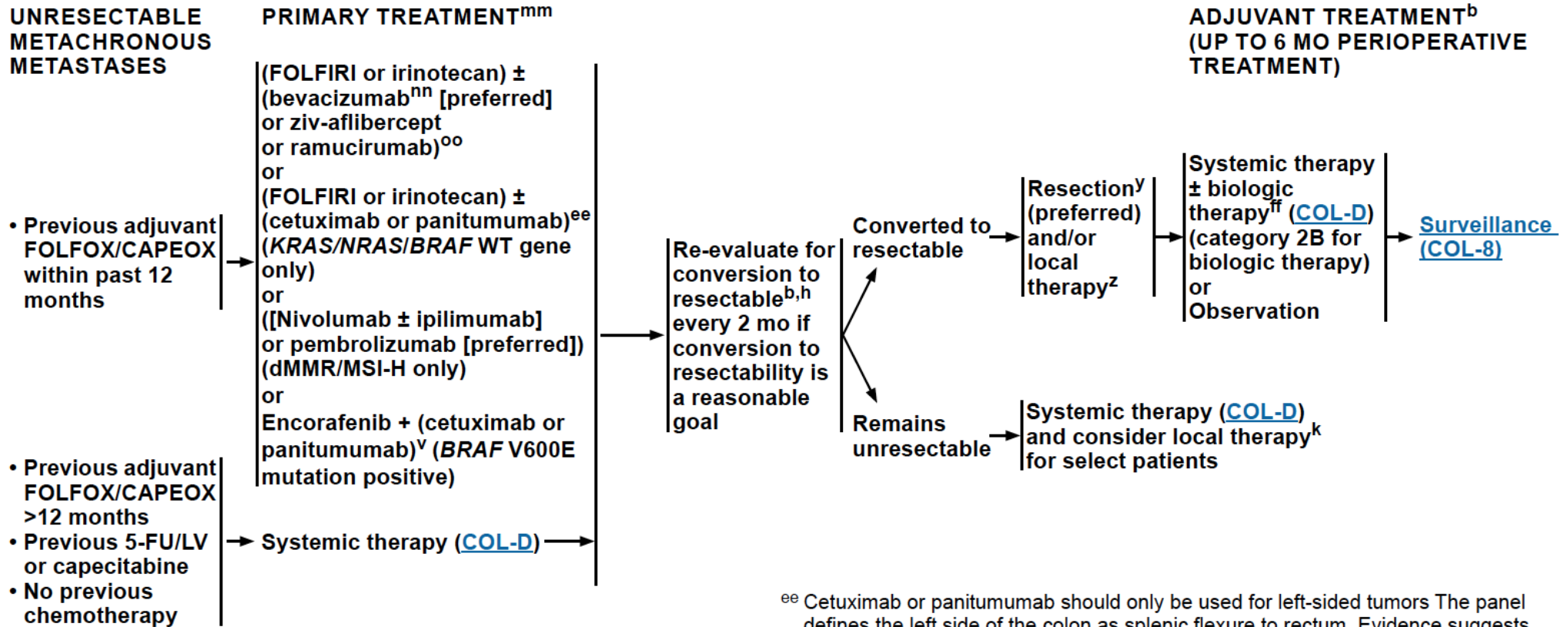
Workup for recurrence



Resectable metachronous metastases



Unresectable metachronous metastases



^{ee} Cetuximab or panitumumab should only be used for left-sided tumors. The panel defines the left side of the colon as splenic flexure to rectum. Evidence suggests

- Sotorasib + panitumumab +/- mFOLFIRI (*KRAS*^{G12C}-MT)
- Encorafenib + cetuximab +/- mFOLFOX (*BRAF*^{V600E}-MT)

Principles of Chemotherapy

LV Dosage:

Leucovorin 400 mg/m² is the equivalent of levoleucovorin 200 mg/m²

Chemotherapy for Advanced/Metastatic disease

All CRC chemotherapy regimens according to patient's condition and guidelines

NHI regulation:

Bevacizumab combine with Irinotecan base or 5-FU base regimens at the 1st line treatment

Cetuximab combine with Irinotecan or oxaliplatin base regimens at the 1st line & the 3rd line treatment

Panitumumab combine with Irinotecan or oxaliplatin base regimens at the 1st line treatment

Regorafenib at the third/fourth[K-ras wild type] line treatment

Adjuvant Chemotherapy Regimen

Oxaliplatin base (including mFOLFOX6, CapeOX, FLOX)

5-FU base chemotherapy (IV form 5-FU, Capecitabine, Ufur/LV)

NHI regulation:

Oxaliplatin: Stage III colon cancer

Xeloda: Stage III colon cancer, stage IV colorectal cancer

5-FU/LV: High risk stage II, stage III and stage IV colorectal cancer

Ufur/LV: High risk stage II, stage III and stage IV colorectal cancer

Chemotherapy Regimens for Advanced/Metastatic Disease (1 of3)

FOLFOX
<i>mFOLFOX6 (may add with Bevacizumab/Panitumumab/Cetuximab)</i>
Oxaliplatin 85 mg/m ² IV over 2 hours, day 1 Leucovorin 400 mg/m ² IV over 2 hours, day 1 5-FU 400 mg/m ² IV bolus on day 1, then 1200 mg/m ² /day x 2 days (total 2400 mg/m ² over 46–48 hours) IV continuous infusion Repeat every 2 weeks
<i>CapeOX(may add with Bevacizumab)</i>
Oxaliplatin 130 mg/m ² IV over 2 hours, day 1 Capecitabine 850–1000mg/m ² twice daily PO for 14 days Repeat every 3 weeks
FOLFIRI <i>(may add with Bevacizumab/Panitumumab/Cetuximab/Ziv-aflibercept/Ramucirumab)</i>
Irinotecan 180 mg/m ² IV over 30–90 minutes, day 1 Leucovorin* 400 mg/m ² IV infusion to match duration of irinotecan infusion, day 1 5-FU 400 mg/m ² IV bolus day 1, then 1200 mg/m ² /day x 2 days (total 2400 mg/m ² over 46–48 hours) continuous infusion Repeat every 2 weeks
FOLFIRINOX <i>(may add with Bevacizumab)</i>
Irinotecan 165 mg/m ² IV day 1, oxaliplatin 85 mg/m ² day 1, leucovorin 400 mg/m ² day 1, fluorouracil 1600 mg/m ² /day x 2 days (total 3200 mg/m ² over 48 hours) continuous infusion starting on day 1. Repeat every 2 weeks

TARGET THERAPY
Repeat every 2 weeks (unless additional mention)
+ <i>Bevacizumab</i>
Bevacizumab 5 mg/kg IV, day 1 or Bevacizumab 7.5 mg/kg IV, day 1 (for Capecitabine based)
+ <i>Panitumumab (KRAS/NRAS WT gene only)</i>
Panitumumab 6 mg/kg IV over 60 minutes, day 1
+ <i>Cetuximab (KRAS/NRAS WT gene only)</i>
Cetuximab 400 mg/m ² IV over 2 hours first infusion, then 250 mg/m ² IV over 60 minutes weekly or Cetuximab 500 mg/m ² IV over 2 hours, day 1
+ <i>Ziv-aflibercept (FOLFIRI)</i>
Ziv-aflibercept 4 mg/kg IV, day 1
+ <i>Ramucirumab² (FOLFIRI)</i>
Ramucirumab 8mg/kg over 60 minutes, day 1
+ <i>Regorafenib (Single use or with FOLFIRI³)</i>
Regorafenib 160 mg PO daily days 1-21 Repeat every 28 days
<i>Trifluridine + tipiracil²</i>
35mg/m ² up to a Max doas of 80 mg per dose (based on trifluridine component) PO twice daily days 1-5 and 8-12 repeat every 28 days

Chemotherapy Regimens for Advanced/Metastatic Disease (2 of3)

Bolus or infusional 5-FU/leucovorin	Irinotecan based
<i>Roswell Park regimen</i>	<i>IROX</i>
Leucovorin 500 mg/m ² IV over 2 hours, days 1, 8, 15, 22, 29, and 36 5-FU 500 mg/m ² IV bolus 1 hour after start of leucovorin, days 1, 8, 15, 22, 29, and 36 Repeat every 8 weeks	Oxaliplatin 85 mg/m ² IV over 2 hours, followed by irinotecan 200 mg/m ² over 30-90 minutes every 3 weeks
<i>Simplified biweekly infusional 5-FU/LV (sLV5FU2)</i>	<i>Irinotecan (may add with Cetuximab)</i>
Leucovorin 400 mg/m ² IV over 2 hours on day 1, followed by 5-FU bolus 400 mg/m ² and then 1200 mg/m ² /day x 2 days (total 2400 mg/m ² over 46-48 hours) continuous infusion Repeat every 2 weeks	Irinotecan 125 mg/m ² IV over 30-90 minutes, days 1 and 8 Repeat every 3weeks or Irinotecan 180 mg/m ² IV over 30-90 minutes, day1 Repeat every 2weeks or Irinotecan 300-350 mg/m ² IV over 30-90 minutes, day 1 Repeat every 3weeks
<i>Weekly</i>	
Leucovorin 20 mg/m ² IV over 2 hours on day 1, 5-FU 500 mg/m ² IV bolus injection 1 hour after the start of leucovorin. Repeat weekly. 5-FU 2600 mg/m ² by 24-hour infusion plus leucovorin 500 mg/m ² . Repeat every week (<i>AIO regimen</i> ⁴ : lecovorin 500 mg/m ² in N/S 250ml over 2 hours followed by 5-FU 2600 mg/m ² in N/S 500ml by 24-hour infusion weekly x6 and 2 weeks off, repeat every 8 weeks)	
	Capecitabine (may add with Bevacizumab)
	850–1250 mg/m ² PO twice daily, days 1–14 Repeat every 3 weeks
<i>Mayo Clinic regimen</i> ⁴	Ufur/LV ¹
Leucovorin 20 mg/m ² /day IV over 30 minutes followed by 5-FU IV bolus 425 mg/m ² /day x 5 days. Repeat every 5 weeks	Leucovorin 20-30 mg/m ² + Ufur 300-500 mg/ m ² PO at day 1 to 28 in every 35 days

Chemotherapy Regimens for Advanced/Metastatic Disease (3 of3)

Modified regimen for CRS@VGHKS	IO
<i>modified mFOLFOX</i>	<i>Nivolumab + ipilimumab</i>
Oxaliplatin 85-100 mg/ m ² IV over 3 hours on day 1 Leucovorin 200 mg/ m ² IV over 1 hours after Oxaliplatin on day 1 5-FU 2600 mg/m ² IV continuous infusion over 18 hours (start on day 1) Repeat every 2 weeks	Nivolumab 3 mg/kg (30 minute IV infusion) and ipilimumab 1 mg/kg (30 minute IV infusion) once every 3 weeks for four doses, then nivolumab 3 mg/kg IV or nivolumab 240 mg IV every 2 weeks.
<i>modified FOLFIRI</i>	
Irinotecan 180 mg/m ² IV over 90 minutes, day 1 Leucovorin 200 mg/m ² IV infusion for 1 hours after irinotecan infusion, day 1 5-FU 2400-3000 mg/m ² continuous infusion over 18 hours (start on day 1) Repeat every 2 weeks	
<i>modified AIO regimen</i>	
leucovorin 250 mg/m ² in N/S 250ml over 1 hours followed by 5-FU 2600 mg/m ² in N/S 500ml by 18-hour infusion weekly x6 and 2 weeks off, repeat every 8 weeks	

¹Japanese regimen, is the equivalent of 5-FU/LV or capecitabine in adjuvant and advanced/metastatic therapy. Also refer to Reference[4], [5] and [6]

²Not available in routine practice in Taiwan now

³As third/fourth line chemotherapy for advanced/metastatic disease, based on reference[10]

⁴At VGHKS

Chemotherapy Regimens for Adjuvant Therapy (1 of 2)

mFOLFOX³	5-FU/leucovorin
Oxaliplatin 85 mg/m ² IV over 2 hours, day 1 Leucovorin 400 mg/m ² IV over 2 hours, day 1 5-FU 400 mg/m ² IV bolus on day 1, then 1200 mg/m ² /day x 2 days (total 2400 mg/m ² over 46–48 hours) IV continuous infusion Repeat every 2 weeks	<i>Rosewell Park regimen (?)</i> Leucovorin 500 mg/m ² given as a 2-hour infusion and repeated weekly x 6. 5-FU 500 mg/m ² given bolus 1 hour after the start of leucovorin and repeated weekly x 6. Every 8 weeks for 4 cycles
FLOX²	<i>Simplified biweekly infusional 5-FU/LV (sLV5FU2)</i>
5-FU 500 mg/m ² IV bolus weekly x 6 + leucovorin 500 mg/m ² IV weekly x 6, each 8-week cycle x 3 with oxaliplatin 85 mg/m ² IV administered on weeks 1, 3, and 5 of each 8-week cycle x 3	Leucovorin 400 mg/m ² IV over 2 hours on day 1, followed by 5-FU bolus 400 mg/m ² and then 1200 mg/m ² /day x 2 days (total 2400 mg/m ² over 46-48 hours) continuous infusion Repeat every 2 weeks
Capecitabine	
1250 mg/m ² PO twice daily, days 1–14 every 3 weeks x 24 wks	
CapeOX	<i>AIO regimen⁴</i>
Oxaliplatin 130 mg/m ² IV over 2 hours, day 1 Capecitabine 850–1000mg/m ² twice daily PO for 14 days Repeat every 3 weeks x 24 weeks	Lecovorin 500 mg/m ² in N/S 250ml over 2 hours followed by 5-FU 2600 mg/m ² in N/S 500ml by 24-hour infusion weekly x6 and 2 weeks off, repeat every 8 weeks
Ufur/LV¹	<i>Mayo Clinic regimen⁴</i>
Leucovorin 20-30 mg/m ² + Ufur 300-500 mg/ m ² PO at day 1 to 28 in every 35 days	Leucovorin 20 mg/m ² /day IV over 30 minutes followed by 5-FU IV bolus 425 mg/m ² /day x 5 days. Repeat every 5 weeks

¹Japanese regimen, is the equivalent of 5-FU/LV or capecitabine in adjuvant and advanced/metastatic therapy. Also refer to Reference[4], [5] and [6]

²FLOX is an alternative to FOLFOX or CapeOx but FOLFOX or CapeOx are preferred

³FOLFOX is reasonable for high-risk or intermediate-risk stage II patients and is not indicated for good- or average-risk patients with stage II colon cancer

⁴At VGHKS

Chemotherapy Regimens for Adjuvant Therapy (2 of 2)

Modified regimen for CRS@VGHKS
<i>modified mFOLFOX</i>
Oxaliplatin 85-100 mg/ m ² IV over 3 hours on day 1 Leucovorin 200 mg/ m ² IV over 1 hours after Oxaliplatin on day 1 5-FU 2600 mg/m ² IV continuous infusion over 18 hours (start on day 1) Repeat every 2 weeks
<i>modified AIO regimen</i>
Lecovorin 250 mg/m ² in N/S 250ml over 1 hours followed by 5-FU 2600 mg/m ² in N/S 500ml by 18-hour infusion weekly x6 and 2 weeks off, repeat every 8 weeks

癌症藥物停藥準則

1. 根據影像學檢查或臨床依據，針對目前癌症用藥反應效果不良者。
2. 癌症用藥期間，產生藥物不良反應者，或初次發生輕微藥物不良反應後，經調降劑量或處置，仍再次發生藥物不良或更嚴重之反應者。
3. 評估 **adverse effects(AEs)** 分級為第三級以上或任何無法承受之併發症者。
4. 評估 **Eastern Cooperative Oncology Group(ECOG) Performance Status** ≥ 3 者。
5. 經病人意願無法接受及配合持續治療，但經醫師解釋說明後，仍是無法接受癌症用藥或拒絕持續治療者。

Reference

1. Major base on NCCN Colon Cancer Clinical Practice Guidelines Version1. 2025
2. ESMO Clinical Practice Guidelines 2014: Gastrointestinal cancers -- section: Metastatic Colorectal Cancer, Early Colon Cancer, Rectal Cancer and AnalCancer
3. NHI regulations for CRCchemotherapy
4. Efficacy of oral UFT as adjuvant chemotherapy to curative resection of colorectal cancer: multicenter prospective randomized trial. Kato T, Ohashi Y, Nakazato H, Koike A, Saji S, Suzuki H, Takagi H, Nimura Y, Hasumi A, Baba S, Manabe T, Maruta M, Miura K, Yamaguchi A. *Langenbecks Arch Surg.* 2002Mar;386(8):575-81.
5. The role of UFT in metastatic colorectal cancer. Bennouna J, Saunders M, Douillard JY. *Oncology.*2009;76(5):301-10.
6. 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. Lembersky BC, Wieand HS, Petrelli NJ, O'Connell MJ, Colangelo LH, Smith RE, Seay TE, Giguere JK, Marshall ME, Jacobs AD, Colman LK, Soran A, Yothers G, Wolmark N. *J Clin Oncol.* 2006 May 1;24(13):2059-64.
7. *Dominique Elias et al.* Complete Cytoreductive Surgery Plus Intraperitoneal ChemohyperthermiaWithOxaliplatin for Peritoneal Carcinomatosis of Colorectal Origin, *J Clin Oncol* 27:681-685.2008
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9. *Hendlisz A, Van den Eynde M, Peeters M et al.* Phase III trial comparing protracted intravenous fluorouracil infusion alone or with yttrium-90 resin microspheres radioembolization for liver-limited metastatic colorectal cancer refractory to standard. *J Clin Oncol* 2010; 28:3687–3694.
10. *Chien-Yu Lu et al.* FOLFIRI and regorafenib combination therapy with dose escalation of irinotecan as fourth-line treatment for patients with metastatic colon cancer according to *UGT1A1* genotyping, *OncoTargets Ther.* 2014; 7:2143–2146

Appendix and Additional Information

1. Dosage of irinotecan in mFOLFIRI + Avstin regimen could be titrated up to $260\text{mg}/\text{m}^2$ in patient with 6TA/6TA in genotyping of UGT1A1. This is based on the ongoing research: **Prospective analysis of UGT1A1 promoter polymorphism for irinotecan dose escalation in metastatic colorectal cancer patients treated with bevacizumab combined with FOLFIRI as the first-line setting** by Dr. Wang