Current Guideline of Ablation for Metastatic Liver Tumor

Shih-Jer Hsu, MD. MMSc.
Department of Internal Medicine and Hepatitis Research Center
National Taiwan University Hospital

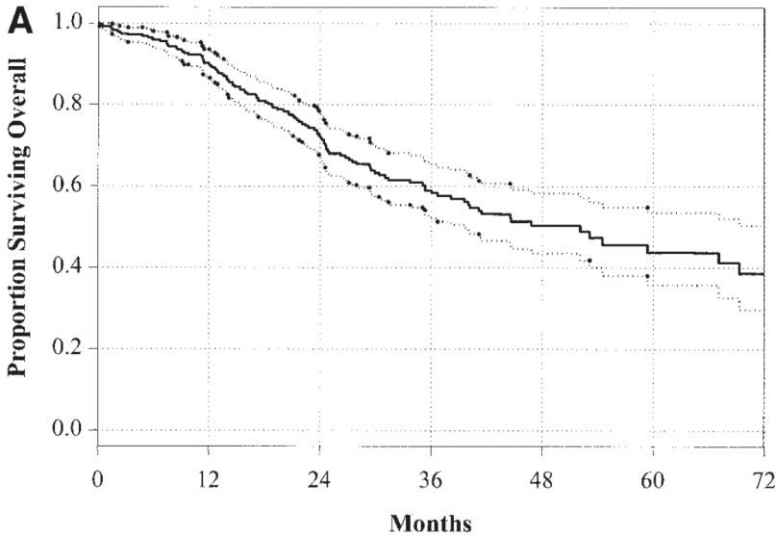
2024/09/15
TATA Autumn Convention

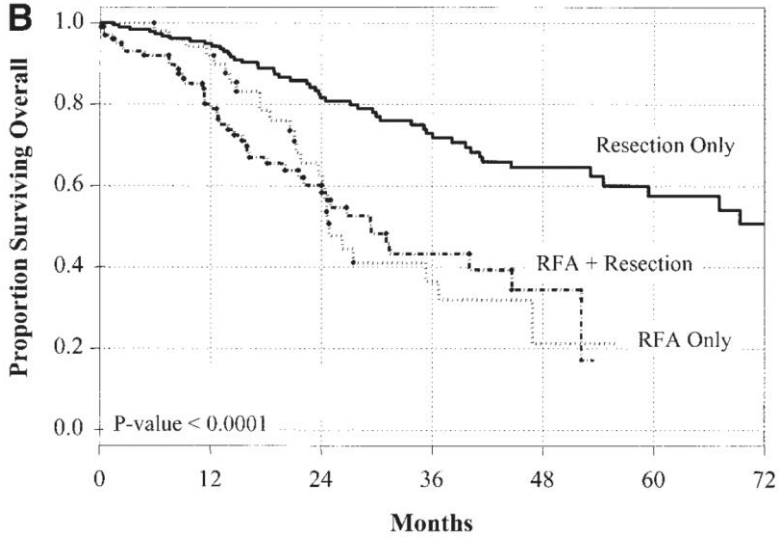
Outcomes Following Resection, RFA and Combined Resection/RFA for CRC Liver Metastases

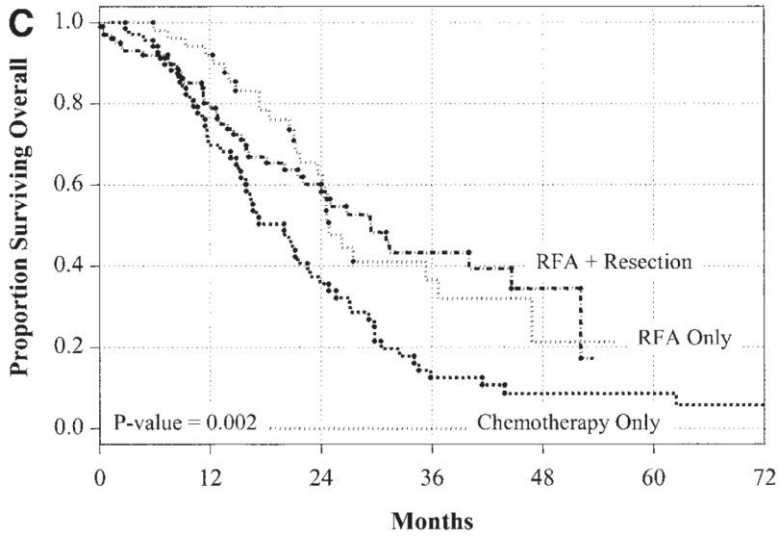
Resection only (n = 190); RFA + Resection (n = 101); RFA only (n = 57); chemotherapy only (n = 70)
RFA was used when patients were considered to be ' unresectable'.

	Overall Survival			Recurrence-free Survival		
Risk Factor	**Hazard Ratio**	**95% CI**	***P***	**Hazard ratio**	**95% CI**	***P***
RFA + resection vs. RFA	1.30	0.74, 2.28	0.36	1.50	0.96, 2.32	0.065
RFA + resection vs. resection only	2.14	1.28, 3.59	0.004	1.73	1.19, 2.51	0.004
RFA vs. resection only	2.79	1.68, 4.62	<0.0001	2.60	1.84, 3.68	<0.0001

CI, confidence interval; RFA, radiofrequency ablation.

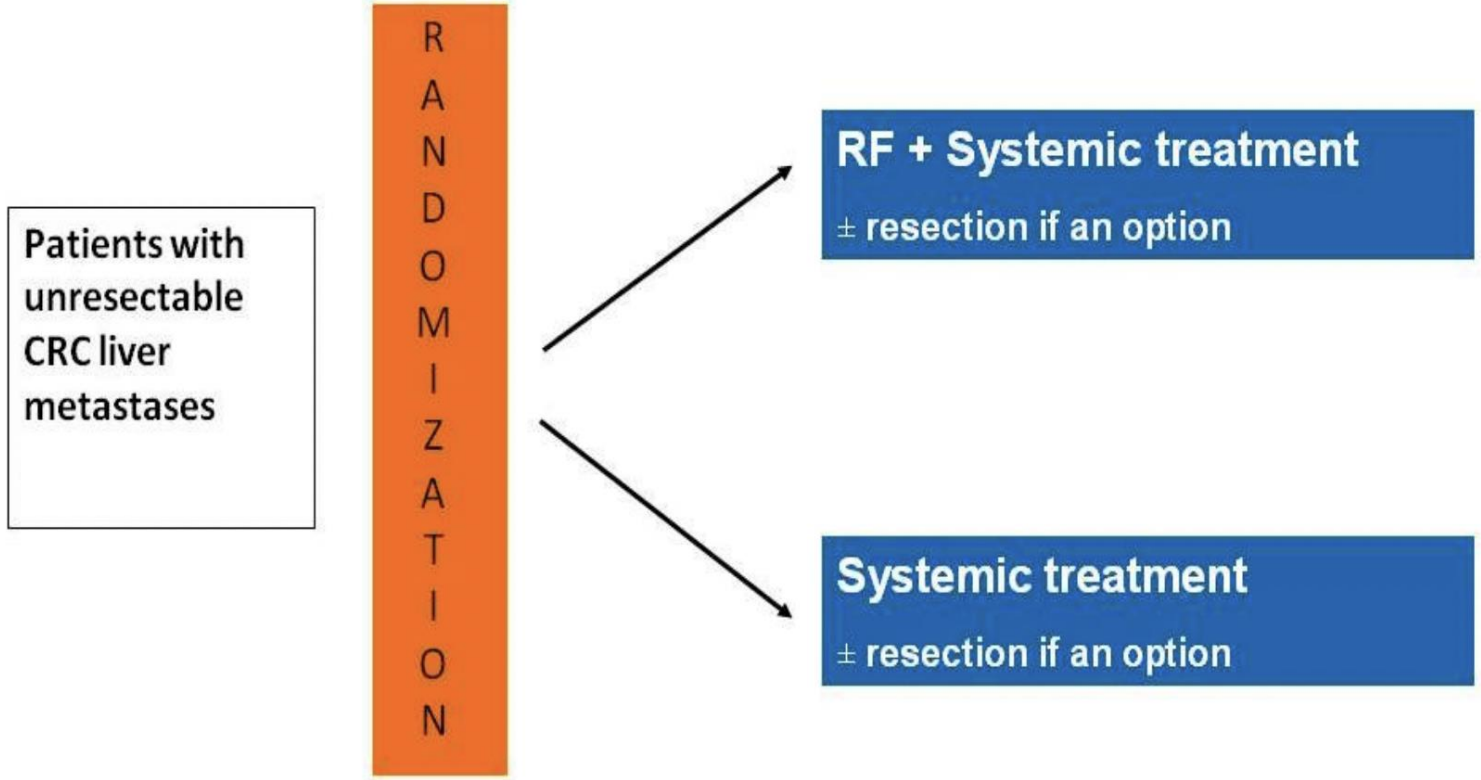






Abdalla EK, et al. Ann Surg. 2004 Jun;239(6):818-25

Benefits of Local Treatment for mCRC: EORTC CLOCC Trial



Designed as phase III trial with primary endpoint OS
Transformed to randomized phase II trial due to decreasing accrual

EORTC: European Organisation for Research and Treatment of Cancer

CLOCC Trial: Baseline Characteristics

Patient and tumor characteristics	Local plus systemic treatment (n = 60) No. (%)	Systemic treatment (n = 59) No. (%)
No. of liver metastases		
1-3	29 (48.3)	18 (30.5)
4-6	18 (30.0)	27 (45.8)
7-9	13 (21.7)	14 (23.7)
Median	4.0	5.0
Synchronicity of liver metastases		
Metachronous metastases	37 (61.7)	31 (52.5)
Synchronous metastases	23 (38.3)	28 (47.5)
T stage of primary cancer		
pT2	9 (15.0)	4 (6.8)
pT3/T4	42 (70.0)/9 (15.0)	48 (81.4)/6 (10.2)
N stage of primary cancer		
pN0	17 (28.3)	21 (35.6)
pN1/N2	22 (36.7)/20 (33.3)	24 (40.7)/12 (20.3)
Adjuvant chemotherapy for primary cancer		
No	50 (83.3)	49 (83.1)
Yes	10 (16.7)	10 (16.9)
Prior chemotherapy for metastatic disease		
No	51 (85.0)	51 (86.4)
Yes	9 (15.0)	8 (13.6)
Previous liver surgery for CRC metastases		
No	51 (85.0)	49 (83.1)
Yes	9 (15.0)	10 (16.9)

Ruers T, et al. J Natl Cancer Inst. 2017 Sep 1;109(9):djx015

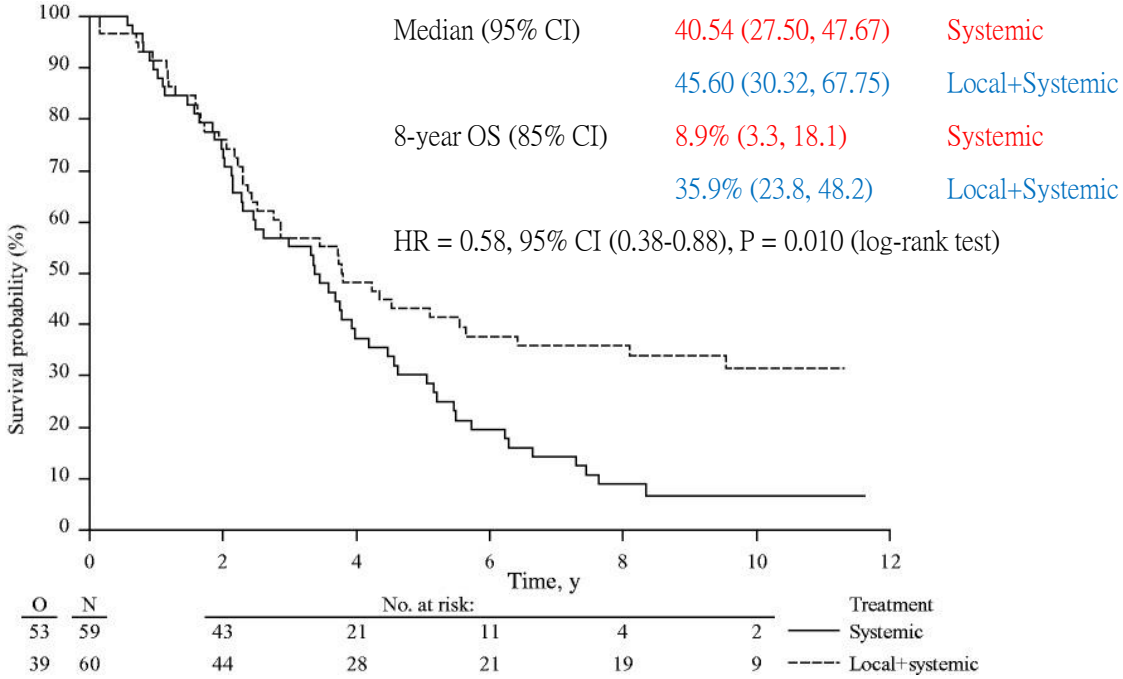
CLOCC Trial: Details of Local Treament

	RFA only (n =30) No. (%)	RFA plus resection (n = 27) No. (%)	Total (n = 57) No. (%)
Means of radiofrequency administration			
At laparotomy	25 (83.3)	26 (96.3)	51 (89.5)
Laparoscopically	1 (3.3)	0 (0.0)	1 (1.8)
Percutaneously	4 (13.3)	0 (0.0)	4 (7.0)
No RFA performed	0 (0.0)	1 (3.7)	1 (1.8)
Worst margin for resected tumors per patient (n = 27), cm			
≥1	NA	10 (37.0)	–
<1	NA	16 (59.3)	–
Residual tumor	NA	1 (3.7)	–
Worst margin for tumors treated by radiofrequency per patient (n = 56), cm		(n = 26)	(n = 56)
≥1	8 (26.7)	5 (19.2)	13 (23.2)
<1	16 (53.3)	17 (65.4)	33 (58.9)
No margin	4 (13.3)	1 (3.8)	5 (8.9)
Unknown	2 (6.7)	3 (11.5)	5 (8.9)
Treatment of at least one liver metastasis unsuccessful			
No	29 (96.7)	26 (96.3)	55 (96.5)
Yes	1 (3.3)‡	1 (3.7)	2 (3.5)

Ruers T, et al. J Natl Cancer Inst. 2017 Sep 1;109(9):djx015

CLOCC Trial: Outcomes

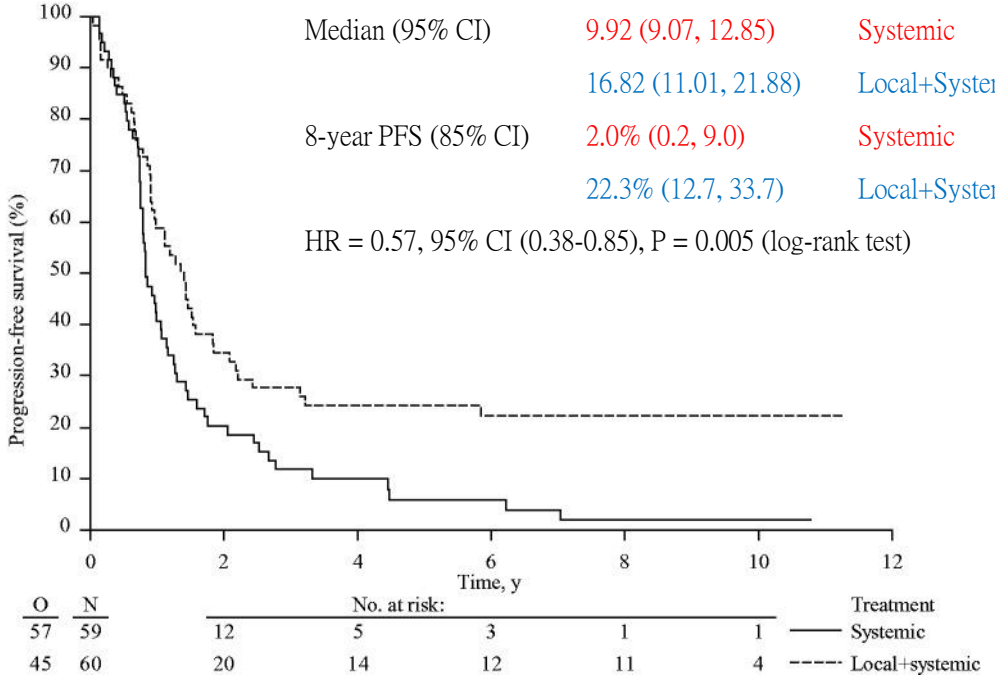
Overall Survival



Median (95% CI)	40.54 (27.50, 47.67)	Systemic
	45.60 (30.32, 67.75)	Local+Systemic
8-year OS (85% CI)	8.9% (3.3, 18.1)	Systemic
	35.9% (23.8, 48.2)	Local+Systemic

HR = 0.58, 95% CI (0.38-0.88), P = 0.010 (log-rank test)

Progression Free Survival



Median (95% CI)	9.92 (9.07, 12.85)	Systemic
	16.82 (11.01, 21.88)	Local+Systemic
8-year PFS (85% CI)	2.0% (0.2, 9.0)	Systemic
	22.3% (12.7, 33.7)	Local+Systemic

HR = 0.57, 95% CI (0.38-0.85), P = 0.005 (log-rank test)

Ruers T, et al. J Natl Cancer Inst. 2017 Sep 1;109(9):djx015

Eur Radiol (2015) 25:3438–3454
DOI 10.1007/s00330-015-3779-z

INTERVENTIONAL

Thermal ablation of colorectal liver metastases: a position paper by an international panel of ablation experts, the interventional oncology sans frontières meeting 2013

Alice Gillams[1] · Nahum Goldberg[2] · Muneeb Ahmed[2] · Reto Bale[3] · David Breen[4] · Matthew Callstrom[5] · Min Hua Chen[6] · Byung Ihn Choi[7] · Thierry de Baere[8] · Damian Dupuy[9] · Afshin Gangi[10] · Debra Gervais[11] · Thomas Helmberger[12] · Ernst-Michael Jung[13] · Fred Lee[14] · Riccardo Lencioni[15] · Ping Liang[16] · Tito Livraghi[17] · David Lu[18] · Franca Meloni[19] · Philippe Pereira[20] · Fabio Piscaglia[21] · Hyunchul Rhim[22] · Riad Salem[23] · Constantinos Sofocleous[24] · Stephen B. Solomon[24] · Michael Soulen[25] · Masatoshi Tanaka[26] · Thomas Vogl[27] · Brad Wood[28] · Luigi Solbiati[29]

Tumor and Technical Considerations

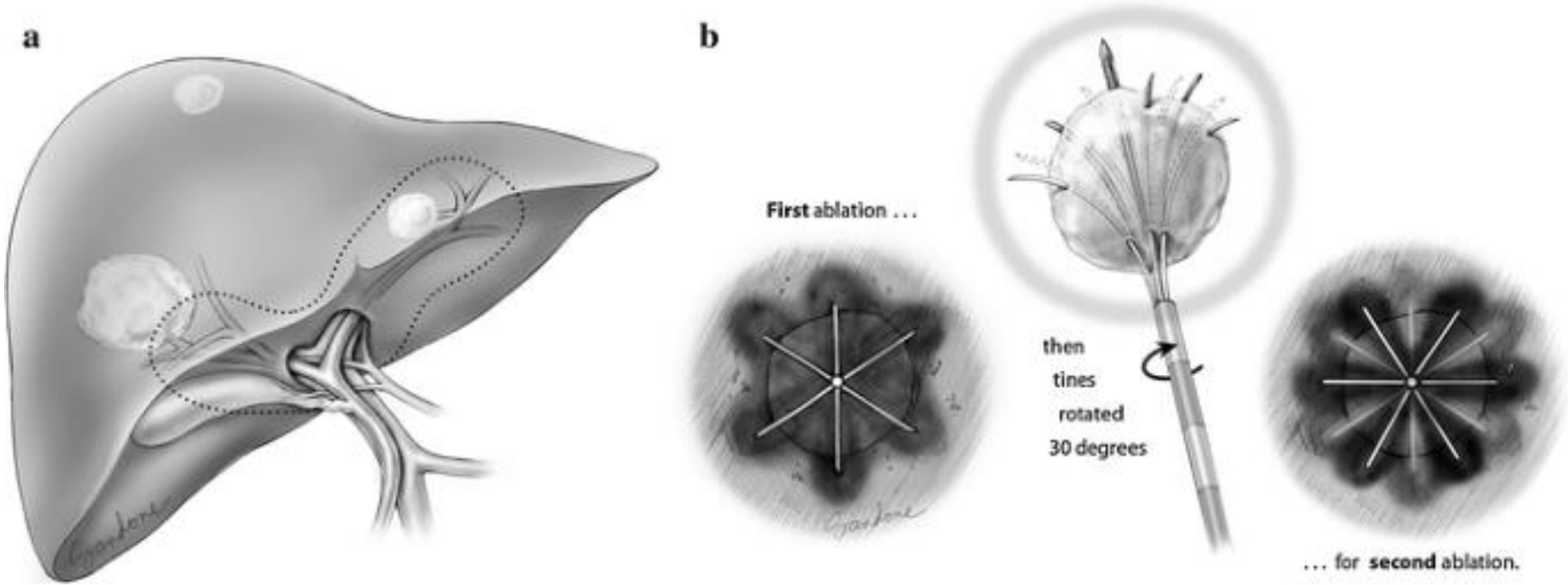
Parameter	Preferred	Caveat
Tumor size	<3 cm	Well located tumors <5 cm may be suitable for ablation
Tumor number	1–3 optimal, <5 preferable Avoid	6–9 maximum
Tumor location next to major bile ducts	Avoid	Consider high flow biliary cooling via nasobiliary tubes or other non-thermal interventional oncology techniques
Tumors located in contact with blood vessels	Suitable for ablation with careful follow-up and repeat treatment if necessary	Consider more intensive RF ablation to compensate for blood flow cooling, could consider IRE or MW
Tumors located within 1 cm of vulnerable structures, e.g. colon	Require displacement from the ablation zone using adjunctive measures, e.g. percutaneous hydro- or gas-dissection	Laparoscopic approach if adequate separation cannot be achieved percutaneously
Extra-hepatic disease (EHD)	Suitable for liver ablation as long as all sites of EHD disease are radically treated	Palliative liver ablation in patients with more extensive EHD is not recommended
Local recurrence should be minimized by:	1. Achieving >1 cm ablation margins in 3D 2. Maximizing operator experience 3. GA should be available as required 4. Optimal definition of the tumor 5. Optimal intra-procedural assessment of the ablation zone	Conscious sedation procedures are an acceptable alternative in unfit patients

Gillams A, et al. Eur Radiol. 2015 Dec;25(12):3438-54.

Tumor Size and Local Recurrence

Author	Open RF ablation, %	Laparoscopic RF ablation, %	Percutaneous RF ablation, %	Size (cm)	Local recurrence, %
Hamada et al. (2012)			28	<3 >3	14 69
Hammill et al. (2011)		5		<3 3 – 5 >5	3 4 27
Nielsen et al. (2013)	13			<3 3 – 5 >5	9 27 45
Solbiati et al. (2012)			12	<2 2–3 All < 3 >3	5 19 10 45
Veltri et al. (2008)			26	<3 >3	33 67
Wang et al. (2013)			48	<2.5 ≥2.5	41 70

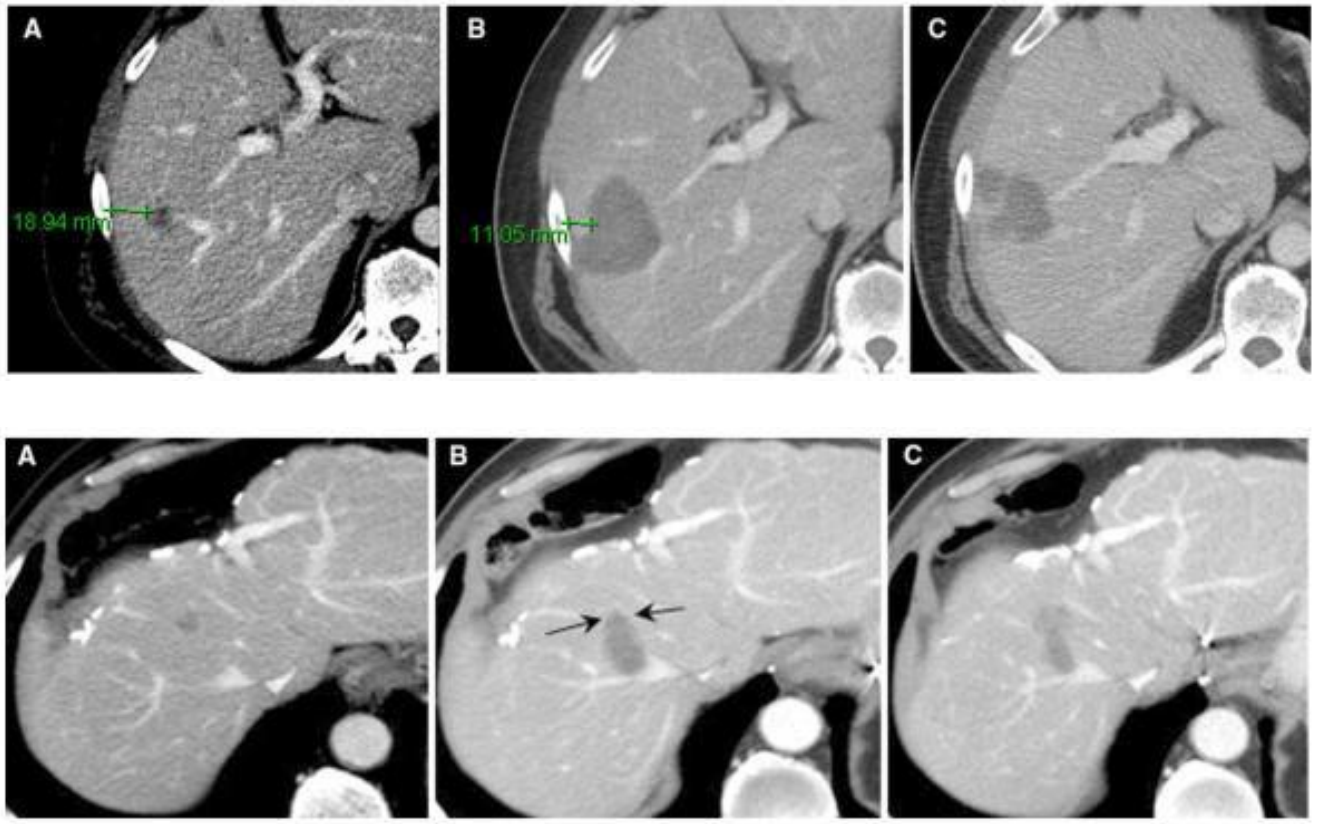
Wang X, et al. Cardiovasc Intervent Radiol. 2013 Feb;36(1):166-75.



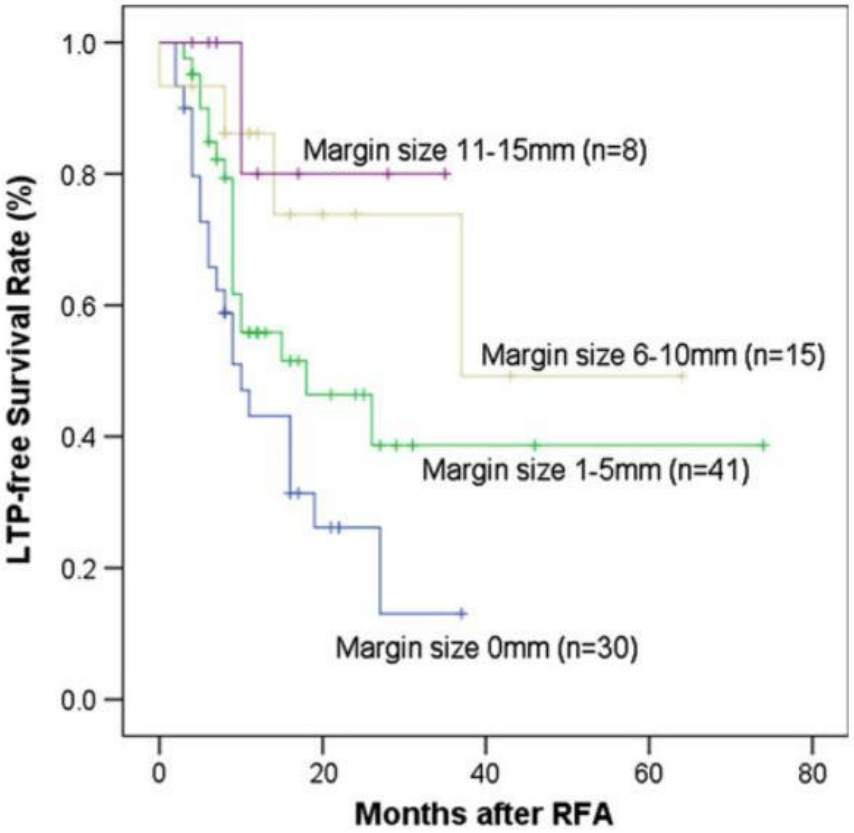
- The goal was a 1-cm margin.
- Ablations resulting in destruction of >20% of the hepatic parenchyma were not performed in a single setting.
- Ablations within 1 cm of the central bile ducts were generally not performed to avoid potential biliary injury.
- Tumors adjacent to large vessels were ablated only if it was thought that an aggressive ablation could overcome the heat-sink effect.

Hammil CW, et al. Ann Surg Oncol. 2011 Jul;18(7):1947-54.

Margin Size and Local Tumor Progression

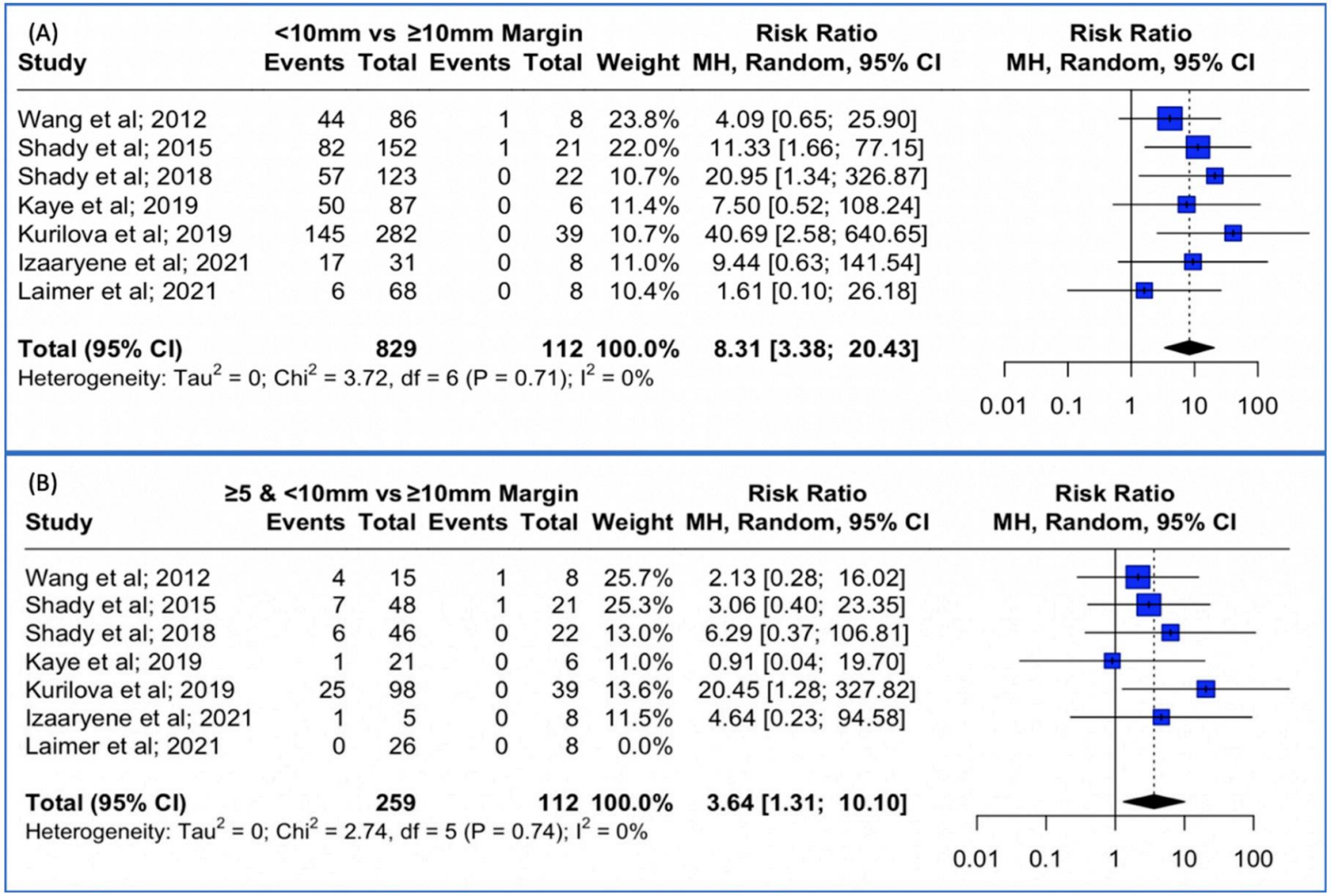


The risk for LTP decreased by 46 % for each 5-mm increase in minimal margin size.



Wang X, et al. Cardiovasc Intervent Radiol. 2013 Feb;36(1):166-75.

Margin Size and Local Tumor Progression



Chlorogiannis D, et al. Cancers (Basel). 2023 Dec 12;15(24):5806.

Clinical Recommendations

Clinical indication	Rationale	Consensus level
Ablation ± chemotherapy is recommended as the treatment of choice in patients with non-resectable but limited liver disease	RCT data shows significantly better disease free survival when ablation is added to chemotherapy Data from large case series shows a 5-year survival of 30 % (17–51 %) in ablation patients which is substantially different from the near 0 % seen after chemotherapy, albeit in different populations	Strong
Ablation ± chemotherapy is recommended in patients with limited liver disease who could otherwise only undergo resection following portal vein embolization or staged resection but are suitable for ablation	5-year survival results are the same following ablation as for resection following downsizing with chemotherapy, portal vein embolization or staged resection without the high morbidity associated with multiple procedures	Strong
Ablation is recommended as the treatment of choice in patients with non-resectable disease due to inadequate liver reserve, including most patients who have had a major liver resection	Risk of liver failure is very low Additional technical considerations include non-standard access, possible concomitant portal hypertension and the relationship of the tumor to major veins or bile ducts that subtend a major portion of the liver remnant	Strong
Ablation is recommended as the treatment of choice in patients with resectable disease who cannot undergo surgery due to medical co-morbidity	Surgical resection remains a major procedure with mortality of <3–5 % and major morbidity 25–30 %. The morbidity can be even higher in the older age group. Percutaneous ablation remains a low morbid, minimally invasive procedure that is well tolerated even by the medically unfit	Strong
Ablation is offered in some centers to patients with resectable disease as part of a ‘test-of-time approach’	Initial ablation does not prevent subsequent resection but does provide time for the tumor biology to declare. Patients with occult non-resectable disease will be spared ineffective surgery	Moderate

Gillams A, et al. Eur Radiol. 2015 Dec;25(12):3438-54.

Clinical Recommendations

Clinical indication	Rationale	Consensus level
Patient choice; patients with ablatable and resectable disease may prefer to undergo ablation	Ablation can be performed as long as the patient has had an opportunity to discuss treatment options with both surgeons and interventional oncologists	Strong
The addition of chemotherapy to ablation is beneficial	Neoadjuvant chemotherapy is advocated in patients with non-ablatable/resectable disease with the goal of downsizing to ablatable/resectable disease. First-line ablation is recommended in small volume disease followed by adjuvant chemotherapy. Ablation should still be performed in patients who cannot undergo/tolerate chemotherapy	Strong
The percutaneous approach is favored over and above the open approach	The open approach to ablation still carries a mortality and an unnecessarily high morbidity. Unless ablation is being performed as part of a surgical resection procedure, a percutaneous approach should be used	Strong
Ablation of small, <3 cm, solitary tumors is not currently an accepted indication but this may become a future indication	Retrospective comparisons suggest very similar outcomes between resection and ablation in these patients. An RCT would be welcomed by this panel of experts	Strong
Ablation is not recommended as a debulking tool	There is no evidence to support debulking in colorectal liver metastases	Strong
An interventional oncologist should be a standing member of the institutional colorectal liver metastasis tumour board	Access to ablation is still uneven and the advice given to patients does not always originate with an interventional oncologist qualified in percutaneous ablation – this needs to be rectified	Strong

Gillams A, et al. Eur Radiol. 2015 Dec;25(12):3438-54.

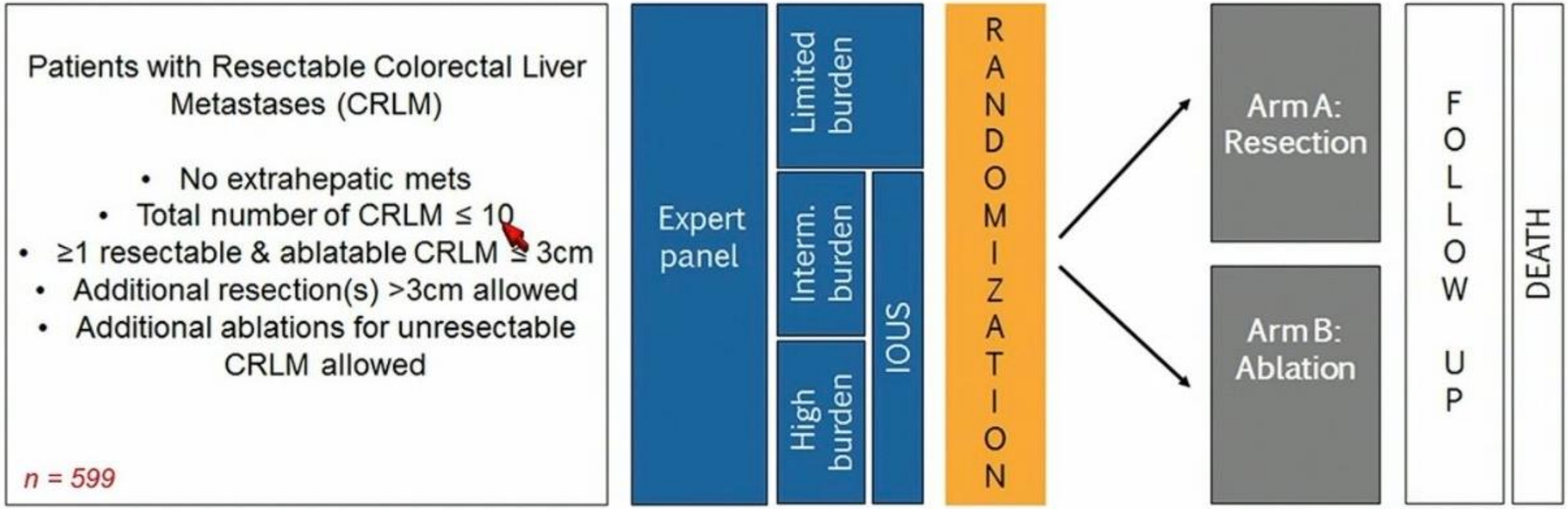
Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

Meeting Abstract: 2024 ASCO Annual Meeting II
FREE ACCESS | Gastrointestinal Cancer—Colorectal and Anal | June 05, 2024

Surgery versus thermal ablation for small-size colorectal liver metastases (COLLISION): An international, multicenter, phase III randomized controlled trial.

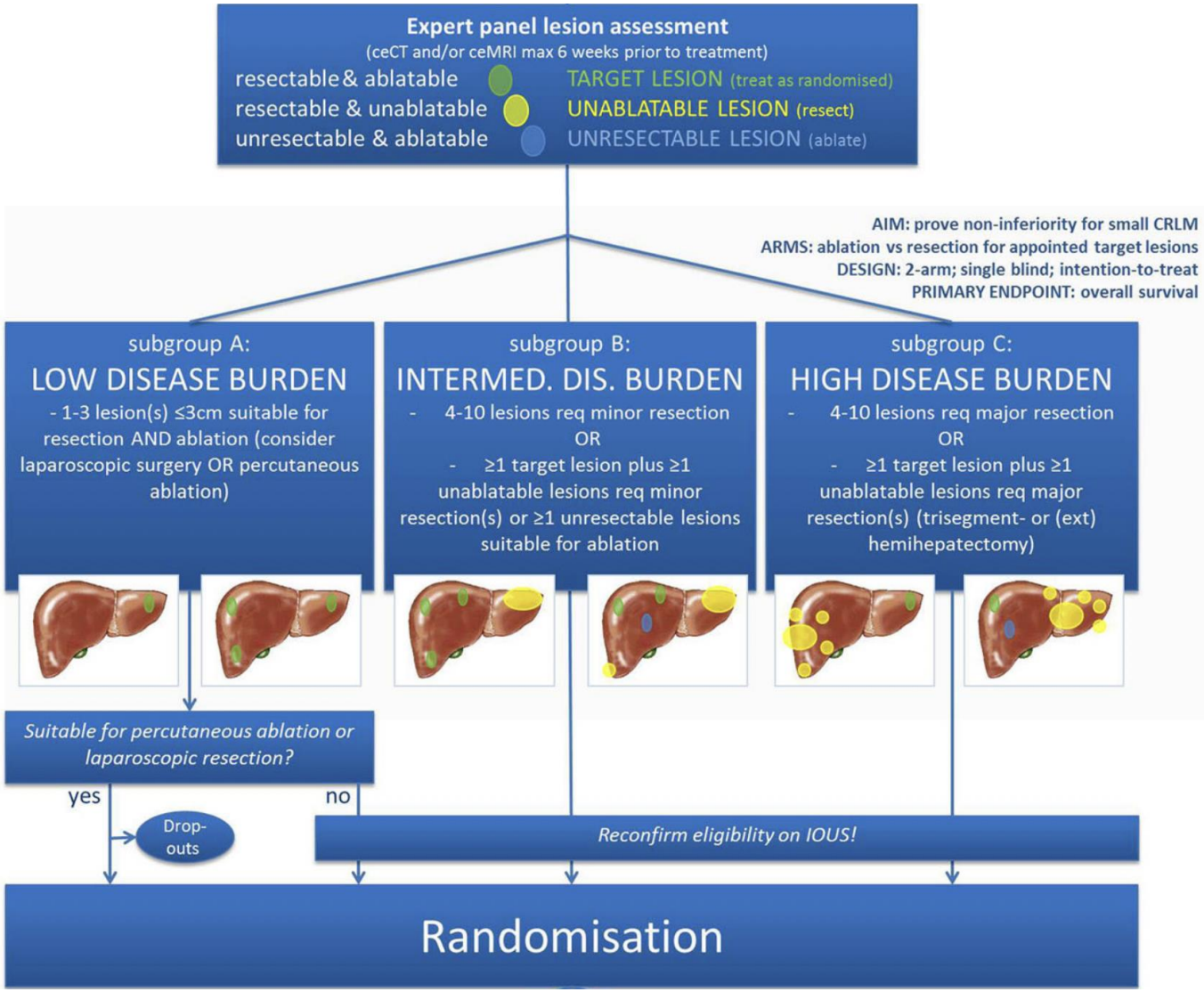
Authors: Martijn Ruben Meijerink, Susan van der Lei, Madelon Dijkstra, Kathelijn S. Versteeg, Tineke E. Buffart, Birgit I. Lissenberg-Witte, Rutger-Jan Swijnenburg, M. Petrousjka van den Tol, and Robbert S. Puijk COLLISION Trial Collaborator Group | AUTHORS INFO & AFFILIATIONS

COLLISION
Colorectal Liver Metastases: surgery vs thermal ablation



Phase III international multicenter randomized controlled trial to prove / disprove hypothesis of non-inferiority of thermal ablation compared to surgical resection for small-size colorectal liver metastases (CRLM)

- Approach (percutaneous, laparoscopic or open) according to local expertise
- If limited disease burden (max 3 CRLM ≤ 3cm) consider percutaneous / laparoscopic approach
- If intermediate or high disease burden randomize after eligibility check (after IOUS) during OR (single-blind)



General 'resectability criteria'	General 'ablatability criteria'
No size limit	Maximum CRLM size ≤3 cm
Aiming at negative (R0) margins	Aiming at a tumour free margin of > 10 mm
Leave sufficient FLR (> 20% normal functioning liver parenchyma; > 30% post-chemotherapy)	Leave sufficient FLR (> 20% normal functioning liver parenchyma; > 30% post-chemotherapy)
Portal vein embolization of the (most) affected liver lobe may be considered for patients with insufficient FLR	To preserve the major bile ducts (common, right and left hepatic duct) a minimum distance (lesion to major bile duct) of 15 mm is required
At least one of three hepatic veins should be preserved and both the portal venous and hepatic arterial blood flow in the future liver remnant should be remain unharmed	Radical ablation(s) with or without surgical resections for additional unablatable lesions
Approachable surgical field, without extensive scar formation, major surgical adhesions and/or intestinal herniations (risk of major morbidity estimated > 20%; risk of mortality estimated > 5%)	To avoid collateral damage to the intestines a minimum distance to the stomach, small bowel and colon of 15 mm should be pursued in open procedures and respected in percutaneous procedures; Pneumo- or hydrodissections to shift bowels are allowed
Maximum total number of CRLM 10	Maximum total number of CRLM 10

Meijerink MR, et al. BMC Cancer. 2018;18(1):821

Baseline Characteristics

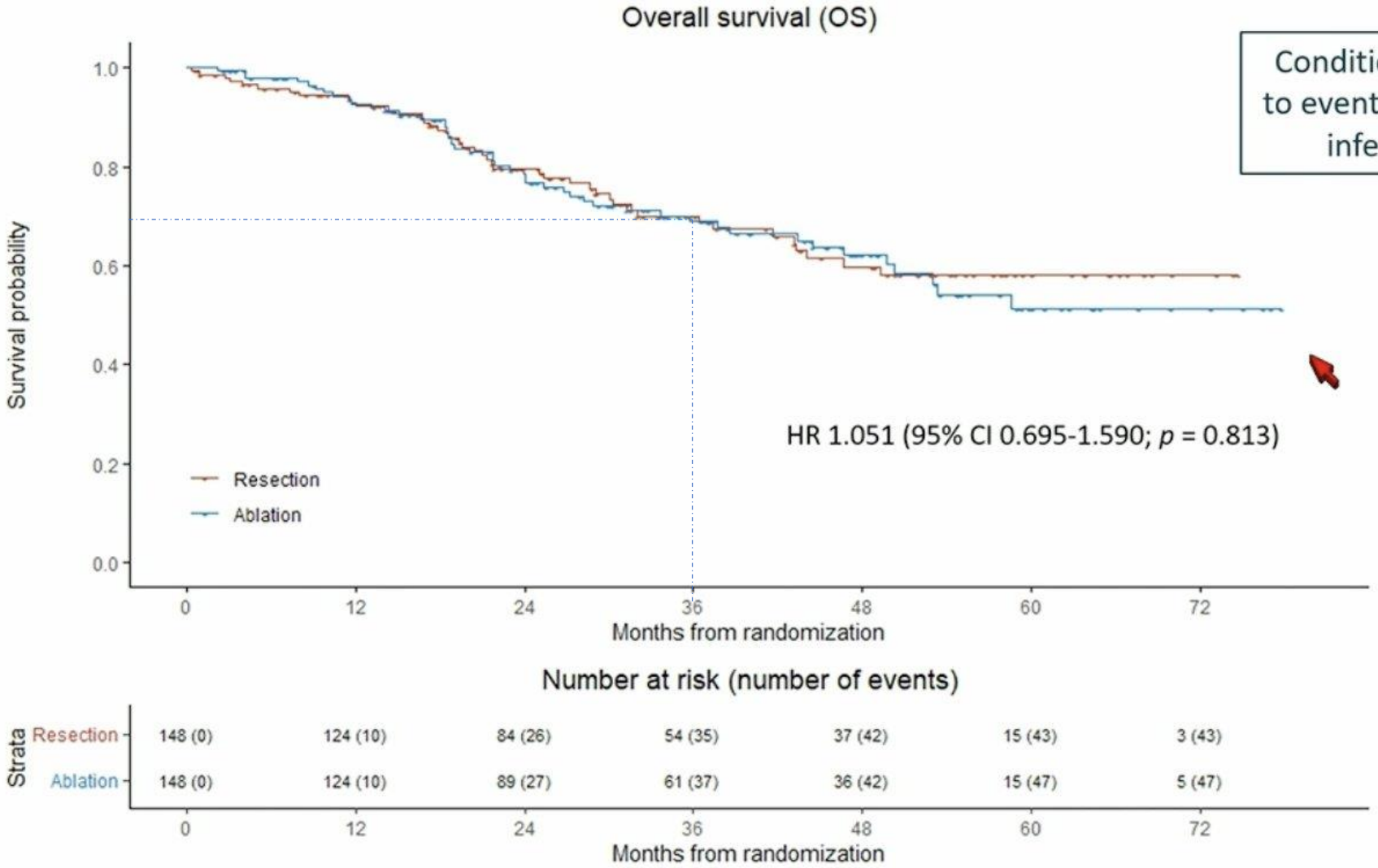
		Group A Resection	Group B Ablation	
Procedure-related characteristics		N = 148	N = 148	
Subgroup	A low disease burden	89 (60.1%)	94 (64.2%)	0.469
	B intermediate disease burden	50 (33.8%)	41 (27.7%)	
	C high disease burden	9 (6.1%)	12 (8.1%)	
Preprocedural systemic therapy	No	112 (75.7%)	118 (79.7%)	0.485
	Yes	36 (24.3%)	30 (20.3%)	
Procedures	Resection alone	90 (60.8%)	0 (0%)	
	Ablation alone	1 (0.7%)	118 (79.7%)	
	Resection & ablation	52 (35.1%)	27 (18.2%)	
	No local treatment	5 (3.4%)	3 (2.1%)	
Approach	Percutaneous	2 (1.4%)	84 (56.8%)	
	Laparoscopic	68 (46.6%)	10 (6.8%)	
	Open	76 (52.1%)	54 (36.5%)	
Anesthesia	General	146 (100%)	111 (75.0%)	
	Propofol	0 (0%)	37 (25.0%)	
Number of CRLM	Median number CRLM (range)	2 (1-10)	2 (1-12)	0.964
Tumor-related characteristics		N = 446	N = 447	
CRLM	Target	304 (68.2%)	349 (78.1%)	
	Non-target (unresectable/unablatable)	142 (31.8%)	98 (21.9%)	
Size CRLM randomization (mm)	Mean size target CRLM (range)	14 (2-34)	13 (3-34)	0.457
Size CRLM treatment (mm)	Mean size target CRLM (range)	14 (2-40)	14 (2-50)	0.459

64% of resection in low disease burden group performed using (robot) laparoscopy
83% of ablation in low disease burden group performed percutaneously

Meijerink MR, et al. ASCO 2024

RESULTS

OVERALL SURVIVAL – PRIMARY ENDPOINT



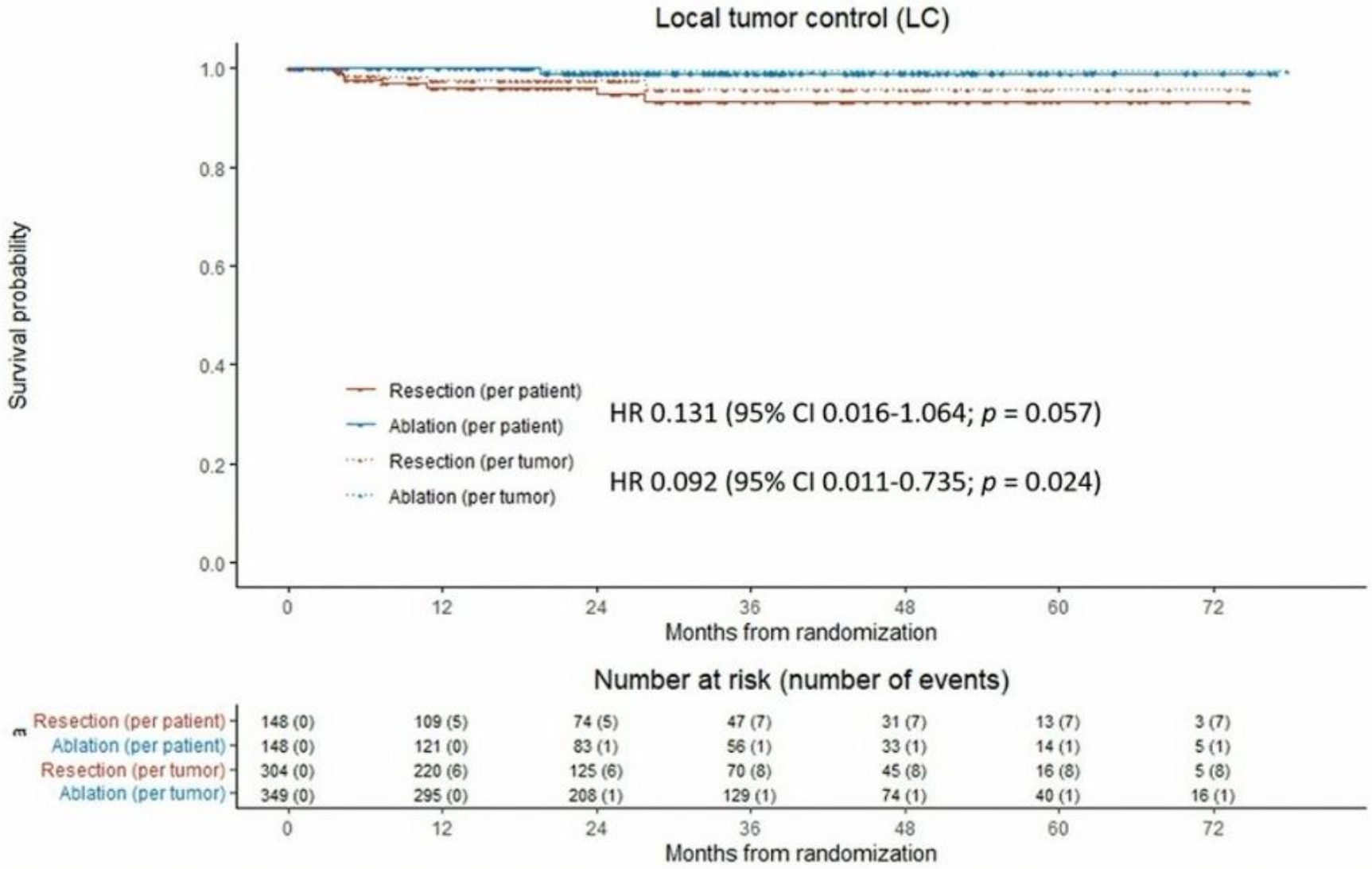
Conditional probability to eventually prove non-inferiority 91%!

HR 1.051 (95% CI 0.695-1.590; p = 0.813)

Meijerink MR, et al. ASCO 2024

RESULTS

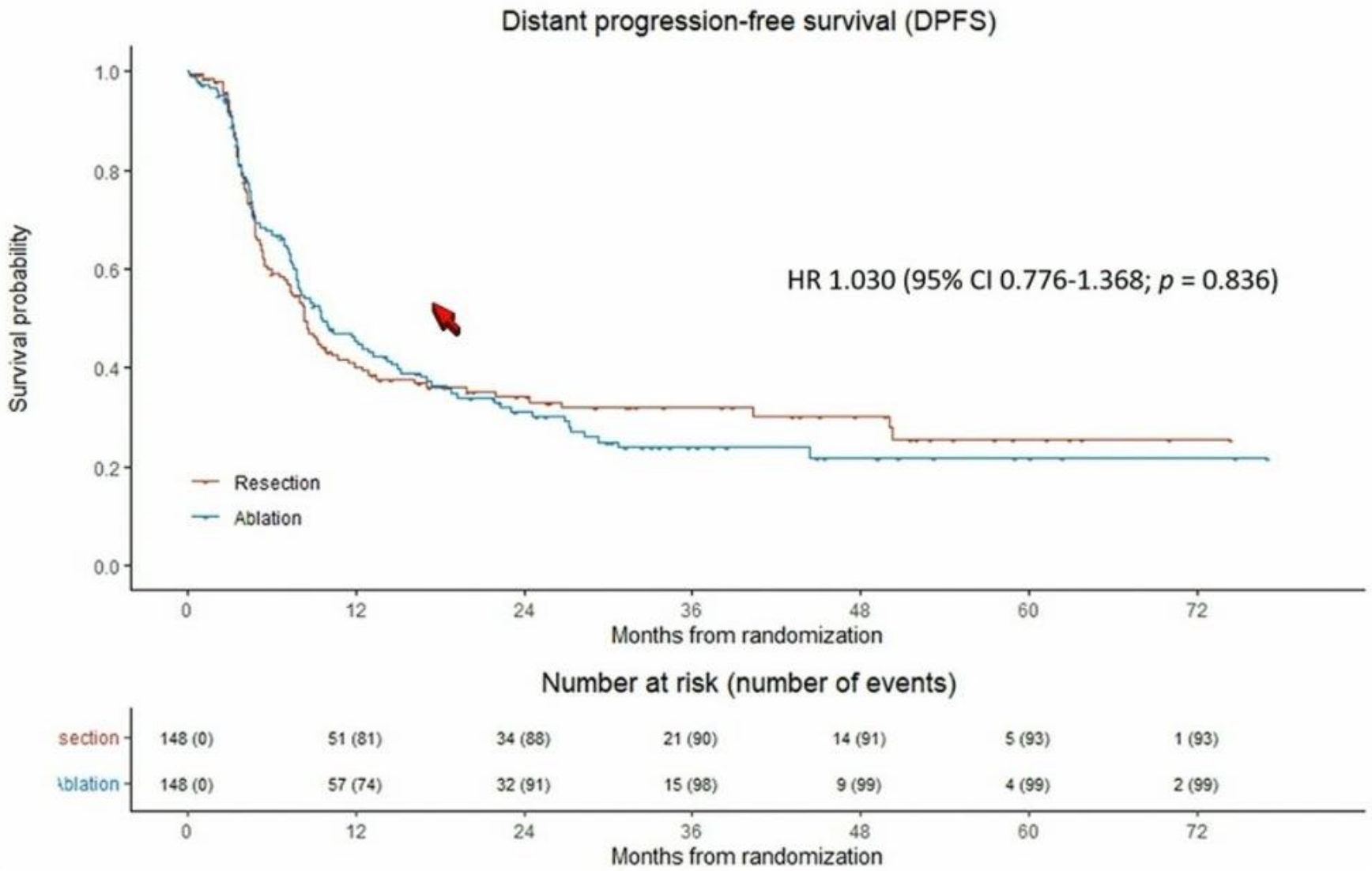
LOCAL CONTROL (TARGET CRLMs) 'INCLUDING REPEAT TREATMENTS'



RESULTS

DISTANT PROGRESSION-FREE SURVIVAL

COLLISION
Colorectal Liver Metastases: surgery vs thermal ablation



Meijerink MR, et al. ASCO 2024

SUMMARY

COLLISION
Colorectal Liver Metastases: surgery vs thermal ablation

- **COLLISION stopped at halftime based on predefined stopping rules for**
  - Showing benefit of the experimental arm (ablation) over standard-of-care (resection)

- **For patients with small-size colorectal liver metastases, thermal ablation compared to standard-of-care surgical resection**
  - Substantially reduced morbidity and mortality
    - treatment related mortality 2.1% (resection) → 0.0% (ablation)
    - all-cause 90-day mortality 2.1% (resection) → 0.7% (ablation)
    - AEs rate 56% (resection) → 19% (ablation) and SAE rate 20% (resection) → 7% (ablation)
  - Was at least as good as surgical resection in locally controlling CRLM
    - no difference in *per-patient* local control: HR 0.131 (95% CI 0.016-1.064; p = 0.057)
    - superior *per-tumor* local control: HR 0.092 (95% CI 0.011-0.735; p = 0.024)
  - Showed no difference in local & distant tumor progression-free survival
  - Did not compromise overall survival (OS)

Meijerink MR, et al. ASCO 2024

Diagnostic Imaging of Colorectal Liver Metastases with CT, MR Imaging, FDG PET, and/or FDG PET/CT: A Meta-Analysis of Prospective Studies Including Patients Who Have Not Previously Undergone Treatment[1]

Radiology

Table 3

Sensitivity Estimates for Each Imaging Modality on a Per-Lesion Basis

Modality*	I^2 Index of Sensitivity (%)†	Mean Sensitivity (%)†
CT ($n = 38$)	70.9 (60.0, 78.9)	74.4 (68.7, 79.3)
MR imaging ($n = 61$)	83.4 (79.4, 86.7)	80.3 (74.6, 85.0)
FDG PET ($n = 8$)	86.4 (76.2, 92.2)	81.4 (66.5, 90.6)
FDG PET/CT ($n = 1$)	NA	66.2 (54.5, 76.2)

* Numbers in parentheses are numbers of data sets.

† Numbers in parentheses are 95% CIs. NA = not applicable.

Table 5

Sensitivity Estimates for Each Subgroup on a Per-Lesion Basis

Subgroup	Mean Sensitivity (%)	
	MR Imaging	CT
Lesion size		
<1 mm	60.2 (54.4, 65.7) [$n = 8$]	47.3 (40.1, 54.5) [$n = 5$]
≥10 mm	89.0 (81.7, 93.7) [$n = 8$]	86.7 (77.6, 92.5) [$n = 5$]
Study year		
Before January 2004	70.2 (63.2, 76.3) [$n = 34$]	73.4 (61.0, 83.0) [$n = 20$]
After January 2004	84.9 (79.3, 89.2) [$n = 27$]	74.9 (69.1, 79.9) [$n = 18$]
Sections		
Single	NA	74.3 (62.4, 83.4) [$n = 12$]
Multiple	NA	74.8 (66.2, 81.8) [$n = 23$]
Phase		
Portal	NA	76.0 (68.0, 82.5) [$n = 14$]
Arterial and portal	NA	68.6 (60.0, 76.1) [$n = 14$]
MR technique		
Unenhanced imaging	78.2 (64.6, 87.6) [$n = 29$]	NA
Contrast-enhanced imaging		
With mangafodipir trisodium	86.0 (83.2, 88.4) [$n = 7$]	NA
With SPIO	79.5 (71.0, 84.4) [$n = 21$]	NA
With gadoterate meglumine or gadopentetate dimeglumine	79.8 (62.6, 90.3) [$n = 4$]	NA

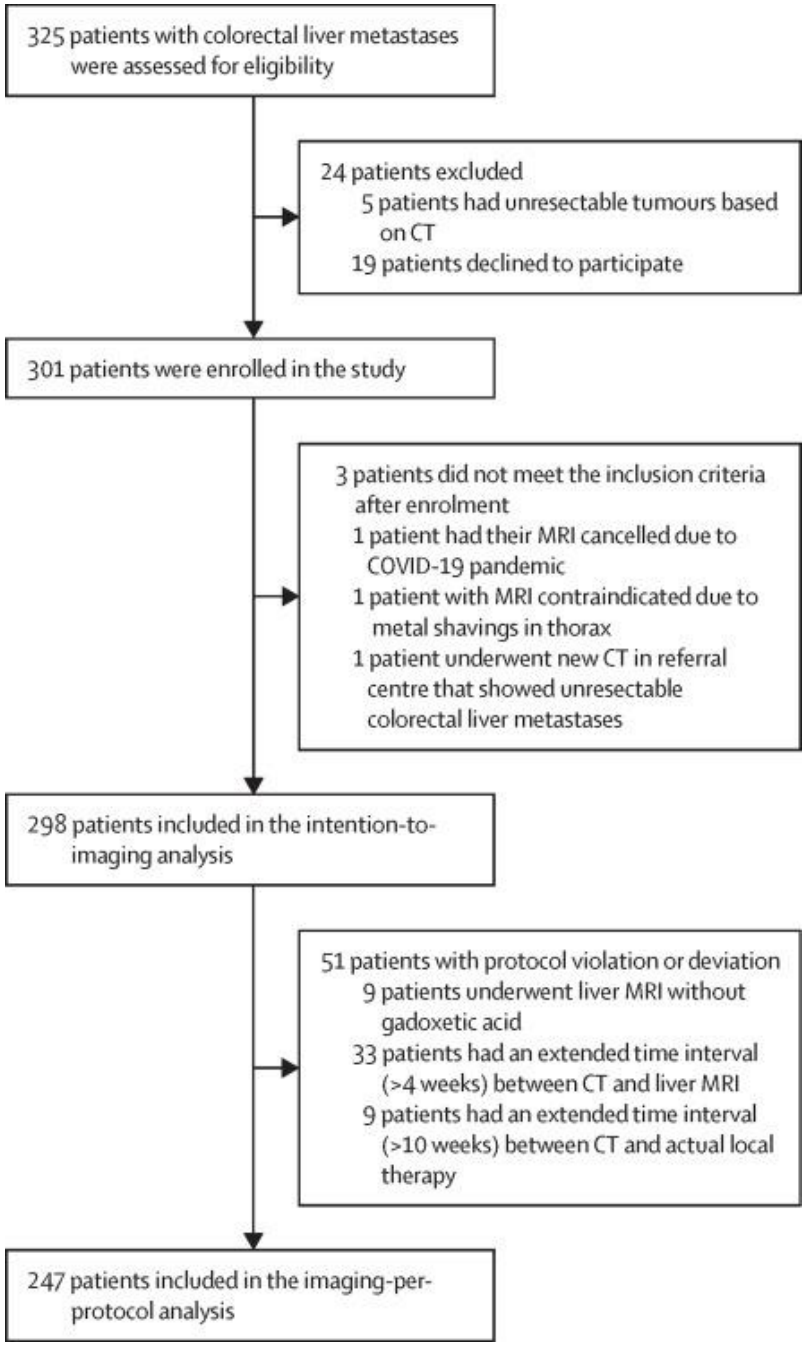
Note.—Numbers in parentheses are the 95% CIs. Numbers in brackets are numbers of data sets. NA = not applicable.

Niekel MC, et al. Radiology. 2010 Dec;257(3):674-84.

Lancet Oncol 2024; 25: 137–46

MRI in addition to CT in patients scheduled for local therapy of colorectal liver metastases (CAMINO): an international, multicentre, prospective, diagnostic accuracy trial

Burak Görgec, Ingrid S Hansen, Gunter Kemmerich, Trygve Syversveen, Mohammed Abu Hilal, Eric J T Belt, Koop Bosscha, Mark C Burgmans, Vincent C Cappendijk, Mathieu D'Hondt, Prof Bjørn Edwin, Arian R van Erkel, Hugo A J Gielkens, Dirk J Grünhagen, Paul D Gobardhan, Henk H Hartgrink, Karin Horsthuis, Elisabeth G Klompenhouwer, Niels F M Kok, Peter A M Kint, Koert Kuhlmann, Wouter K G Leclercq, Daan J Lips, Bart Lutin, Monique Maas, Hendrik A Marsman, Prof Martijn Meijerink, Yannick Meyer, Mario Morone, Jan Peringa, Jasper P Sijberden, Otto M van Delden, Janneke E van den Bergh, Inge J S Vanhooymissen, Maarten Vermaas, François E J A Willemssen, Marcel G W Dijkgraaf, Patrick M Bossuyt, Rutger-Jan Swijnenburg, Åsmund A Fretland, Cornelis Verhoef, Marc G Besselink*, Jaap Stoker*, for the CAMINO Study Group*



	All patients (n=298)
No change in local treatment plan	206 (69%)
Change in local treatment plan	92 (31%)
More extensive local therapy	40 (13%)
More extensive local therapy (minor to minor)	32 (11%)
More extensive local therapy (minor to major)	8 (3%)
Less extensive local therapy	11 (4%)
Less extensive local therapy (minor to minor)	10 (3%)
Less extensive local therapy (major to minor)	1 (<1%)
No local treatment	34 (11%)
From local therapy to induction systemic therapy	15 (5%)
From local therapy to palliative systemic therapy	11 (4%)
From local therapy to no local therapy due to benign lesions on contrast-enhanced MRI	8 (3%)
Other	7 (2%)
From resection to selective internal radiotherapy	1 (<1%)
From resection to liver transplantation due to irresectability	1 (<1%)
From thermal ablation to follow-up of colorectal liver metastases	1 (<1%)
From one-stage to two-stage hepatectomy	1 (<1%)
From resection to thermal ablation (same localisation)	2 (1%)
From resection to resection of a different segment than initially determined based on contrast-enhanced CT	1 (<1%)

Data are n (%).

Table 2: **Primary outcome of changes in local treatment plan of the intention-to-image population**

Görgec B, et al. Lancet Oncol. 2024 Jan;25(1):137-146.

Parameters Associated with Change in Treatment Plan after MR

	Univariable analysis odds ratio (95% CI)	p value
Age	1·02 (0·99–1·05)	0·062
Sex		
Female	1 (ref)	..
Male	1·17 (0·71–1·93)	0·55
BMI	1·04 (0·98–1·10)	0·14
WHO performance status		
Grade 0	1 (ref)	..
Grade 1	0·88 (0·52–1·49)	0·62
Grade 2	3·39 (0·55–20·87)	0·19
Grade 3	..	..
Grade 4	..	..
Hepatic steatosis on contrast-enhanced CT		
No	1 (ref)	..
Yes	1·22 (0·47–3·17)	0·68
Site of colorectal carcinoma		
Coecum	1 (ref)	..
Ascending colon	1·96 (0·52–7·34)	0·32
Transverse colon	5·00 (1·12–22·41)	0·035
Descending colon	1·18 (0·26–5·43)	0·84
Sigmoid colon	2·74 (0·85–8·77)	0·090
Rectosigmoid	2·65 (0·69–10·15)	0·16
Rectum	2·24 (0·70–7·12)	0·17
Previous resection primary colorectal carcinoma		
No	1 (ref)	..
Yes	0·43 (0·25–0·74)	0·0020

	Univariable analysis odds ratio (95% CI)	p value
(Continued from previous column)		
Previous liver surgery for colorectal liver metastases		
No	1 (ref)	..
Yes	0·77 (0·39–1·50)	0·44
Time of diagnosis of colorectal liver metastases		
Metachronous	1 (ref)	..
Synchronous	2·12 (1·27–3·56)	0·0040
Type of colorectal liver metastases		
Primary	1 (ref)	..
Recurrence	0·92 (0·43–1·94)	0·82
Locoregional recurrence after previous local therapy	1·12 (0·27–4·61)	0·87
Disease-free survival between primary colorectal carcinoma and first colorectal liver metastases within 12 months		
No	1 (ref)	..
Yes	1·74 (0·98–3·08)	0·060
Size of largest lesion	0·96 (0·94–0·98)	0·0003
Pre-interventional systemic therapy		
No systemic therapy	1 (ref)	..
Neoadjuvant systemic therapy	1·10 (0·62–1·97)	0·747
Induction systemic therapy	0·88 (0·40–1·99)	0·76
Number of lesions	1·26 (1·12–1·42)	0·0001
Distribution		
Unilobar	1 (ref)	..
Bilobar	2·11 (1·26–3·53)	0·0040

Görgec B, et al. Lancet Oncol. 2024 Jan;25(1):137-146.

NCCN Guidelines Colon Cancer: Principles of Imaging

- Initial Workup/Staging
  - Consider FDG-PET/CT (skull base to mid-thigh)
    - In selected patients considered for image-guided liver-directed therapies (ie, thermal ablation, radioembolization).
  - If liver-directed therapy or surgery is contemplated, a hepatic MRI with intravenous routine extracellular or hepatobiliary GBCA is preferred over CT to assess exact number and distribution of metastatic foci for local treatment planning.
- Monitoring
  - FDG-PET/CT can be considered for assessment of response and liver recurrence after image-guided liver-directed therapies (ie, thermal ablation, radioembolization).
- Surveillance
  - FDG-PET/CT can be considered for assessment of response and liver recurrence after image-guided liver-directed therapies (ie, thermal ablation, radioembolization) or serial CEA elevation during follow-up.

NCCN Guidelines Colon Cancer: Principles of Image Guided Tumor Ablation

- Thermal ablation creates tumor cell death through deposition of tumoricidal heat (radiofrequency or microwave) or cold (cryoablation) in the tumor and surrounding margins.
- Non-thermal ablation such as irreversible electroporation creates tumor cell death through electrical pulses that create irreversible membrane pores and cellular lysis/destruction.

NCCN Guidelines Colon Cancer: Principles of Liver Tumor Ablation

- Thermal ablation can be considered alone, or in conjunction with surgery, in appropriately selected patients with small metastases that can be treated with margins. All original sites of disease need to be amenable to thermal ablation or resection.
- Image guided thermal ablation may be considered in selected surgical candidates or medically non-surgical candidates with small tumor that can be completely ablated with margins.
- Image guided thermal ablation can be considered in selected patients with recurrence after hepatectomy or ablation as long as all visible disease can be ablated with margins.
- Image guided non-thermal ablation (irreversible electroporation) can be considered in patients that cannot be safely resected or ablated with margins due to proximity to central bile ducts or other structures that cannot be protected.

TREATMENT

Resectable[n] synchronous liver and/or lung metastases only pMMR/MSS

ADJUVANT TREATMENT[b] (UP TO 6 MO PERIOPERATIVE TREATMENT) (resected metastatic disease)

Synchronous or staged colectomy[aa] with liver or lung resection (preferred) and/or local therapy[bb]
or
Neoadjuvant therapy (for 2–3 mo) FOLFOX (preferred) or CAPEOX (preferred) or FOLFIRI (category 2B) or FOLFIRINOX (category 2B) followed by synchronous or staged colectomy[aa] and resection (preferred) and/or local therapy[bb] of metastatic disease
or
Colectomy,[aa] followed by chemotherapy (for 2–3 mo) FOLFOX (preferred) or CAPEOX (preferred) or FOLFIRI (category 2B) or FOLFIRINOX (category 2B) and staged resection (preferred) and/or local therapy[bb] of metastatic disease

→ **FOLFOX (preferred)**
or
CAPEOX (preferred)
or
Capecitabine or 5-FU/leucovorin

→ **Surveillance (COL-8)**

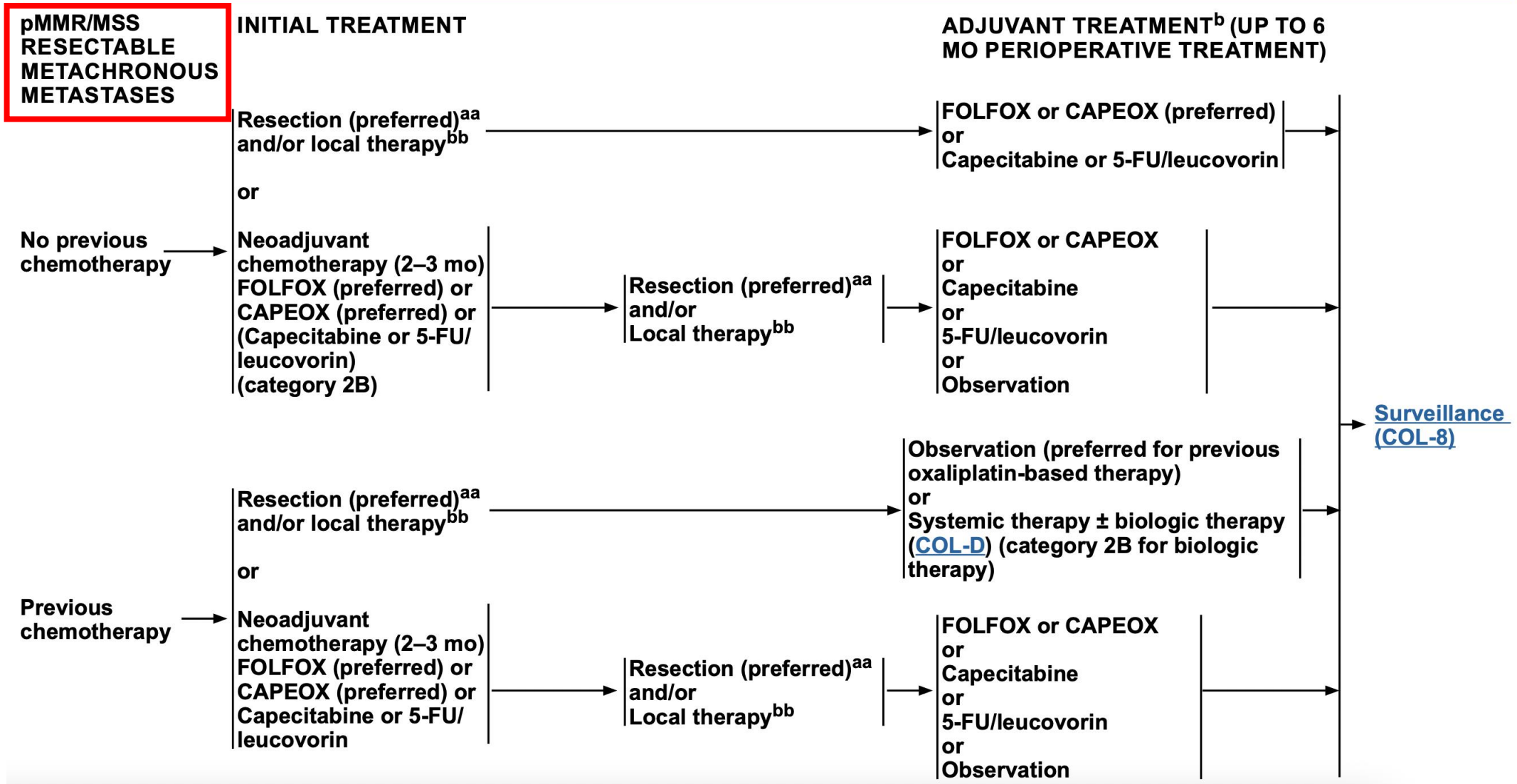
[aa] Hepatic artery infusion ± systemic 5-FU/leucovorin (category 2B) is also an option at institutions with experience in both the surgical and medical oncologic aspects of this procedure.

[bb] Resection is preferred over locally ablative procedures (eg, image-guided thermal ablation or stereotactic body RT [SBRT]). However, these local techniques can be considered for liver or lung oligometastases

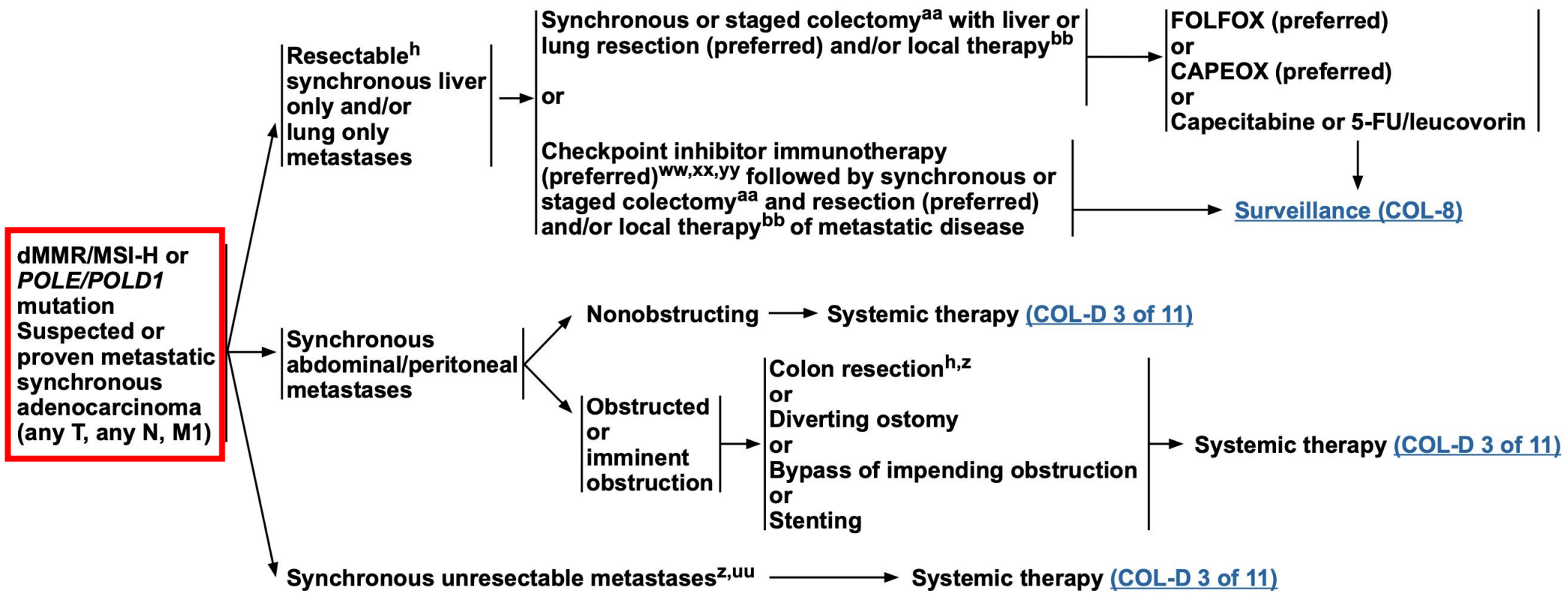
National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2024
pMMR/MSS Colon Cancer

NCCN Guidelines Index
Table of Contents
Discussion

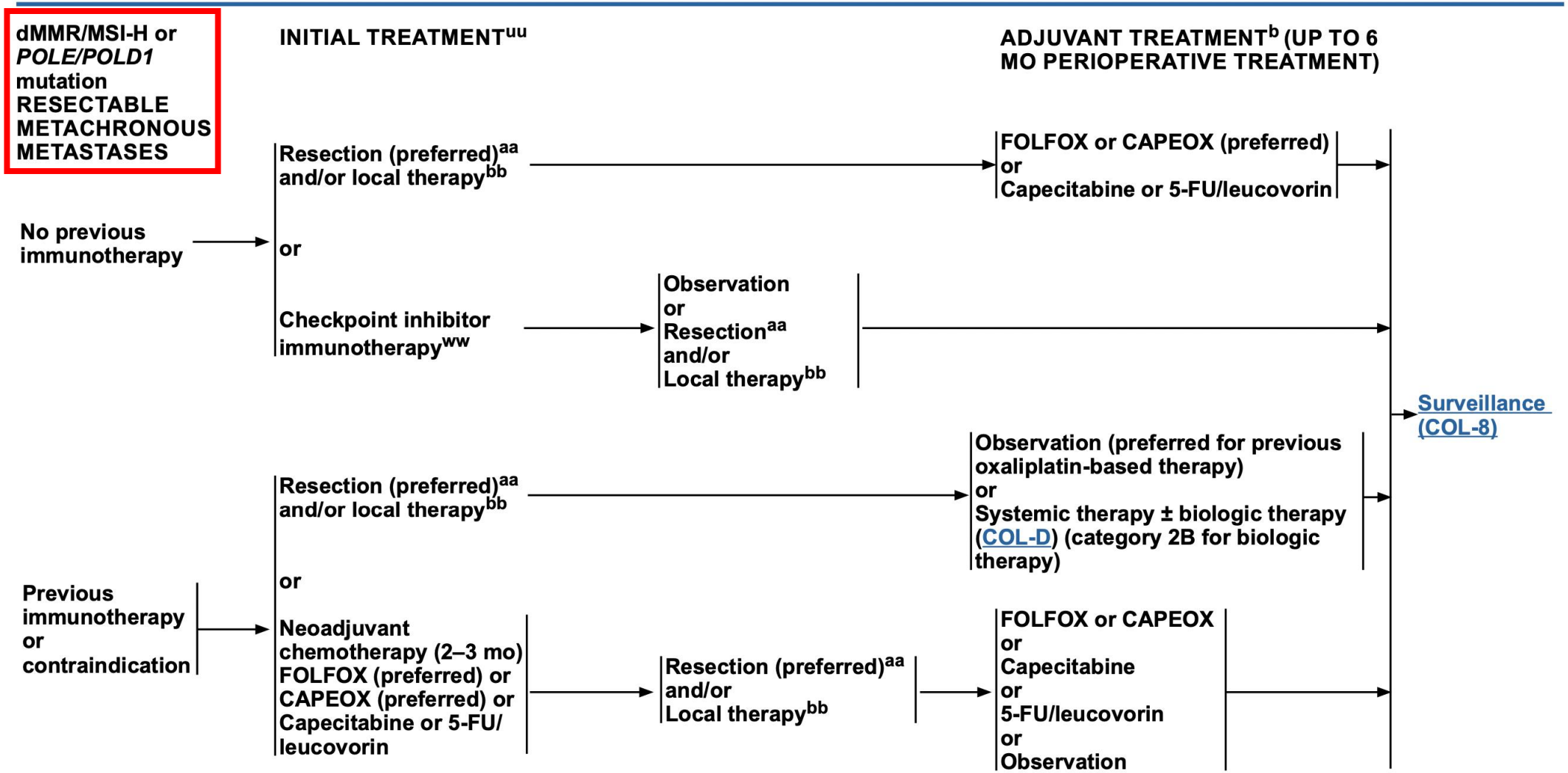


NCCN Guidelines Version 5.2024
dMMR/MSI-H Colon Cancer



NCCN Guidelines Version 5.2024
dMMR/MSI-H Colon Cancer

NCCN Guidelines Index
Table of Contents
Discussion



Locoregional Treatment Improves Outcomes of Liver Metastases from Gastropancreatic NET

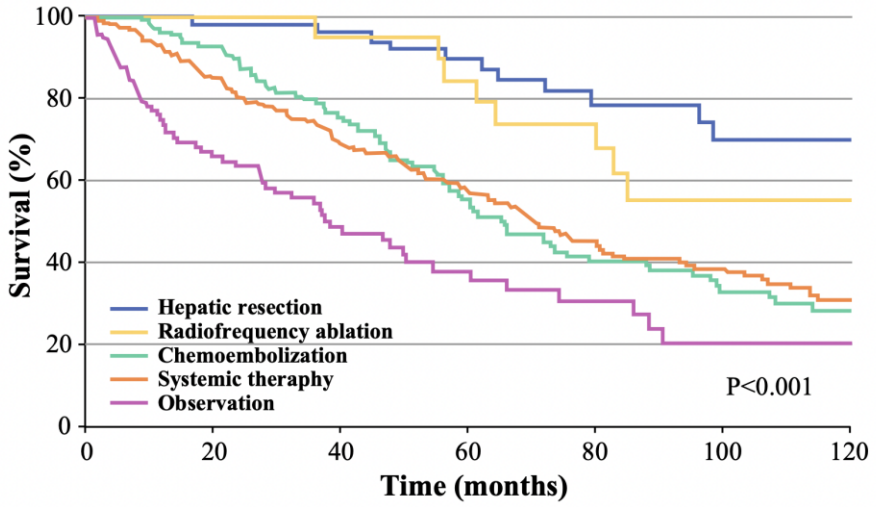
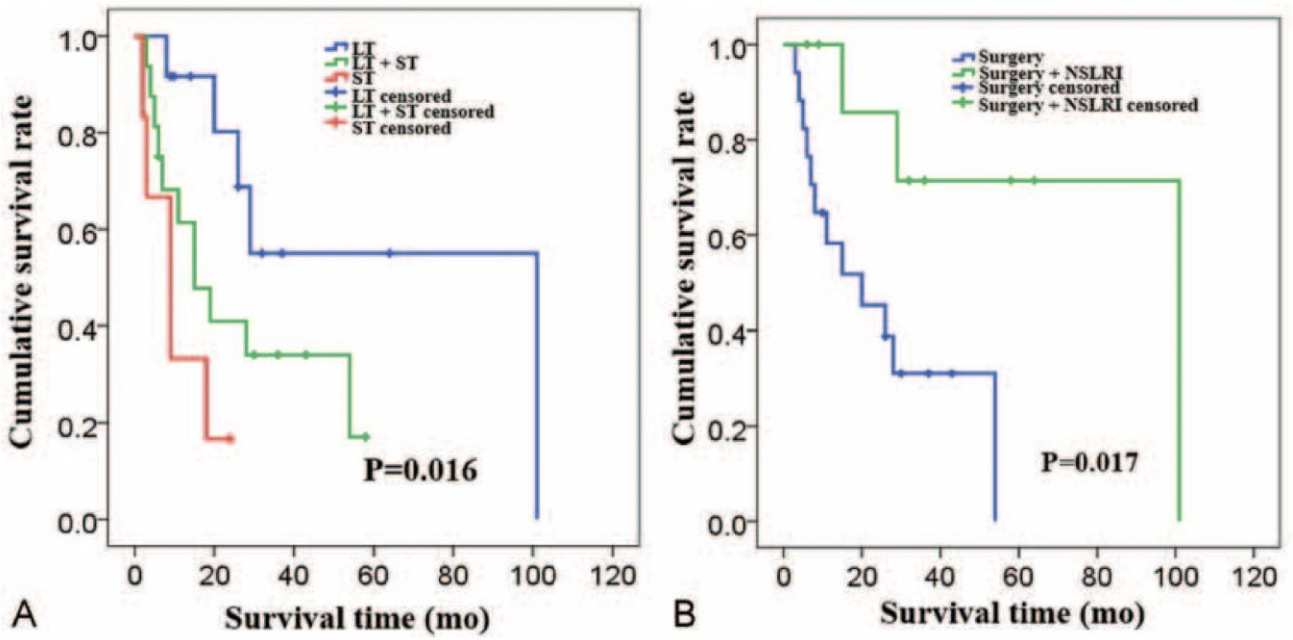


FIG. 1 Kaplan–Meier overall survival curves for patients with neuroendocrine tumor liver metastases ($n = 649$) based on primary treatment modality

LT: Local therapy
ST: Systemic therapy

NSLRI: Non-surgical LRT



Fairweather M, et al. Ann Surg Oncol. 2017 Aug;24(8):2319-2325.
Du S, et al. Medicine (Baltimore). 2015 Aug;94(34):e1429.

NCCN Guidelines Neuroendocrine Tumors: Principles of Liver-directed Therapy

- Liver-directed therapies (eg, liver resection, thermal ablation, chemoembolization) for hepatic metastases from NETs following pancreatoduodenectomy are associated with increased risk for cholangitis and liver abscess.
- Percutaneous thermal ablation, often using microwave energy (radiofrequency and cryoablation are also acceptable), can be considered for oligometastatic liver disease, generally up to four lesions each smaller than 3 cm. Feasibility considerations include safe percutaneous imaging-guided approach to the target lesions, and proximity to vessels, bile ducts, or adjacent non-target structures that may require hydro- or aero-dissection for displacement.

NCCN Guidelines Version 2.2024 NE-F
NCCN Guidelines Version 2.2024 NE-K

MANAGEMENT OF LOCOREGIONAL ADVANCED DISEASE AND/OR DISTANT METASTASES OF THE GASTROINTESTINAL TRACT

SUBSEQUENT THERAPY

Clinically significant disease progression[kk] →

Systemic therapy (NE-H 1 of 9)

or

Locoregional therapy options

- **Liver-directed therapy for liver-predominant disease (NE-K)**
- **Consider RT (NE-I) ± concurrent fluoropyrimidine-based chemotherapy for locally advanced unresectable disease (excluding small bowel mesenteric)**
- **Palliative RT for oligometastatic disease and/or symptomatic metastases (excluding mesenteric masses) (NE-I)**

NCCN Guidelines Version 2.2024
Neuroendocrine Tumors of the Pancreas (Well-Differentiated Grade 1/2)

NCCN Guidelines Index
Table of Contents
Discussion

MANAGEMENT OF LOCOREGIONAL ADVANCED DISEASE AND/OR DISTANT METASTASES

SUBSEQUENT THERAPY

Disease progression[z] →

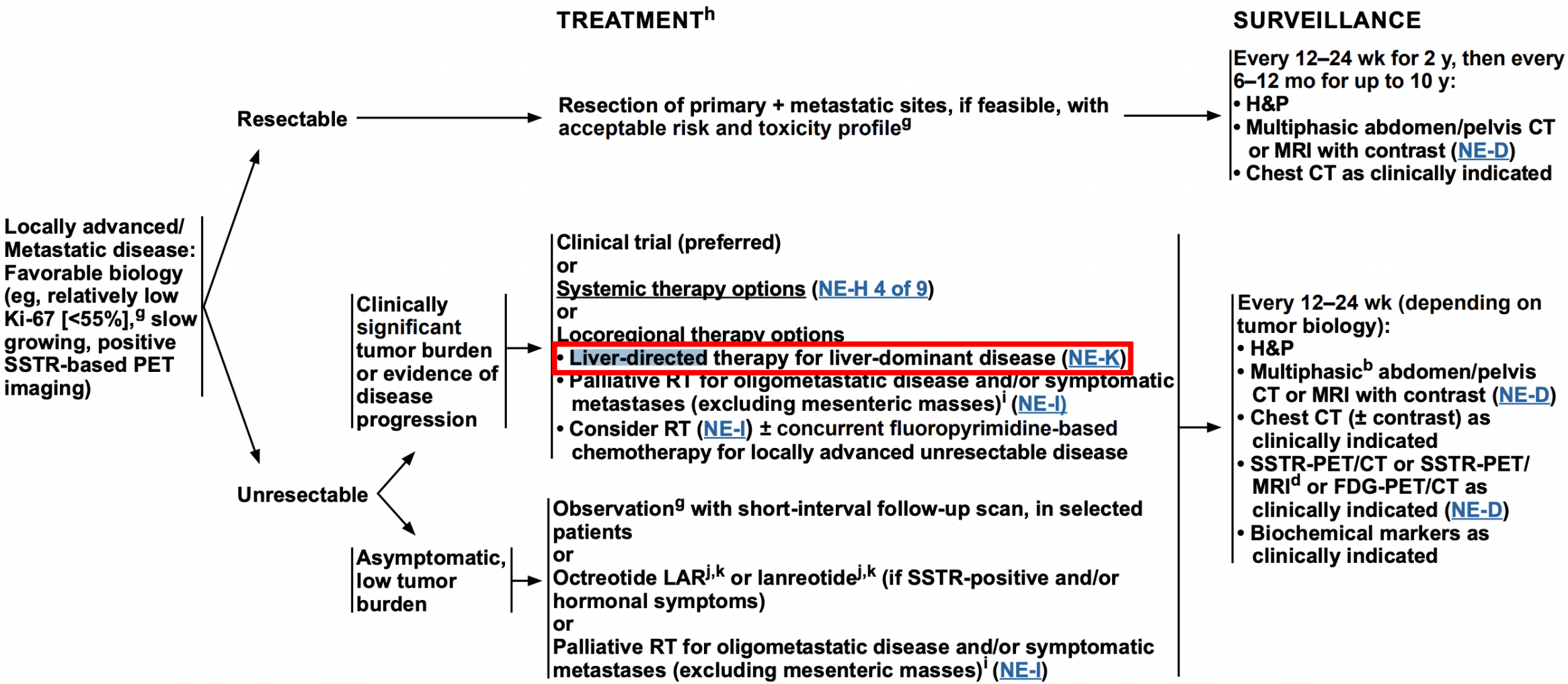
Clinical trial
or
Systemic therapy (NE-H 3 of 9)
or
Locoregional therapy options

- **Consider liver-directed therapy for liver-predominant disease[ee] (NE-K)**
- **Consider RT (NE-I) ± concurrent fluoropyrimidine-based chemotherapy for locally advanced unresectable disease (excluding small bowel mesenteric)**
- **Palliative RT for oligometastatic disease and/or symptomatic metastases (excluding mesenteric masses) (NE-I)**

NCCN Guidelines Version 2.2024
Well-Differentiated, Grade 3 Neuroendocrine Tumors

NCCN Guidelines Index
Table of Contents
Discussion

MANAGEMENT OF LOCALLY ADVANCED/METASTATIC DISEASE: FAVORABLE BIOLOGY



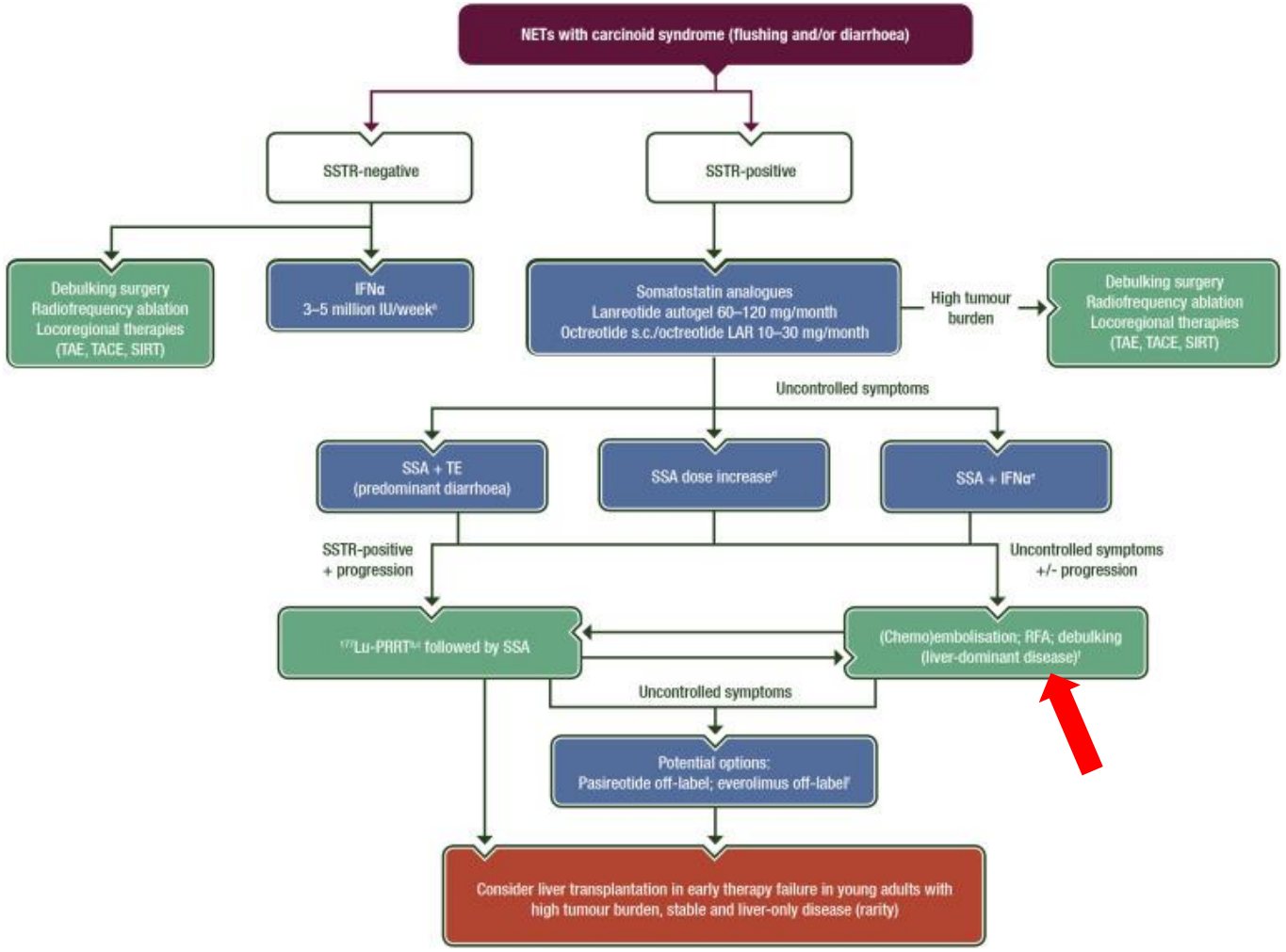
NCCN Guidelines Version 2.2024
Well-Differentiated, Grade 3 Neuroendocrine Tumors

NCCN Guidelines Index
Table of Contents
Discussion

MANAGEMENT OF LOCALLY ADVANCED/METASTATIC DISEASE: UNFAVORABLE BIOLOGY

	TREATMENT	SURVEILLANCE
Locally advanced/Metastatic disease: Unfavorable biology (relatively high Ki-67 [≥55%],[g] rapid growth rate, FDG-avid tumors, negative SSTR-based PET imaging)	Clinical trial (preferred) or Systemic therapy options (NE-H 4 of 9) or Locoregional therapy options • Consider RT (NE-I) ± concurrent fluoropyrimidine-based chemotherapy for locally advanced unresectable disease • Consider addition of liver-directed therapy (embolization, selective internal RT, ablation, SBRT)[l] (NE-K) • Palliative RT for oligometastatic disease and/or symptomatic metastases (excluding mesenteric masses)[i] (NE-I)	Every 8–12 wk (depending on tumor biology) • H&P • Multiphasic[b] abdomen/pelvis CT or MRI with contrast (NE-D) • Chest CT (± contrast) as clinically indicated • FDG-PET/CT as clinically indicated (NE-D) • Biochemical markers as clinically indicated (NE-E)

ESMO Guidelines for Metastatic NET

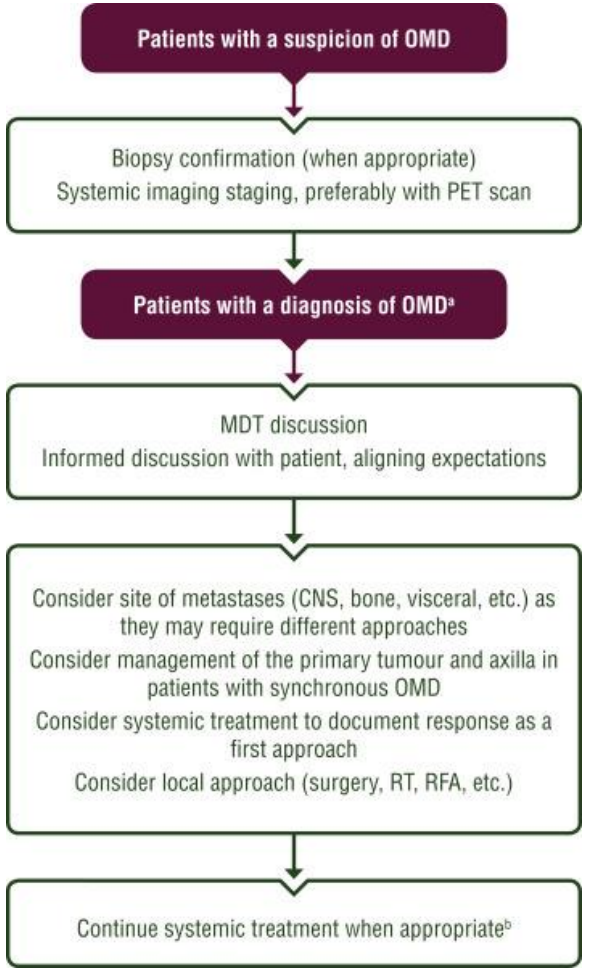


- To determine the efficacy of RFA in NET liver metastases, a systematic review had been performed
- Fifty-four percent of patients presented with symptoms, with 92% reporting symptom improvement following RFA (alone or in combination with surgery).
- The median duration of symptom improvement was 14–27 months.
- However, recurrence was common (63%–87%).

Mohan H, et al. J Vasc Interv Radiol. 2015 Jul;26(7):935-942
Pavel M, et al. Ann Oncol. 2020 Jul;31(7):844-860.

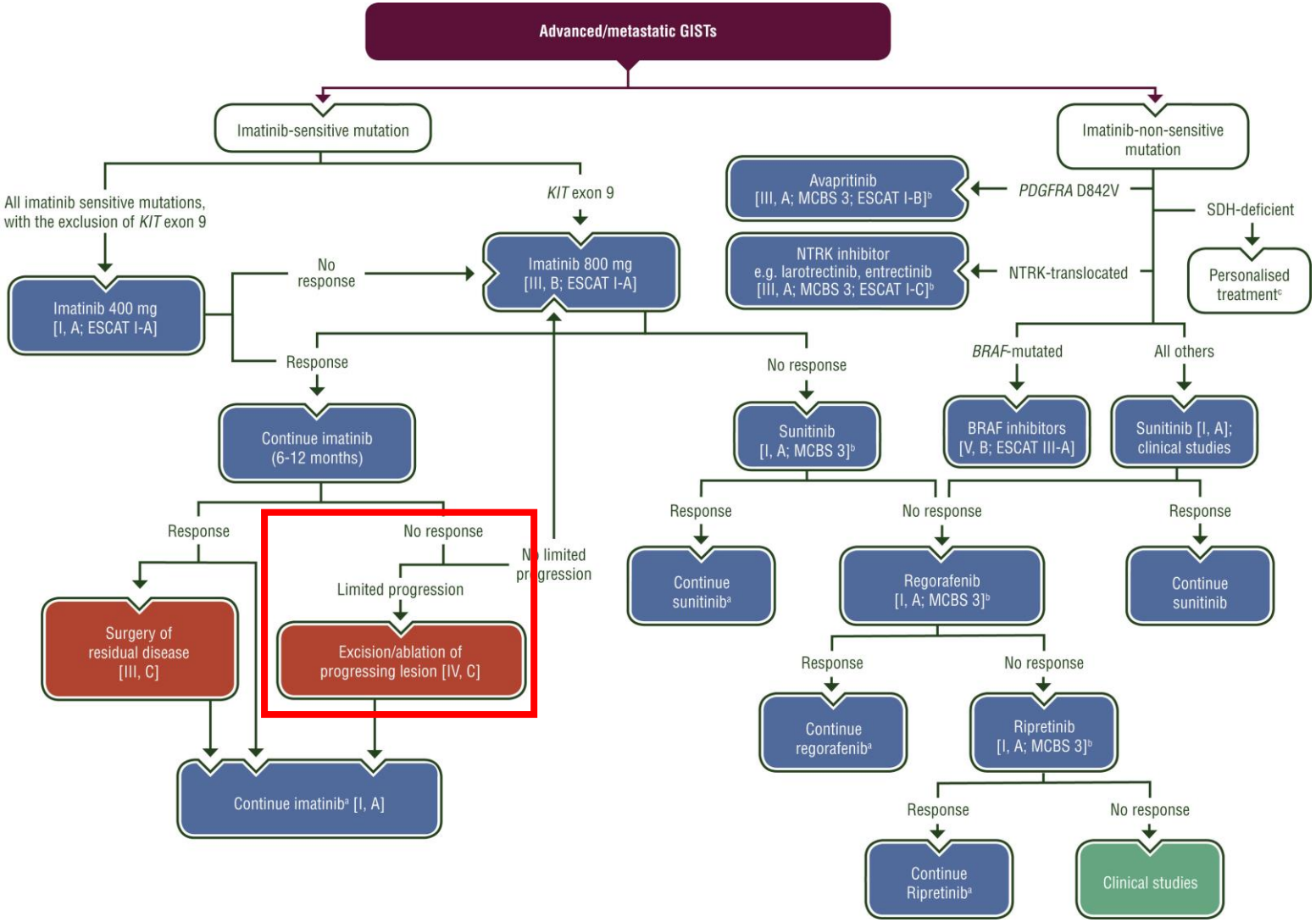
ESMO Guidelines for Metastatic Breast Cancer

- Oligometastatic disease (OMD)
  - The dynamics in chronic metastatic conditions should be reviewed to identify induced/recurrent OMD. Complete imaging history should be available for decisions on OMD care [V, B].
  - Patients with OMD should be discussed in a multidisciplinary context to individualize management [V, B].
  - Multimodality treatment approaches involving LRT [e.g. high conformal radiotherapy (RT), image-guided ablation, selective internal radiotherapy and/or surgery] combined with systemic treatments are recommended, tailored to the disease presentation in the individual patient [V, B].
  - Local ablative therapy to all metastatic lesions may be offered on an individual basis after discussion in a multidisciplinary setting [II, C]; however, it is unknown if this leads to improved OS.



Gennari A, et al. Ann Oncol. 2021 Dec;32(12):1475-1495.

ESMO Guidelines for Metastatic GIST



Casali PG, et al. Ann Oncol. 2022 Jan;33(1):20-33.

Conclusions

- Ablation therapy, such as radiofrequency and microwave ablation, is increasingly utilized for treating liver metastases, particularly in patients with small tumors or those who are not suitable candidates for surgery.
- Current practices emphasize its role in treating metastases from colorectal cancer, neuroendocrine tumors, and select other primaries when the metastatic burden is limited.
- Technological advances in imaging and precision guidance have improved the safety and efficacy of ablation, allowing for more targeted treatments with fewer complications.
- The role of ablation in managing metastatic liver tumors continues to evolve, contributing to both curative and palliative treatment strategies in a multidisciplinary setting.