

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

2021年5月修訂

Kaohsiung Veterans General Hospital

Colon Cancer Clinical Practice Guidelines

Colorectal Cancer Multidisciplinary Team

May 2021 *version 1*

Content **Colon Cancer Clinical Practice Guidelines**

P.3-4	<u>Revisionsummary</u>
P.5	<u>Malignant polyp</u>
P.6	<u>Resectable primary coloncancer</u>
P.7	<u>Adjuvant therapy for stage I-II coloncancer</u>
P.8	<u>Adjuvant therapy for stage III coloncancer</u>
P.9	<u>Metastatic synchronous adenocarcinoma from largebowel</u>
P.10	<u>Resectable synchronous liver and/or lung metastasesonly</u>
P.11	<u>Unresectable synchronous liver and/or lung metastasesonly</u>
P.12	<u>Synchronous abdominal/peritonealmetastases</u>
P.13-16	<u>Chemotherapy for advanced or metastaticdisease</u>
P.17	<u>Workup forrecurrence</u>
P.18	<u>Resectable metachronous metastases</u>
P.19	<u>Unresectable metachronous metastases</u>
P.20	<u>Principles of chemotherapy</u>
P.21-23	<u>Chemotherapy regimens for advanced/metastaticdisease</u>
P.24-25	<u>Chemotherapy regimens for adjuvanttherapy</u>
P.26	<u>TNM classification & staging of coloncancer</u>
P.27	<u>Reference</u>
P.28	<u>Appendix & additionalinformation</u>

<Revision Summary>

in Version 1 2021 of the VGHKS ColonCancer Clinical Practice Guidelines from Version 1 2020 include:

1. [Pre-OP workup](#)(p.6):

- MMR/MSI testing
- MDT evaluation

2. Unresectable Synchronous Metastases or Medically Inoperable Treatment (p.12):

- Add HIPEC regimen: oxaliplatin or mitomycin C

3. [Regimen added](#)(p.13):

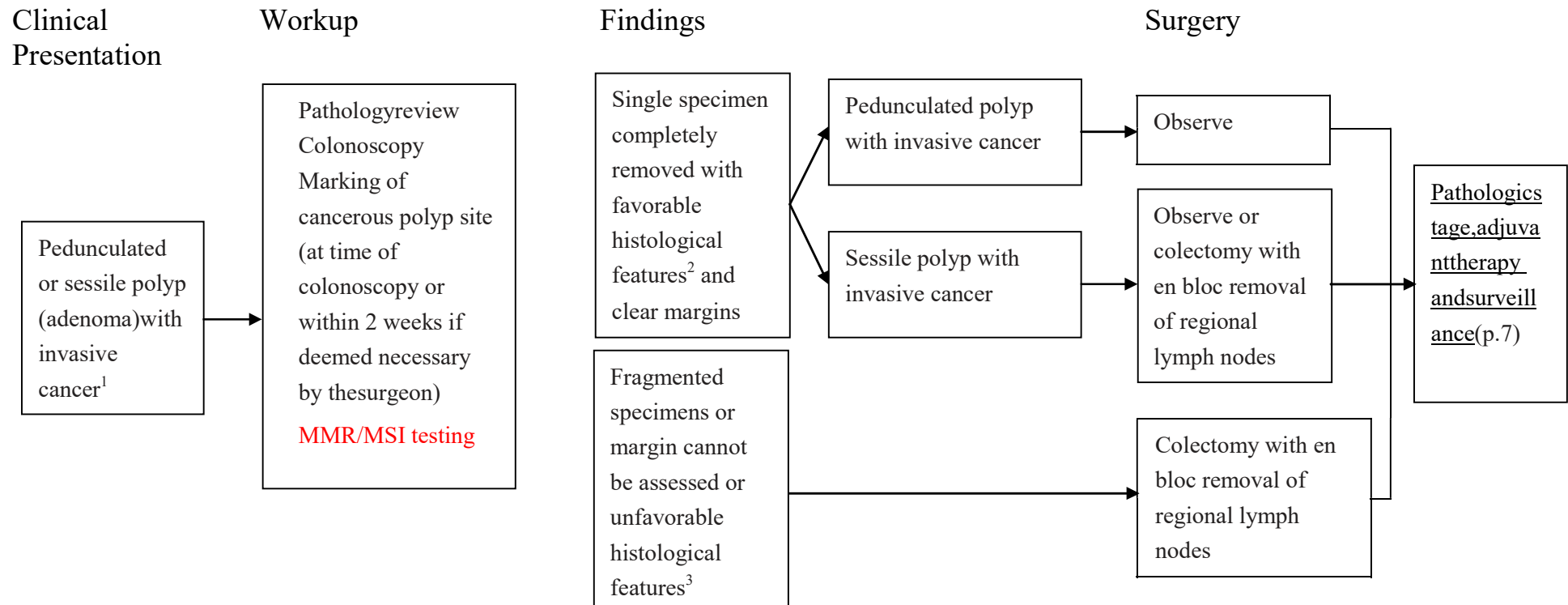
Trifluridine + tipiracil +/- bevacizumab

Add backbone with FOLFOXIRI for BRAF-mutant.

Dabrafenib + trametinib + (cetuximab or panitumumab)

BRAF V600E mutation (+)

Malignant polyp

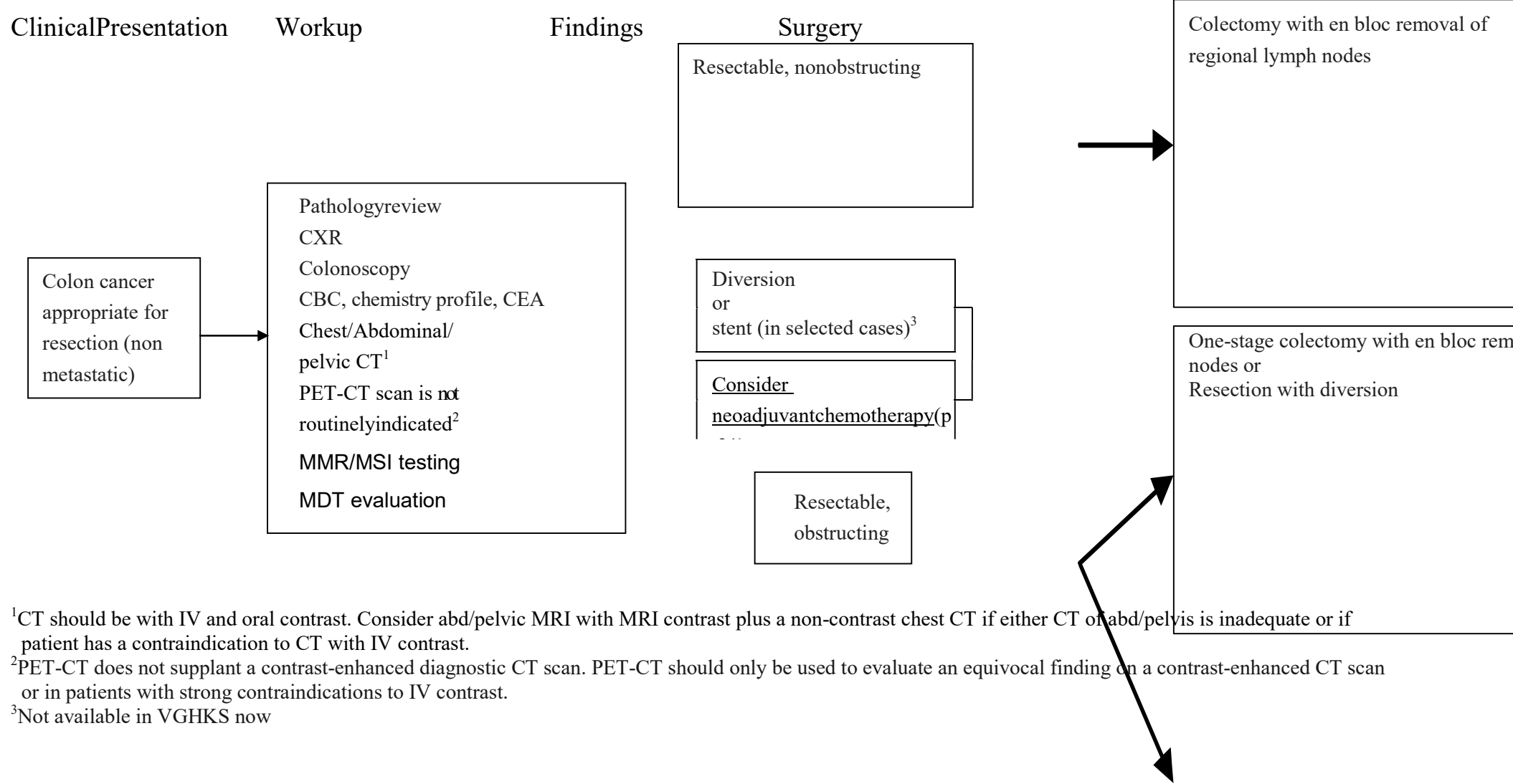


¹A malignant polyp is defined as one with cancer invading through the muscularis mucosae and into the submucosa (pT1). pTis is not considered a “malignant polyp”.

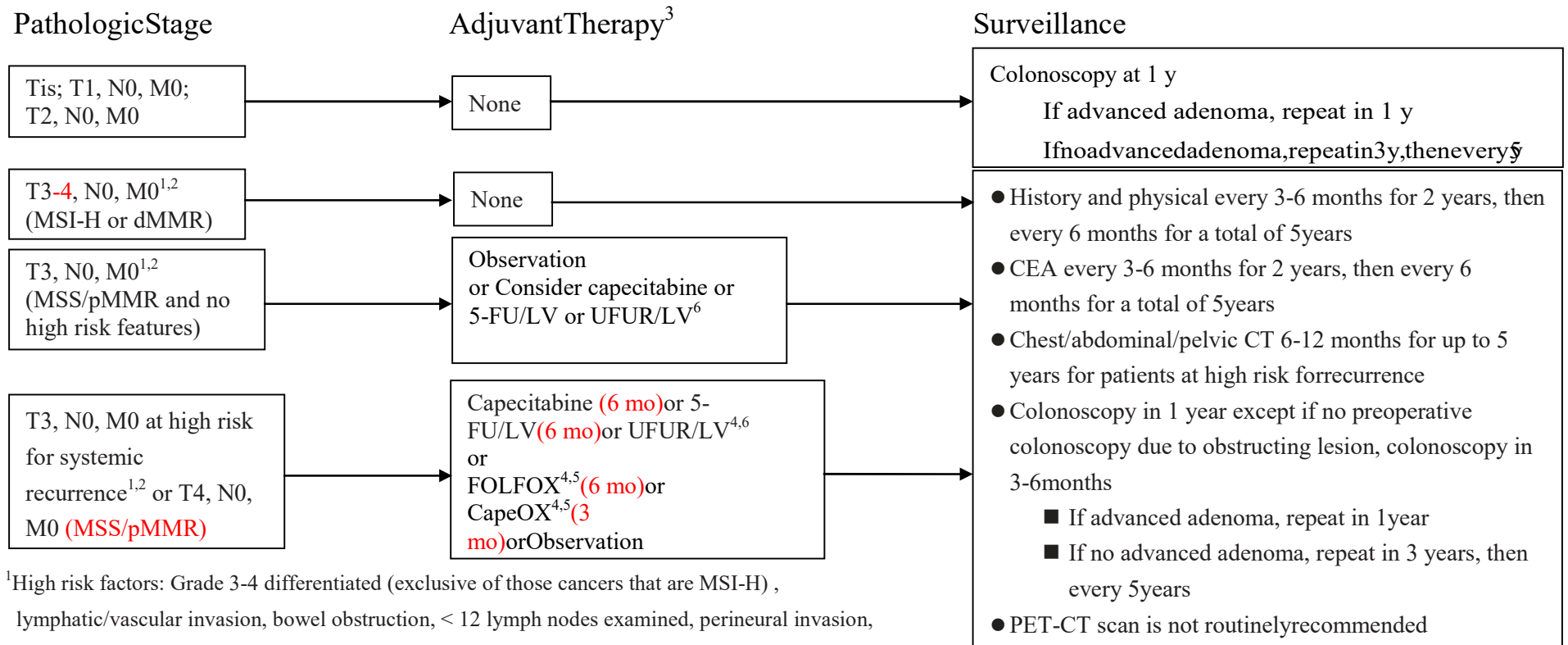
²Favorable histological features: Grade 1 & 2, no angiolymphatic invasion and negative margin of resection

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.

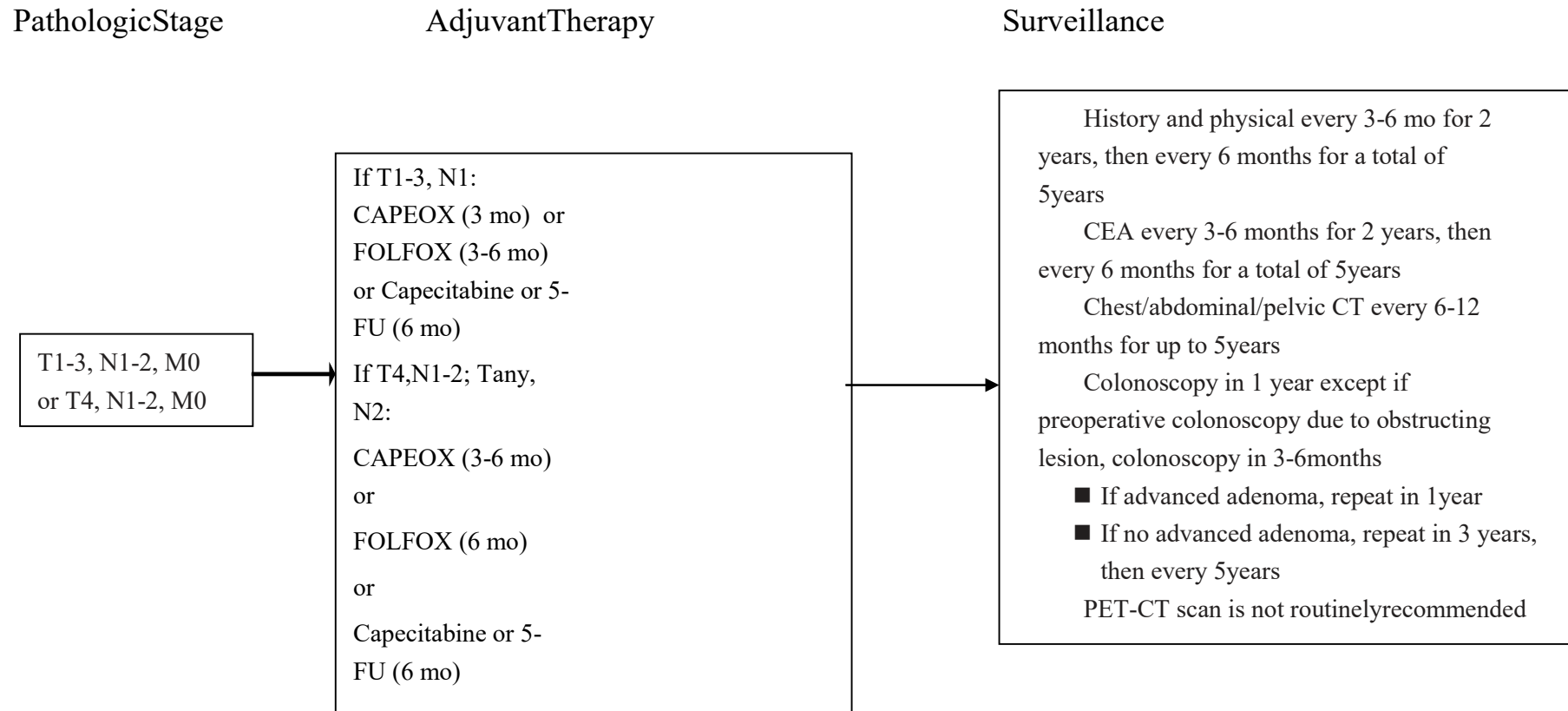
³Bevacizumab, cetuximab, panitumumab, or irinotecan should be not used in the adjuvant setting for stage II or III patients outside the setting of a clinical trial

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](#)

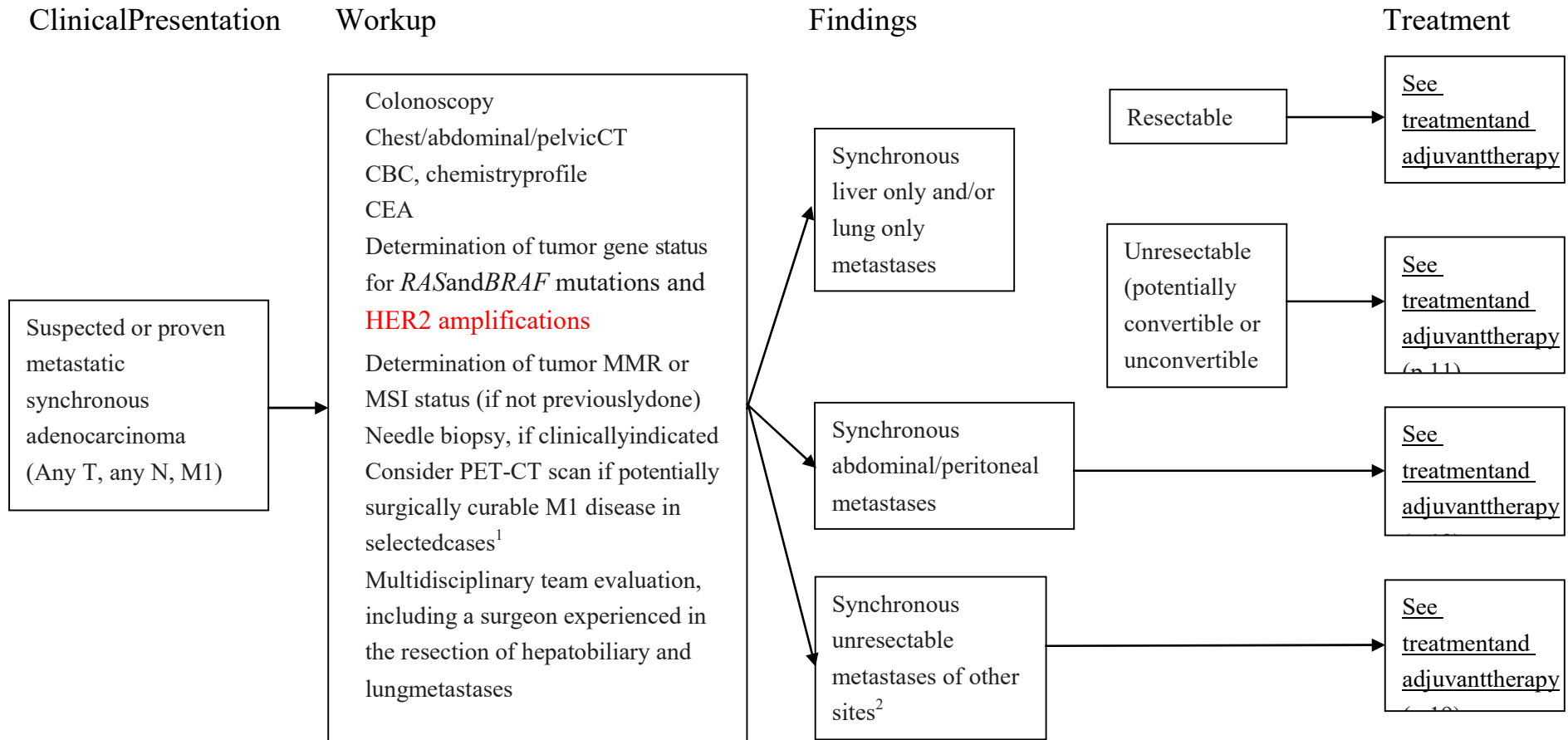
Adjuvant therapy for stage III colon cancer



¹ PLoS One. 2017 Mar 22;12(3):e0174280. Oral tegafur-uracil as metronomic therapy following intravenous FOLFOX for stage III colon cancer.

² Japanese regimen, also see [Chemotherapy Regimens](#)

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

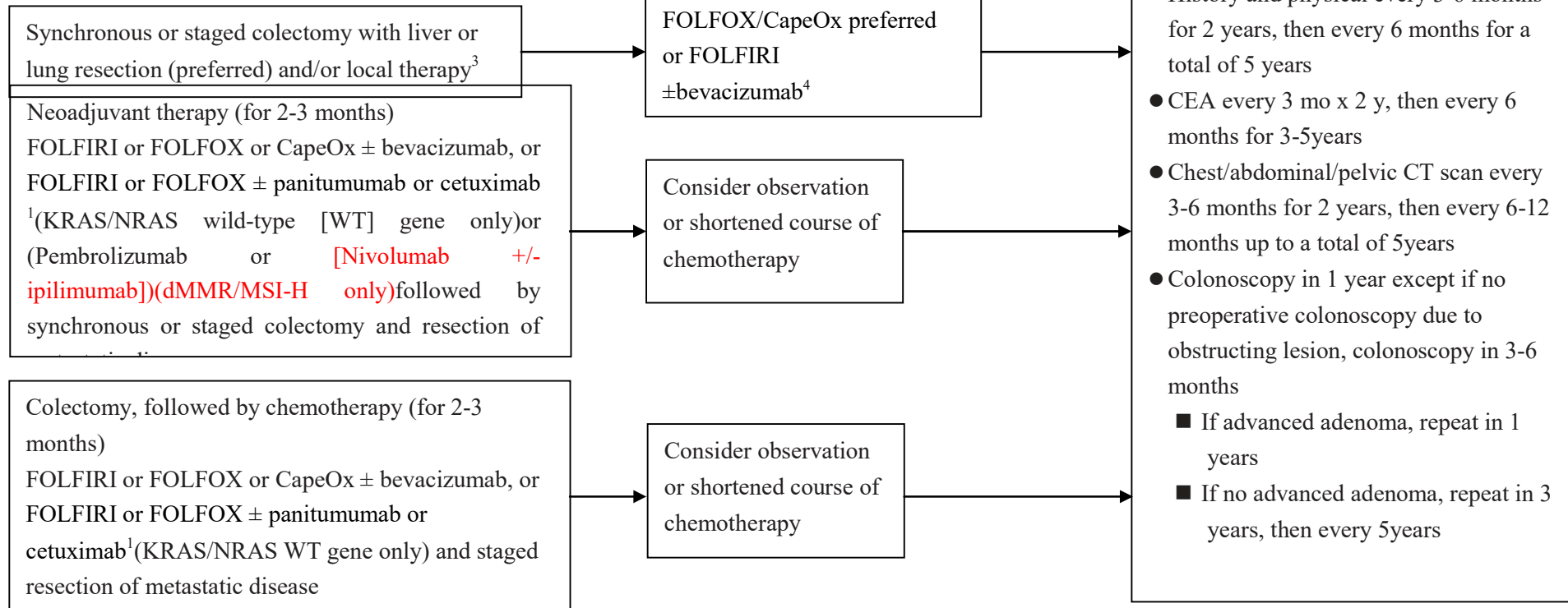
ADJUVANT THERAPY

Resectable metastatic disease
6 months peri-OP treatment preferred²

SURVEILLANCE

If patient stage IV, NED:

- History and physical every 3-6 months for 2 years, then every 6 months for a total of 5 years
- CEA every 3 mo x 2 y, 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 years
 - If no advanced adenoma, repeat in 3 years, then every 5 years



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 FOLFOXIRI ± panitumumab or cetuximab [KRAS /NRAS WT gene only] or, FOLFOXIRI ± bevacizumab)

[Nivolumab +/- ipilimumab] (dMMR/MSI-H only)

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

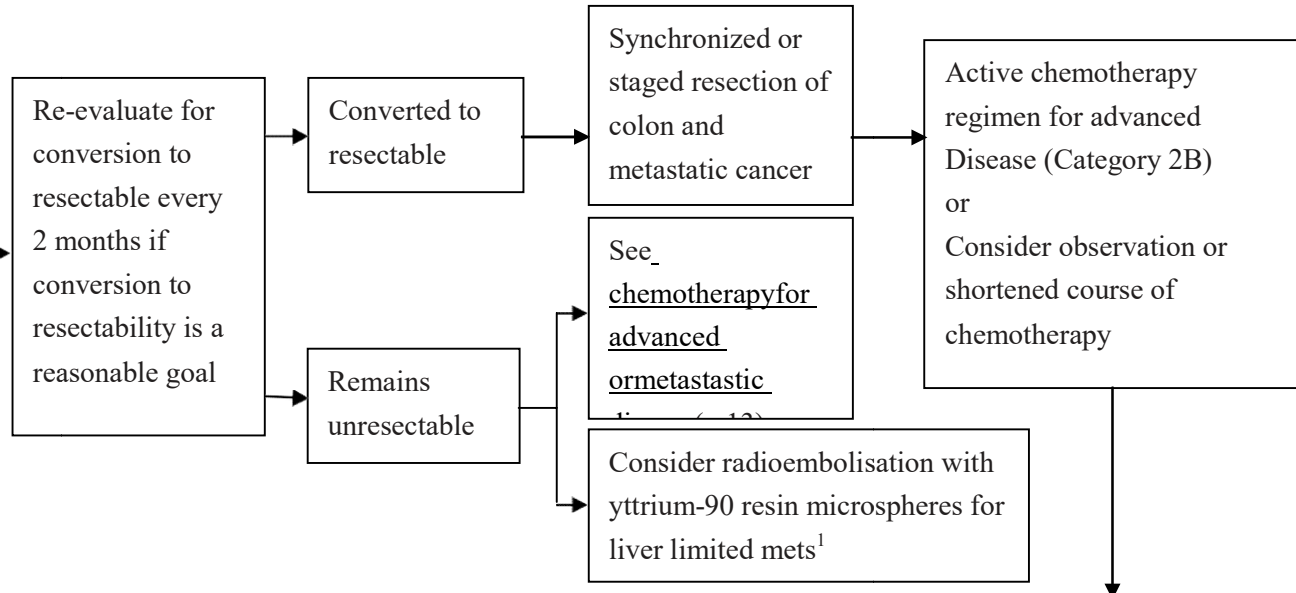
SURVEILLANCE

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

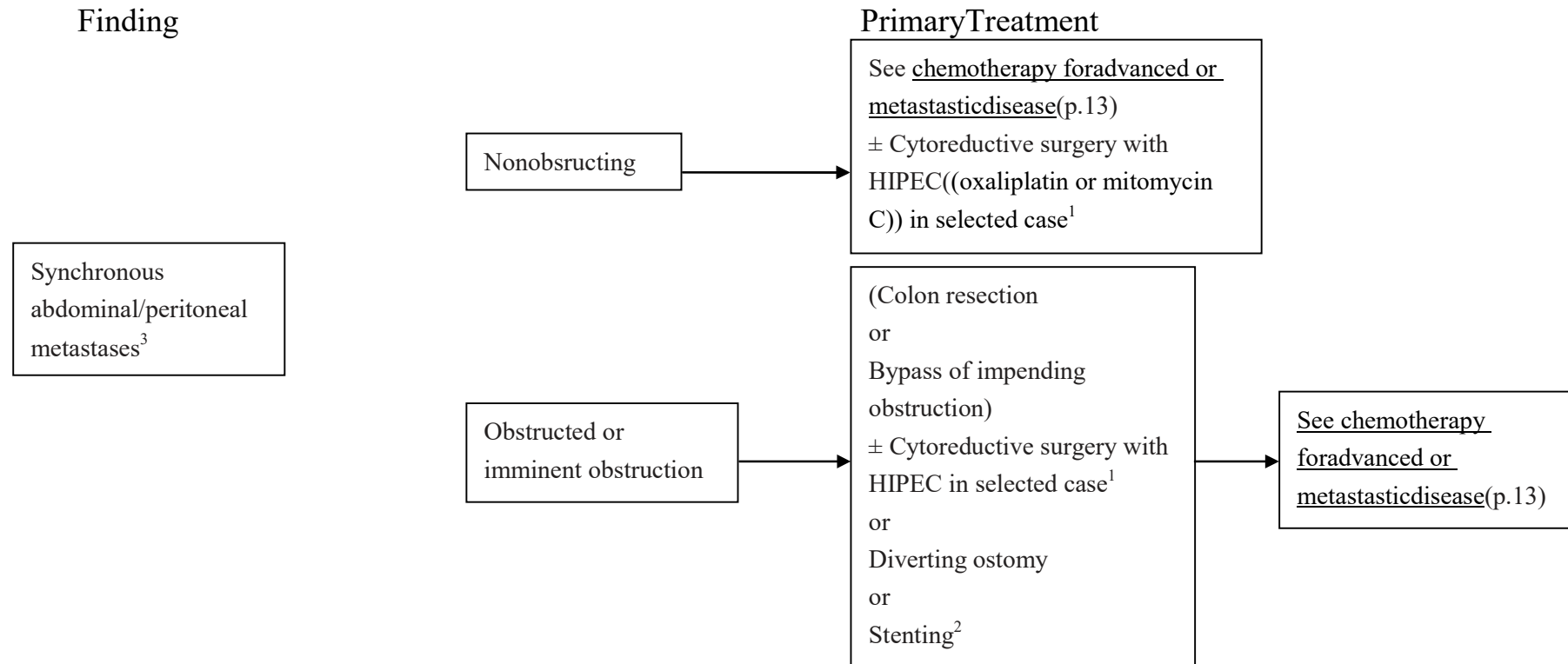
ADJUVANT THERAPY

6 months peri-OP treatment preferred



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

Synchronous abdominal/peritoneal metastases

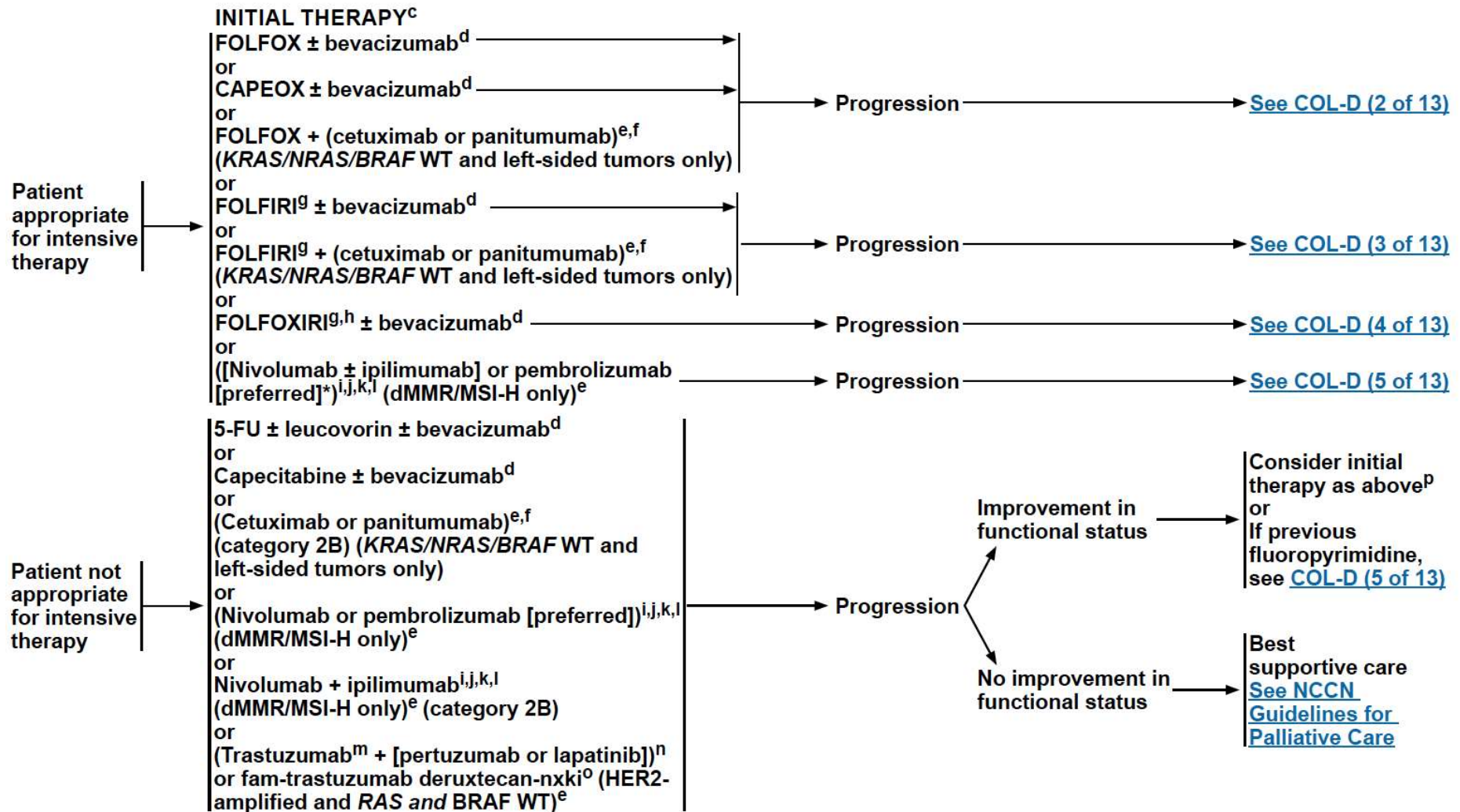


¹HIPEC = Hyperthermic Intraperitoneal Chemotherapy; Not documented in NCCN guideline 2015 v2 but in ESMO guideline 2014 (evidence grade IVB). Also refer to Reference [7], [8]

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)

SUBSEQUENT THERAPY^{C,I,S}

FOLFIRI^g or irinotecan^g
 or
 FOLFIRI^g + (bevacizumab^{d,t} [preferred] or ziv-aflibercept^{t,u} or ramucirumab^{t,u})
 or
 Irinotecan^g + (bevacizumab^{d,t} [preferred] or ziv-aflibercept^{t,u} or ramucirumab^{t,u})

or

FOLFIRI^g + (cetuximab or panitumumab)^v (KRAS/NRAS/BRAF WT only)^e
 or
 Irinotecan^g + (cetuximab or panitumumab)^v (KRAS/NRAS/BRAF WT only)^e
 or
 Encorafenib + (cetuximab or panitumumab)^w (BRAF V600E mutation positive)^e

([Nivolumab ± ipilimumab] or pembrolizumab [preferred])^{i,j,k,l} (dMMR/MSI-H only)^e
 or
 (Trastuzumab^m + [pertuzumab or lapatinib])ⁿ or fam-trastuzumab deruxtecan-nxki^o (HER2-amplified and RAS and BRAF WT)^e

See Subsequent Therapy ←

Irinotecan^g + (cetuximab or panitumumab)^v (KRAS/NRAS/BRAF WT only)^e

or
 Regorafenib^x

or
 Trifluridine + tipiracil ± bevacizumab^{d,x}

or
 ([Nivolumab ± ipilimumab] or pembrolizumab [preferred])^{i,j,k,l} (dMMR/MSI-H only)^e

or
 (Trastuzumab^m + [pertuzumab or lapatinib])ⁿ or fam-trastuzumab deruxtecan-nxki^o (HER2-amplified and RAS and BRAF WT)^e

See Subsequent Therapy ←

Regorafenib^x

or
 Trifluridine + tipiracil ± bevacizumab^{d,x}

or
 ([Nivolumab ± ipilimumab] or pembrolizumab [preferred])^{i,j,k,l} (dMMR/MSI-H only)^e

or
 (Trastuzumab^m + [pertuzumab or lapatinib])ⁿ or fam-trastuzumab deruxtecan-nxki^o (HER2-amplified and RAS and BRAF WT)^e

See Subsequent Therapy ←

Regorafenib^x
 or
 Trifluridine + tipiracil ± bevacizumab^{d,x}

Regorafenib^{x,y}
 or
 Trifluridine + tipiracil^y ± bevacizumab^{d,x}
 or
 Best supportive care
[See NCCN Guidelines for Palliative Care](#)

Previous oxaliplatin-based therapy without irinotecan

Dabrafenib +/- trametinib or

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

Chemotherapy for advanced or metastatic disease (1 of 4)

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

SUBSEQUENT THERAPY^{c,r,s}

FOLFOX or CAPEOX
or
FOLFOX + bevacizumab^d
or
CAPEOX + bevacizumab^d
or
FOLFOX +
(cetuximab or panitumumab)^v
(*KRAS/NRAS/BRAF* WT only)^e

or

Irinotecan^g +
(cetuximab or panitumumab)^v
(*KRAS/NRAS/BRAF* WT only)^e
or
Encorafenib +
(cetuximab or panitumumab)^w
(*BRAF* V600E mutation positive)^e

or

([Nivolumab ± ipilimumab] or pembrolizumab
[preferred])^{i,j,k,l} (dMMR/MSI-H only)^e
or
(Trastuzumab^m + [pertuzumab or lapatinib])ⁿ
or fam-trastuzumab deruxtecan-nxki^o
(HER2-amplified and *RAS* and *BRAF* WT)^e

See Subsequent Therapy ←

Irinotecan^g + (cetuximab or panitumumab)^v
(*KRAS/NRAS/BRAF* WT only)^e

Regorafenib^x
or
Trifluridine + tipiracil ± bevacizumab^{d,x}

([Nivolumab ± ipilimumab] or pembrolizumab
[preferred])^{i,j,k,l} (dMMR/MSI-H only)^e
or
(Trastuzumab^m + [pertuzumab or lapatinib])ⁿ
or fam-trastuzumab deruxtecan-nxki^o
(HER2-amplified and *RAS* and *BRAF* WT)^e

See Subsequent Therapy ←

FOLFOX or CAPEOX
or
([Nivolumab ± ipilimumab]
or pembrolizumab [preferred])^{i,j,k,l}
(dMMR/MSI-H only)^e

(Trastuzumab^m + [pertuzumab
or lapatinib])ⁿ or fam-trastuzumab
deruxtecan-nxki^o (HER2-amplified
and *RAS* and *BRAF* WT)^e

See Subsequent Therapy ←

Regorafenib^x
or
Trifluridine + tipiracil
± bevacizumab^{d,x}

Regorafenib^x
or
Trifluridine
+ tipiracil ±
bevacizumab^{d,x}

Regorafenib^{x,y}
or
Trifluridine
+ tipiracil^y ±
bevacizumab^{d,x}
or
Best supportive
care
[See NCCN
Guidelines for
Palliative Care](#)

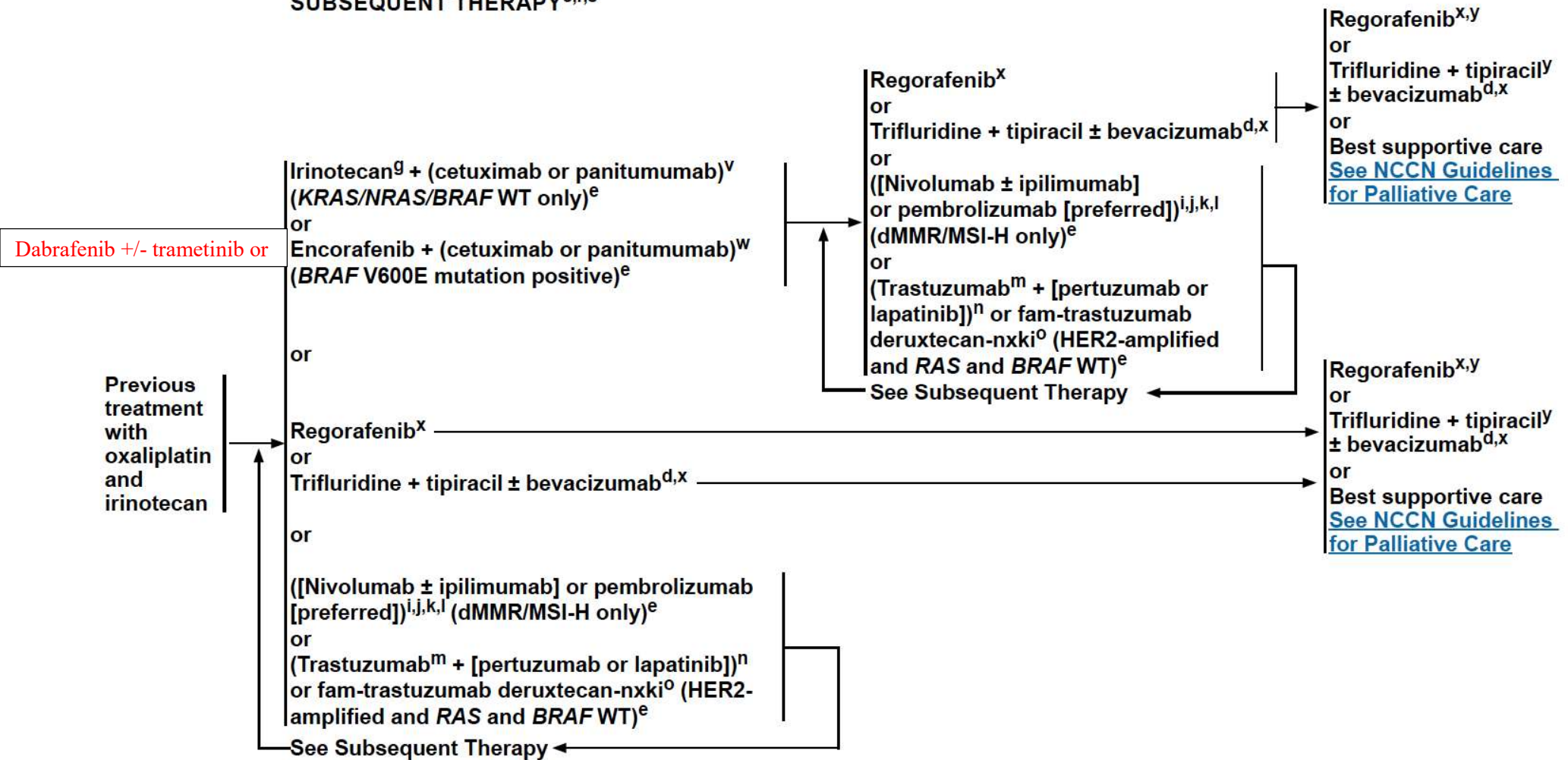
Previous
irinotecan-
based therapy
without
oxaliplatin

Dabrafenib +/- trametinib or

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

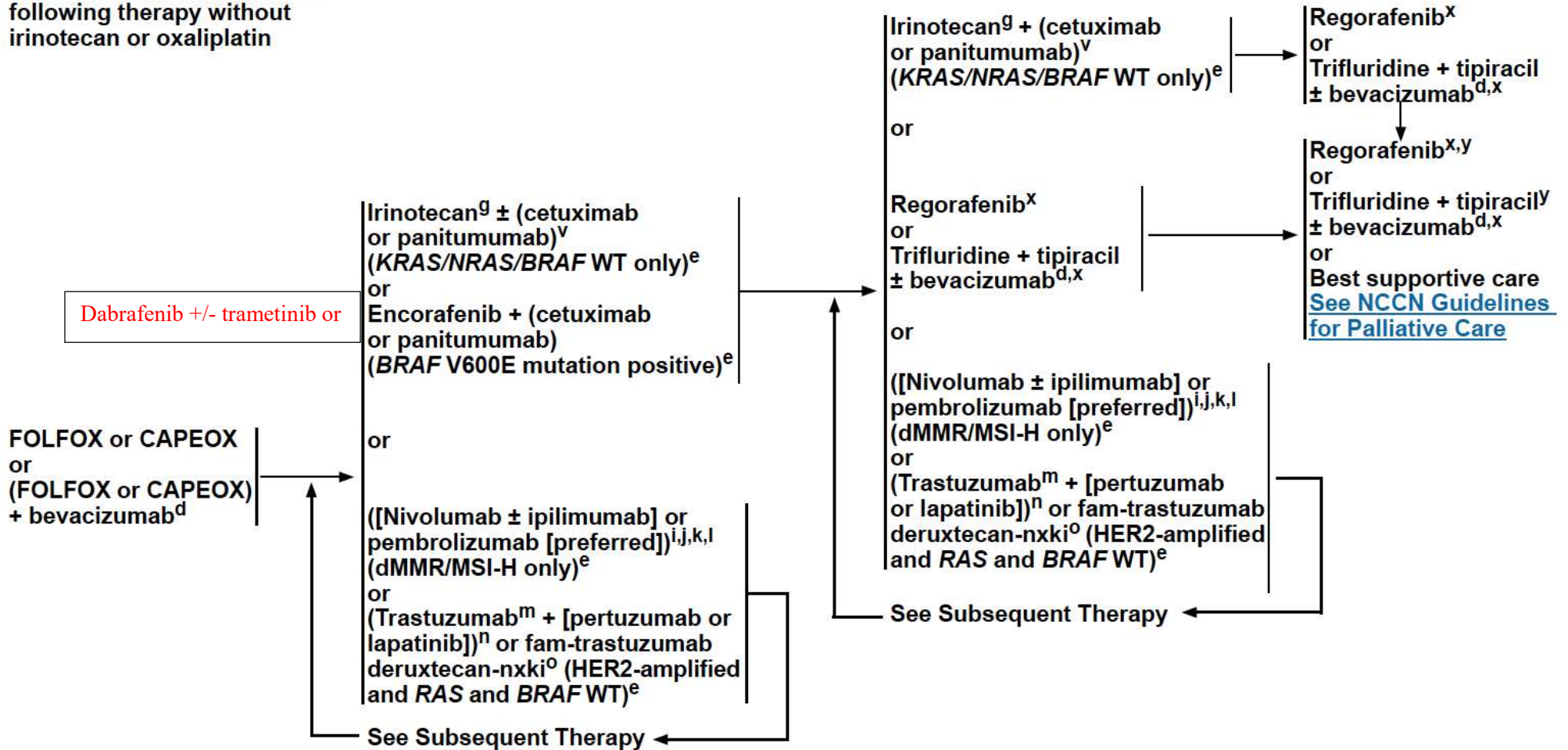
Chemotherapy for advanced or metastatic disease (1 of 4)

SUBSEQUENT THERAPY^{c,r,s}

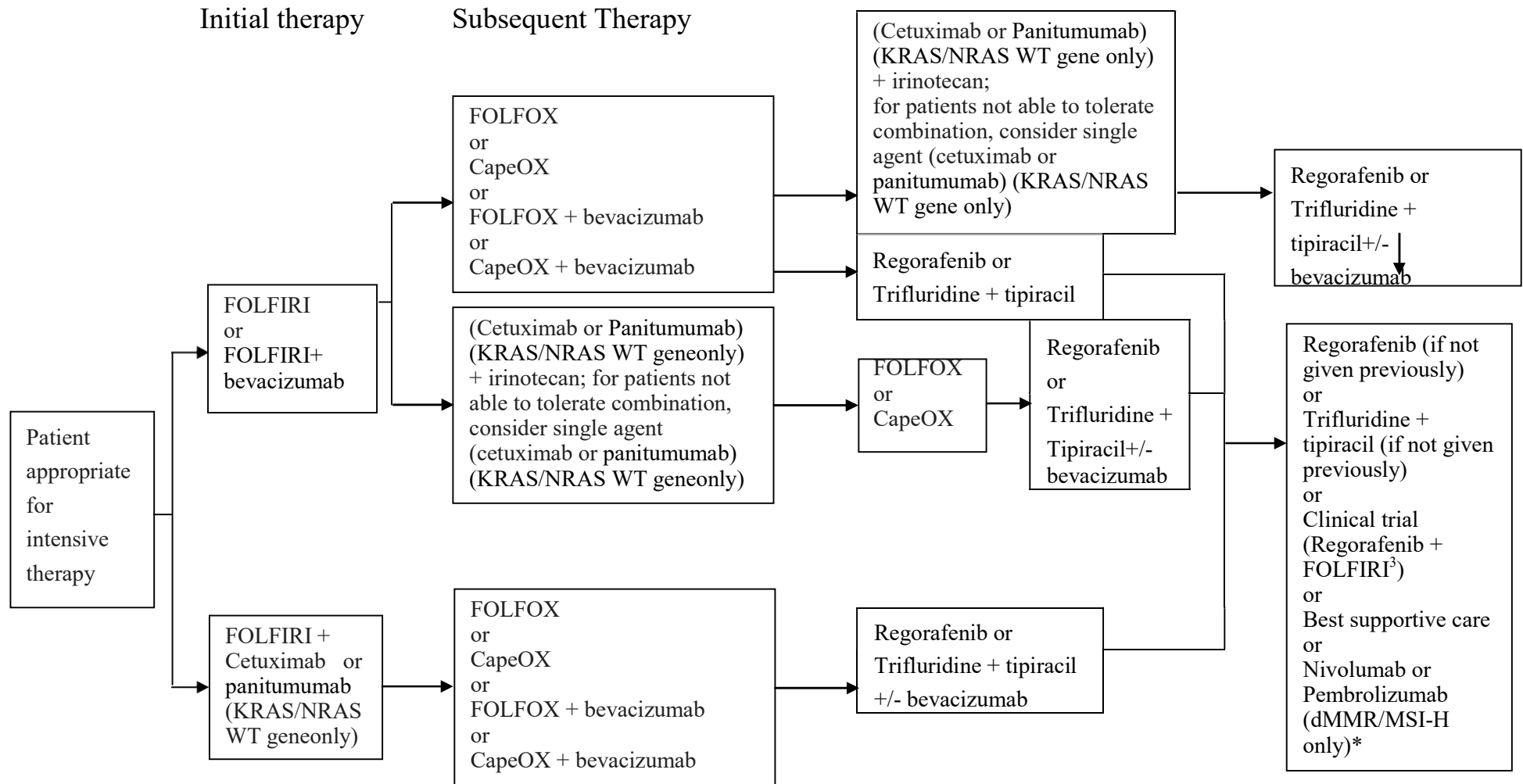


Chemotherapy for advanced or metastatic disease (1 of 4)

SUBSEQUENT THERAPY^{c,r,s}
following therapy without
irinotecan or oxaliplatin



Chemotherapy for advanced or metastatic disease (2 of 4)



*PD-1 blockade in tumors with mismatch-repair deficiency. N Engl J Med 2015;372:2509-2520. Nivolumab +/- ipilimumab in treatment of patients with metastatic colorectal cancer (mCRC) with

Chemotherapy for advanced or metastatic disease (2 of 4)

Initial therapy Subsequent Therapy

and without high microsatellite instability (MSI-H): CheckMate-142 Interim results [abstract]. ASCO Meeting Abstracts 2016;34:350

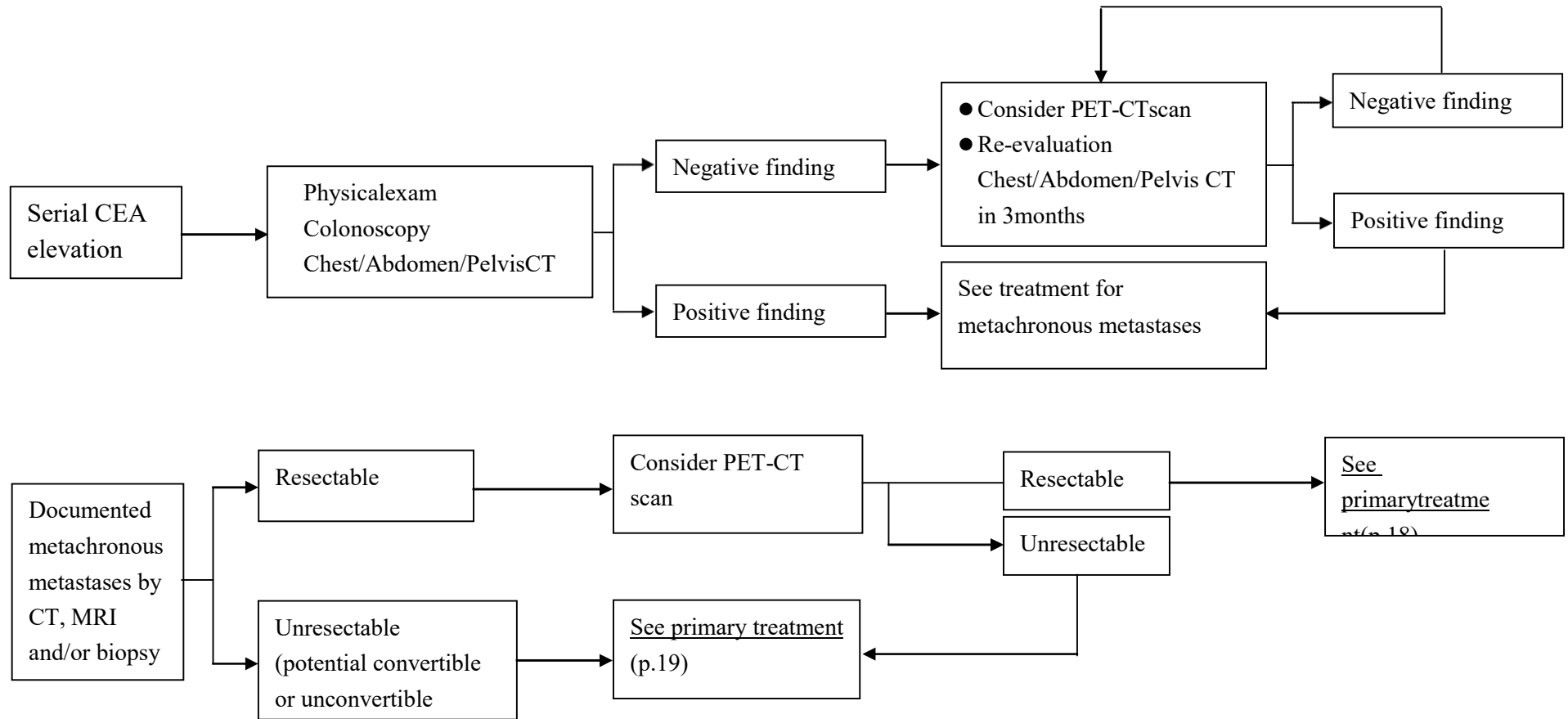
Chemotherapy for advanced or metastatic disease (3 of 4)

Chemotherapy for advanced or metastatic disease (4 of 4)

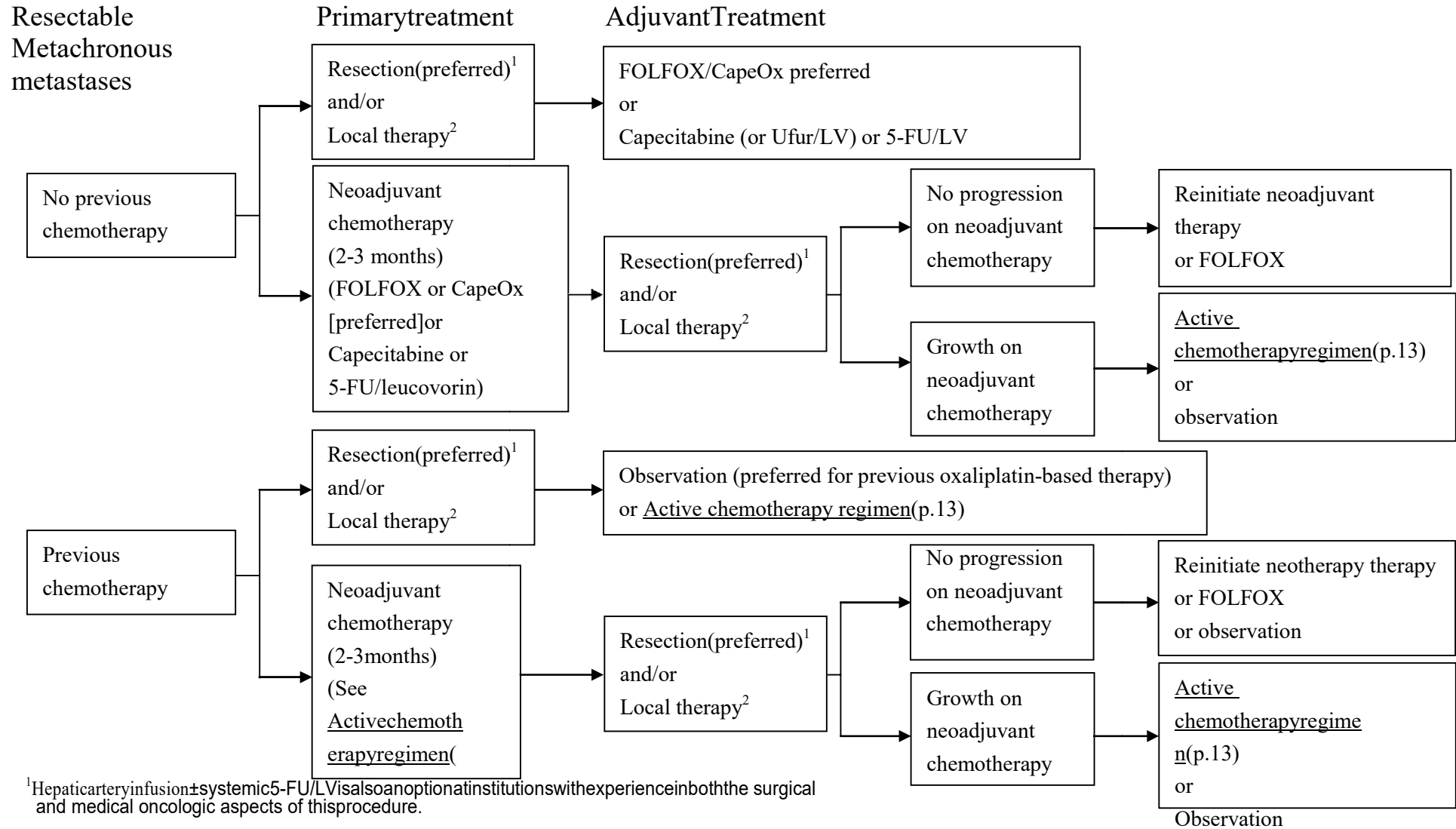
Workup for recurrence

Recurrence

Workup



Resectable metachronous metastases



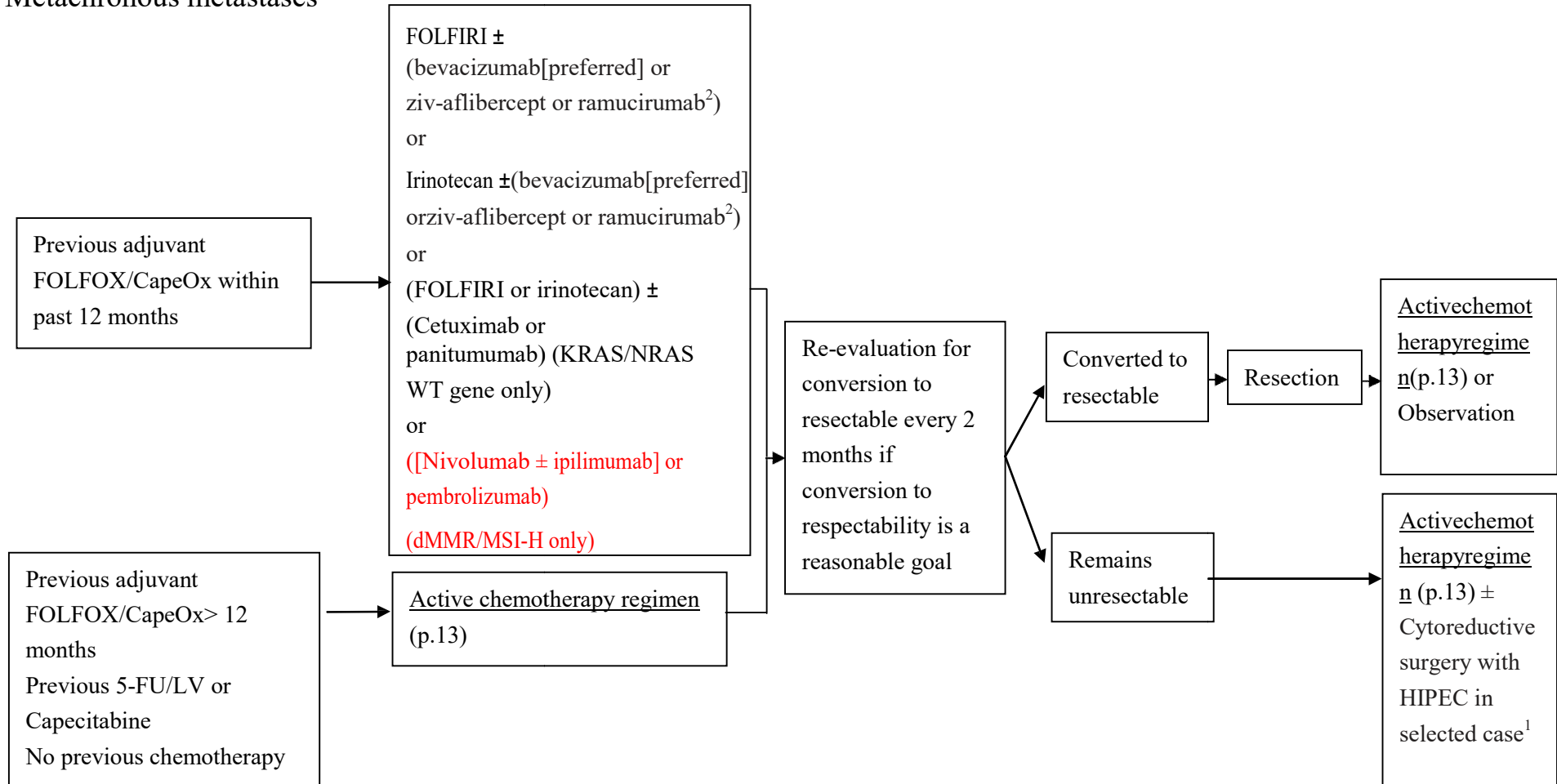
¹Hepatic artery infusion ± systemic 5-FU/LV is also an option at institutions with experience in both the surgical and medical oncologic aspects of this procedure.

²Resection is preferred over locally ablative procedures (eg, image-guided ablation or SBRT). However, these local techniques can be considered for liver oligometastases

Unresectable metachronous metastases

Unresectable
Metachronous metastases

Primary treatment



Unresectable metachronous metastases

¹See footnote “1” in Synchronous abdominal/peritoneal metastases

²Not available in routine practice in Taiwan now

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
FOLFOXIRI <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	Leucovorin 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 of2)

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

Definitions for T, N, M	
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 ^a
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into the pericolorectal tissues
T4a	Tumor penetrates to the surface of the visceral peritoneum ^b
T4b	Tumor directly invades or is adherent to other organs or structures ^{b,c}
Regional Lymph Nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	Noregionallymphnodemetastasis
N1a	Metastasis in one regional lymph node
N1b	Metastasis in 2-3 regional lymph nodes
N1c	Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
N2a	Metastasis in 4-6 regional lymph nodes
N2b	Metastasis in seven or more regional lymph nodes
Distant Metastasis (M)	
M0	M0 No distant metastasis
M1	M1 Distant metastasis
M1a	Metastasis confined to one organ or site (eg, liver, lung, ovary, onregional node)
M1b	Metastases in more than one organ/site or the peritoneum

7 th AJCC Colorectal cancer staging				Dukes [*]	MAC [*]
Group	T	N	M		
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	T1-2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3-4a	N1/N1c	M0	C	C2
	T2-3	N2a	M0	C	C1/C2
	T1-2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3-4a	N2b	M0	C	C2
	T4b	N1-2	M0	C	C3
IVA	anyT	anyN	M1a	-	-
IVB	anyT	anyN	M1b	-	-

Note: cTNM = clinical classification, pTNM = pathologic classification. Prefix “y” = classification after neoadjuvant pretreatment (eg, ypTNM). Patients who have a complete pathologic response are ypT0N0cM0 that may be similar to Stage Group 0 or I. Prefix “r” = recurred after a disease-free interval (rTNM).

*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

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. 2021
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 ChemohyperthermiaWith Oxaliplatin for Peritoneal Carcinomatosis of Colorectal Origin, *J Clin Oncol* 27:681-685.2008
8. *Vic J. Verwaal et al.* 8-Year Follow-up of Randomized Trial: Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy Versus Systemic Chemotherapy in Patients with Peritoneal Carcinomatosis of Colorectal Cancer, *Annals of Surgical Oncology* 15(9):2426–2432.2008
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-YuLu 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 260mg/m² in patient with 6TA/6TA in genotyping of UGT1A1. This is based on the ongoing reseach: **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