

Table S1 Twenty-six patients were recruited into the control group for the following reasons

Reasons	N
Poor financial status	24
Previous myocardial infarction	1
Grade 3 hypertension	1

Table S2 Number of cycles and relative dose intensities of mFOLFOXIRI regimen, according to treatment group

Variable	mFOLFOXIRI plus bevacizumab (n=54)	mFOLFOXIRI alone (n=26)
No. of cycles per patient, median [range]	8 [2–12]	6 [1–9]
No. of cycles per patient prior to local ablative treatment, median [range] [†]	8 [3–10]	5.5 [2–9]
No. of cycles per patient prior to liver metastasectomy, median [range] [‡]	8 [3–9]	6 [4–9]
Relative dose intensity with respect to planned, mean [range], %		
Oxaliplatin	95.2 [78.3–100.0]	95.4 [83.8–100.0]
Irinotecan	91.9 [77.4–100.0]	91.9 [83.8–100.0]
5-Fluorouracil	91.1 [71.3–100.0]	92.1 [77.1–100.0]

[†], only patients received local ablative treatment; [‡], only patients received liver metastasectomy. FOLFOXIRI, 5-fluorouracil, folinic acid, oxaliplatin, and irinotecan; mFOLFOXIRI, modified FOLFOXIRI.

Table S3 Second line therapy for patients with disease progression, according to treatment group

Regimen	N (%) [†]	
	mFOLFOXIRI plus bevacizumab (n=33)	mFOLFOXIRI alone (n=12)
Triplet chemotherapy plus bevacizumab	5 (15.2)	1 (8.3)
Doublet chemotherapy plus bevacizumab	24 (72.7)	3 (25.0)
Doublet chemotherapy	2 (6.1)	6 (50.0)
Capecitabine	0 (0)	1 (8.3)
Regorafenib plus PD-1 inhibitor	2 (6.1)	0 (0)
Fruquintinib	0 (0)	1 (8.3)

Percentages may not total 100 because of rounding. [†], only patients receiving second line therapy were included. FOLFOXIRI, 5-fluorouracil, folinic acid, oxaliplatin, and irinotecan; mFOLFOXIRI, modified FOLFOXIRI; PD-1, programmed death-1.

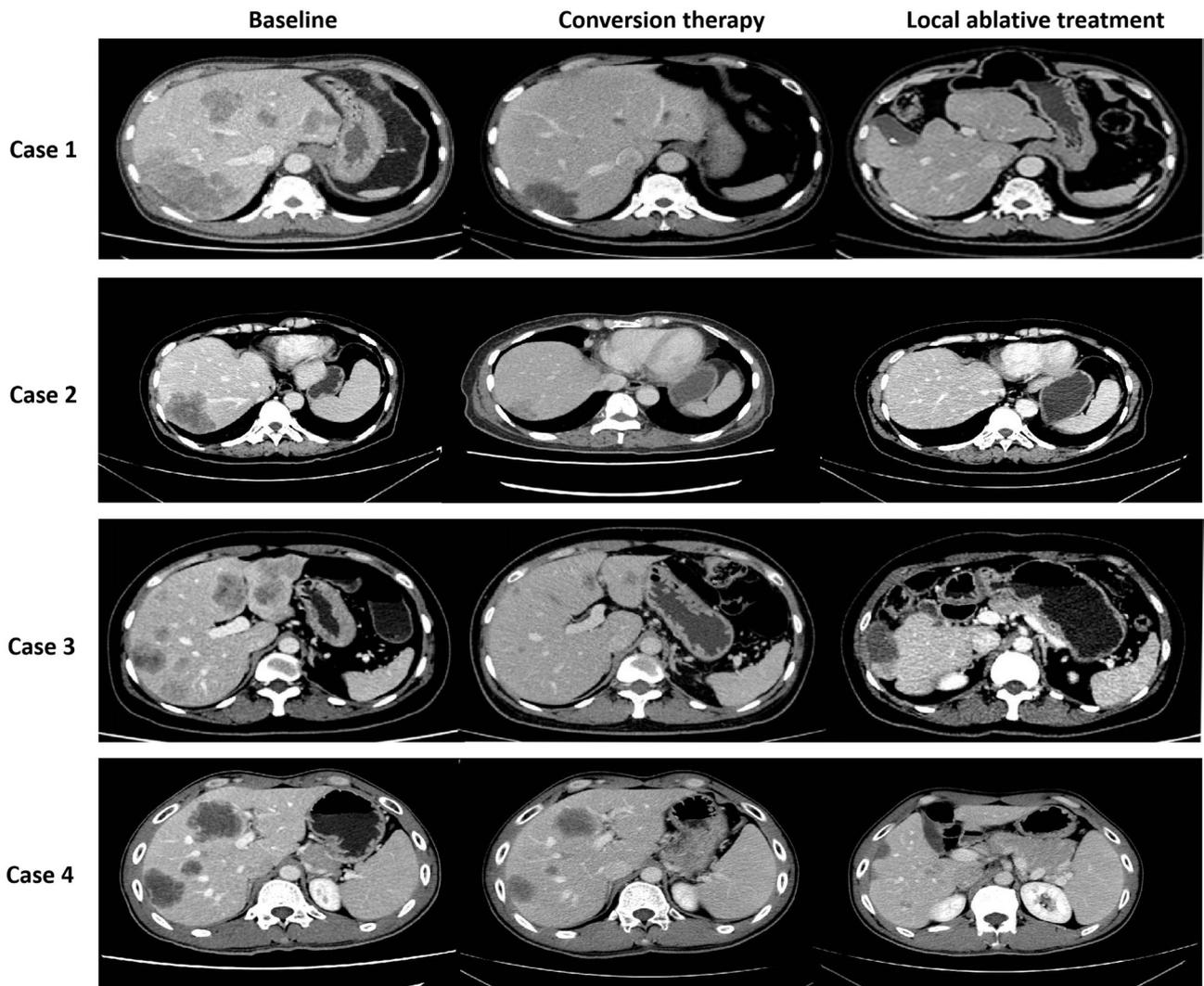


Figure S1 Radiographic images of four cases before and after treatment in the two groups. Case 1: the patient in the experimental group attained NED; Case 2 (only the largest lesions was shown): the patient in the control group attained NED; Case 3: the patient in the experimental group did not attain NED; Case 4: the patient in the control group did not attain NED. NED, no evidence of disease.

Table S4 Clinical studies involving triplet chemotherapy-based regimen as conversion therapy for patients with initially unresectable CRLMs

Schedule	Gene status	N	RR (%)	R0 resection (%)	mPFS (months)	mOS (months)
FOLFOXIRI (Falcone <i>et al.</i> , 2007) (11)	Unknown	39	Not reported	36	Not reported	23.4
FOLFIRINOX (Ychou <i>et al.</i> , 2008) (19)	Unknown	34	70.6	26.5	Not reported	36
FOLFOXIRI + bevacizumab (Masi <i>et al.</i> , 2010) (20)	Unknown	30	80	40	16.9	Not reported
FOLFOXIRI + cetuximab (Garufi <i>et al.</i> , 2010) (21)	Unknown	43	79.1	60	14	37
FOLFIRINOX (Ychou <i>et al.</i> , 2013) (12)	Unknown	30	73	30	11.9	Not reported
FOLFOXIRI + bevacizumab (Gruenberger <i>et al.</i> , 2015) (13)	Unknown	41	81	49	18.6	Not reached
mFOLFOXIRI (Hu <i>et al.</i> , 2021) (8)	<i>RAS/BRAF</i> wild-type	34	76.5	20.6	14.2	33.2
mFOLFOXIRI + cetuximab (Hu <i>et al.</i> , 2021) (8)	<i>RAS/BRAF</i> wild-type	67	95.5	35.8	15.5	Not reached
mFOLFOXIRI (Shen <i>et al.</i> , present study)	<i>RAS/BRAF/PIK3CA</i> mutation	26	60.0	3.8	9.1	35.3
mFOLFOXIRI+ bevacizumab (Shen <i>et al.</i> , present study)	<i>RAS/BRAF/PIK3CA</i> mutation	54	77.4	7.4	12.6	42.6

CRLMs, colorectal liver-limited metastases; FOLFOXIRI, 5-fluorouracil, folinic acid, oxaliplatin, and irinotecan; FOLFIRINOX, fluorouracil, leucovorin, oxaliplatin, and irinotecan; mFOLFOXIRI, modified FOLFOXIRI; mOS, median overall survival; mPFS, median progression-free survival; RR, response rate.

Table S5 Site of first disease progression among patients who underwent LATs, according to treatment group

LATs and site of first progression	N (%)	
	mFOLFOXIRI plus bevacizumab (n=32)	mFOLFOXIRI alone (n=16)
R0 resection plus thermal ablation	11 [†]	1
Site treated by surgical resection	1 (9.1)	0 (0.0)
Site treated by thermal ablation	0 (0.0)	0 (0.0)
Any other liver lesions	5 (45.5)	0 (0.0)
Extrahepatic lesions only	2 (18.2)	0 (0.0)
Without disease progression	3 (27.3)	1 (100.0)
Complete thermal ablation	10	7
Site treated by thermal ablation	1 (10.0)	1 (14.3)
Any other liver lesions	4 (40.0)	1 (14.3)
Extrahepatic lesions	1 (10.0)	2 (28.6)
Without disease progression	4 (40.0)	3 (42.9)
Thermal ablation	8	4
Site treated by thermal ablation	0 (0.0)	0 (0.0)
Any other liver lesions	4 (50.0)	4 (100.0)
Extrahepatic lesions	1 (12.5)	0 (0.0)
Without disease progression	3 (37.5)	0 (0.0)
R2 resection	3	4 [¶]
Site treated by surgical resection	0 (0.0)	0 (0.0)
Any other liver lesions	3 (100.0)	2 (50.0)
Extrahepatic lesions	0 (0.0)	0 (0.0)
Without disease progression	0 (0.0)	2 (50.0)

[†], one patient underwent R0 resection plus thermal ablation and stereotactic body radiation therapy; [¶], one patient underwent R2 resection plus thermal ablation and transarterial chemoembolisation. FOLFOXIRI, 5-fluorouracil, folinic acid, oxaliplatin, and irinotecan; LATs, local ablative treatments; mFOLFOXIRI, modified FOLFOXIRI.

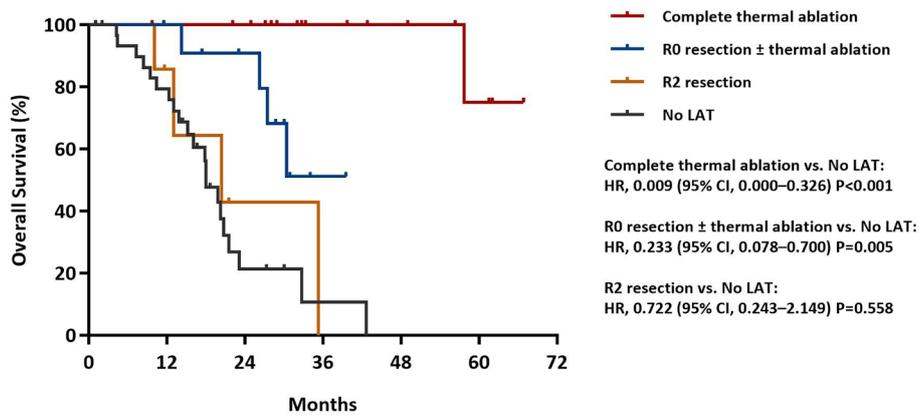


Figure S2 Kaplan-Meier curves of overall survival, according to means of LAT. CI, confidence interval; HR, hazard ratio; LAT, local ablative treatment.