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ANNUAL MEETING

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**Transplant Oncology in a Modern Era - Colorectal Liver Metastases
What's the right bridge to transplant?**

Ablation or Arterial Embolization

Orlando Jorge M. Torres

Department of Gastrointestinal Surgery

Hepatopancreatobiliary Unit

Maranhão Federal University - Brazil

Liver transplant for CRLM

Unresectable liver-limited mCRC patients	Resectable After 1L CT?	Frontline approach	Fup	Relapse pattern	Resectable after 2L CT?	Salvage approach	Fup	Relapse pattern	Resectable after 3L CT?	Salvage approach
	Yes	Resection	NED	Unresectable liver-limited	Yes	Resection	NED	Unresectable liver-limited	Yes	Resection
No (SD/PR ≥ 6 months)	Transplant	Unlikely transplantable for expected poor disease control in subsequent lines								
No PD or SD/PR < 6 months	2L	Unlikely transplantable for expected poor disease control in subsequent lines								
				No (SD/PR ≥ 6 months)	Transplant	Unlikely transplantable for expected poor disease control in subsequent lines				
				No (PD or SD/PR < 6 months)	3L CT	Unlikely transplantable for expected poor disease control in subsequent lines				
								No (SD/PR ≥ 6 months)	Transplant	
								No (PD or SD/PR < 6 months)	4L CT	

Figure 1. Real-world scenarios of application of liver transplantation in liver-limited mCRC.

1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; CT, chemotherapy; Fup, follow-up; mCRC, metastatic colorectal cancer; NED, no evidence of disease; PD, progressive disease; PR, partial response; QoL, quality of life; SD, stable disease.

CHEMOTHERAPY

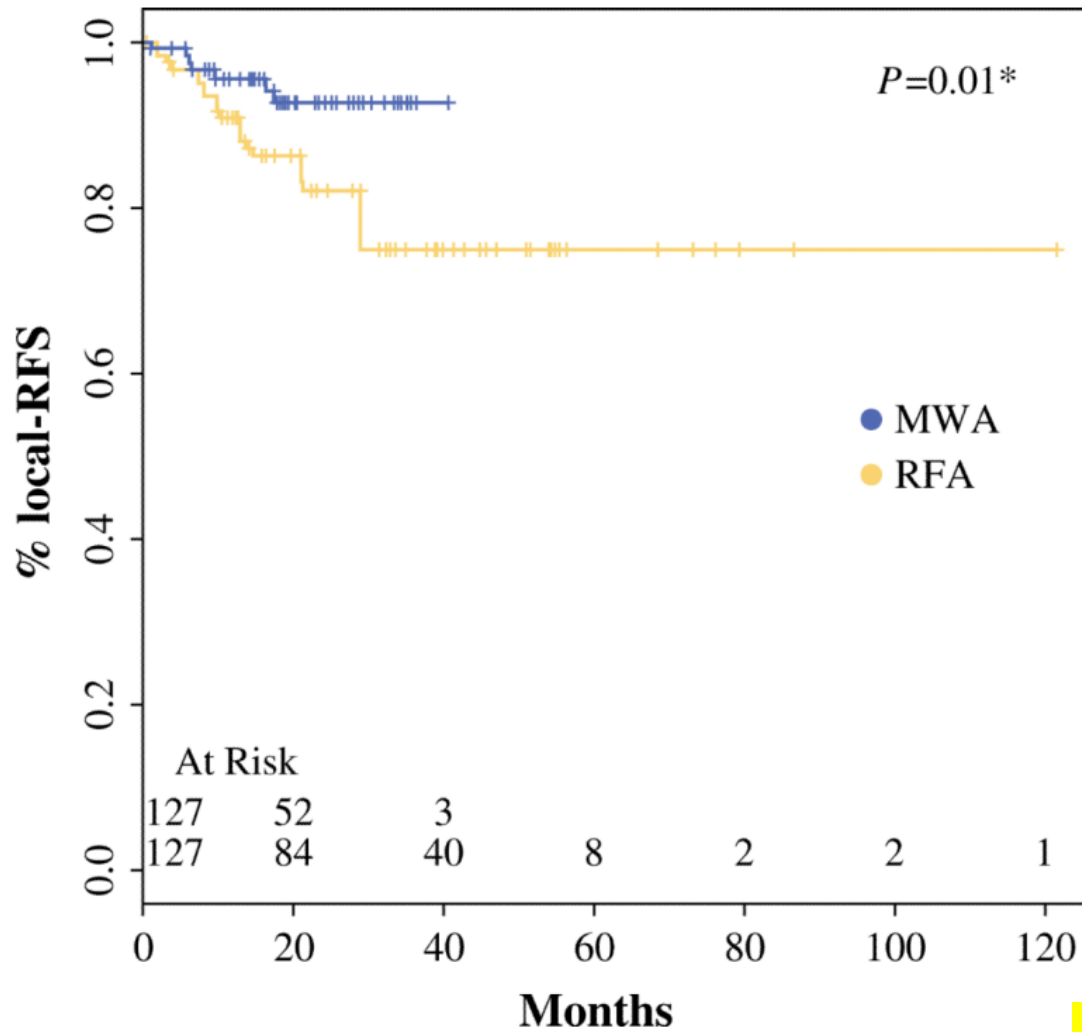
Interventional therapies for CRLM

Indication	Treatment Options
Improve surgical candidacy	Portal vein embolization
	Lobar TARE
	Combine ablation with surgical resection
Therapies with Curative Intent	Ablation +/- Systemic chemotherapy
	Radiation Segmentectomy
	Firstline Chemotherapy plus TARE
Therapies with Palliate Intent	TARE
	TACE

Ablation for CRLM

- Microwave ablation (MWA)
- Irreversible electroporation (IRE)
- Radiofrequency ablation (RFA)
- Cryoablation

ABLATION



Microwave

Thermal ablation for CRLM

Table 4 Summary of recommendations. Tumour and technical considerations

Parameter	Preferred	Caveat
Tumour size	<3 cm	Well located tumours <5 cm may be suitable for ablation
Tumour number	1–3 optimal, <5 preferable	6–9 maximum
Tumour location next to major bile ducts	Avoid	Consider high flow biliary cooling via nasobiliary tubes or other non-thermal interventional oncology techniques
Tumours 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
Tumours 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 minimised by:	<ol style="list-style-type: none"> 1. Achieving >1 cm ablation margins in 3D 2. Maximising operator experience 3. GA should be available as required 4. Optimal definition of the tumour 5. Optimal intra-procedural assessment of the ablation zone 	Conscious sedation procedures are an acceptable alternative in unfit patients

Tumor size

Microwave ablation

TABLE 4. Univariate analysis of factors associated with local tumor progression in MWA-treated patients

Variables	p
Sex (male vs. female)	0.372
Age (≤ 65 vs. > 65 years)	0.415
White blood cell count ($\leq 8 \times 10^3/L$ vs. $> 8 \times 10^3/L$)	0.554
Neutrophil-to-lymphocyte ratio (≤ 2 vs. > 2)	0.297
Primary tumor (HCC vs. metastasis)	0.624
Metastasis type (colorectal vs. non-colorectal)	0.198
Tumor location (favorable vs. unfavorable)	0.339
Tumor size (≤ 3 cm vs. > 3 cm)	0.012

HCC = hepatocellular carcinoma; MWA = microwave ablation

p = 0.012

Tumor size

Liver transplant for CRLM

Table 5

Prognostic factors and survival outcomes after LT for CRLM

Factor	Comparison	Impact on OS	References/Appendix
Pre-LT LRT	LRT vs. none	No OS benefit at 1 or 5 years	Appendix 7
Pre-LT resection	Resection vs. none	No OS benefit at 1 or 5 years	Appendix 7
Donor type	LDLT vs. DDLT	No pooled difference; variable individual reports	Kaltenmeier 2024; Byrne 2024; Rajendran 2023; Appendix 8
Tumor sidedness	Right vs. left/rectum	Right-sided tumors had lower 1- and 3-year OS	Appendix 9
Chemo response	Partial vs. poor	Responders had higher OS	Appendix 10
CEA level	≥80 vs. < 80	High CEA predicted poor OS	Appendix 10
Oslo score	3–4 vs. 0–2	Higher scores are associated with worse OS	Appendix 10
Tumor size	≥5.5 cm vs. < 5.5 cm	Larger lesions predicted poor OS	Appendix 10
MTV	≥70 cm ³ vs. < 70 cm ³	High MTV strongly predicted poor OS	Grut 2023; Wehrle 2024; Appendix 10

Tumor size

Liver transplant for colorectal liver metastasis

TABLE 2. Summary of the TransMet Trial and Supporting Registry Studies and Meta-Analyses

Study	Design	No. of Patients	Key Inclusion Criteria	5-Year OS	5-Year DFS
TransMet trial ⁷²	Multicenter RCT (LT + chemotherapy v chemotherapy alone)	94 randomly assigned: 47 LT + chemotherapy v 47 chemotherapy alone Per-protocol: 36 LT + chemotherapy v 38 chemotherapy alone	1. Age 18-65 years 2. ECOG 0-1 3. Permanently uCRLM 4. BRAF wild-type 5. Response to ≤ 3 lines of chemotherapy (≥ 3 months) 6. CEA ≤ 80 ng/mL 7. No extrahepatic disease	ITT: 56.6% (LT + chemotherapy) v 12.6% (chemotherapy alone); HR, 0.37; $P = .0003$ Per-protocol: 73.2% (LT + chemotherapy) v 9.3% (chemotherapy alone); HR, 0.16; $P < .0001$	19.9% (LT + chemotherapy) v 0% (chemotherapy alone)
Norwegian combined series ⁷⁵	Prospective cohort (SECA-I, SECA-II, and subsequent studies)	61	Various (Oslo criteria refined over time)	50.40%	18.30%
Meta-analysis by Dawood et al ⁷⁷	Systematic review and meta-analysis	403 patients (16 studies)	Varied	53% (95% CI, 45 to 61)	13% (95% CI, 4 to 7)
Meta-analysis by Sayed Ahmed et al ⁷⁸	Systematic review and meta-analysis	377 patients (20 studies)	Varied	54%	16%
Meta-analysis by Varley et al ⁷⁹	Systematic review and meta-analysis	48 patients (3 studies)	Varied	50%-80%	35%-56%

Abbreviations: CEA, carcinoembryonic antigen; CRLM, colorectal liver metastasis; DFS, disease-free survival; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; ITT, intention-to-treat; LT, liver transplant; OS, overall survival; RCT, randomized controlled trial; uCRLM, unresectable CRLM.



Perspective

Liver transplantation for colorectal liver metastases: What do we need to know?



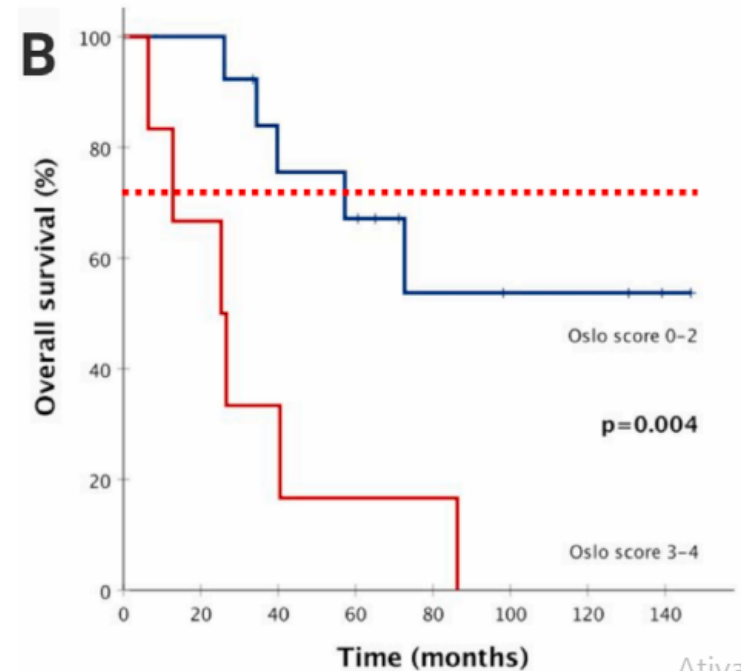
Oslo Score (0–4)

Tumor Diameter > 5.5 cm

CEA > 80 µg/L

Less than 2 year interval between
primary resection and LT

Progressive disease at time of LT



Tumor size

Liver transplant for colorectal liver metastasis

Table 1. Eligibility criteria in main clinical trials on liver transplantation in liver-limited CRC

	SECA-I	SECA-II	TransMet
Confirmation of no extrahepatic disease	CT scan, FDG–PET–CT and bone scan	CT scan and FDG–PET–CT	CT scan and FDG–PET–CT
Assessment of unresectability	National, centralized at one centre	National, centralized at one centre	International, centralized
Age	Not specified	Not specified	18-65 years
Primary tumour	Resected	Resected	Resected
ECOG-PS	0/1	0/1	0/1
Line of chemotherapy	Not specified	Not specified	≤3
Response to CT (RECIST criteria)	Not specified	<ul style="list-style-type: none"> • At least 10%. • If >20 lesions (see below) at least 30%. • If <10% eligible if 20% response achieved after TACE or ⁹⁰Y-spheres 	At least stable disease lasting ≥3 months
Radiological criteria	Not specified	<ul style="list-style-type: none"> • No lesion >10 cm before the start of CT • If >20 lesions all <5 cm 	Not specified
Molecular criteria	Not specified	Not specified	<i>BRAF</i> wild-type
Biochemical criteria	Not specified	Not specified	CEA level <80 ng/ml or ≥50% decrease from baseline
Other criteria	—	At least 1-year time span from CRC diagnosis and date of being listed on the transplantation list	—

CEA, carcinoembryonic antigen; CT, computed tomography; ECOG-PS, Eastern Cooperative Group performance status; FDG-PET, [¹⁸F]2-fluoro-2-deoxy-D-glucose–positron emission tomography; (m)CRC, (metastatic) colorectal cancer; TACE, transarterial chemoembolization.

Tumor size

Studies describing the role of TACE in CRLM

TABLE 7 Studies describing the role of TACE in CRLM.

Study	Study design	Country/Region	Sample Size	Patients	Follow up/Inclusion period	Results	Additional data
Maraj et al. (121) 2023	Retrospective study	Canada	120	328 procedures of irinotecan-eluting microspheres TACE was performed in unresectable CRLM with <75% hepatic parenchymal disease, limited extrahepatic tumor burden and previous locoregional treatment.	Included patients between 2012 to 2020	Technical success rate was 85%; Median OS of 12.7 months; The OS improved if the patient has prior ablation (P<0.05), <25% hepatic tumor burden (P<0.001), and previously resected primary disease (P<0.05)	5% intra-procedural adverse events including groin hematoma, pseudoaneurysm, peri-procedural pain and hepatic artery dissection; 6% post-procedural adverse events including post-embolic cholecystitis, perforated gastric ulcer, bleeding duodenal ulcer and biloma.
Vogl et al. (122) 2018	Retrospective study	Germany	452	Total: 452 patients with CRLM unresponsive to systemic chemotherapy; TACE as palliative option: 233 patients; TACE followed by ablation as neoadjuvant therapy: 219 patients	Included patients between 2001 and 2015	OS and PFS in palliative group were 12.6 and 5.9 months respectively and in neoadjuvant group was 25.8 and 10.8 months respectively.	Extrahepatic metastases in both palliative and neoadjuvant group; Tumor number, location, average size of metastases in neoadjuvant group.
Gruber-Rouh et al. (123) 2013	Retrospective study	Germany	564	564 patients underwent TACE; Mean number of sessions: 6	Included patients between 1999 and 2011	Partial response: 16.7%; Stable disease: 48.2%; Progressive disease: 16.7%; 1-, 2-, and 3-year survival rates: 62%, 28%, and 7% respectively; Median survival from the start of TACE: 14.3 months	Predictors of survival: Indication of TACE and initial tumor response
Nishiofuku et al. (124) 2013	Prospective trial	Japan	24	24 patients treated with FOLFOX prior to TACE	Phase I patient recruitment from February 2008 to July 2008; Phase II patient recruitment from September 2008 to January 2010; Mean follow up duration was 17.4 months	Tumor response rate: 61.1%; Median hepatic PFS: 8.8 months; OS: 21.1 months	Grade 3 thrombocytopenia: 12.5%; Grade 3 AST elevation: 33.3%; Grade 3 ALT elevation: 12.5%; Grade 3 hyponatremia: 8.3%; Grade 3 cholecystitis: 4.2%

Median OS 12.7 months

Median OS 12.6 months

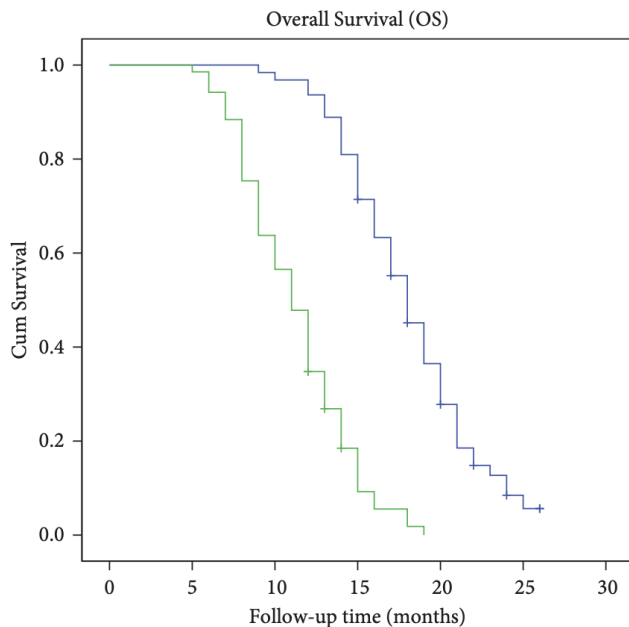
**1, 2, and 3-year survival
62%, 28%, and 7%**

Median hPFS 8.8 months

TACE

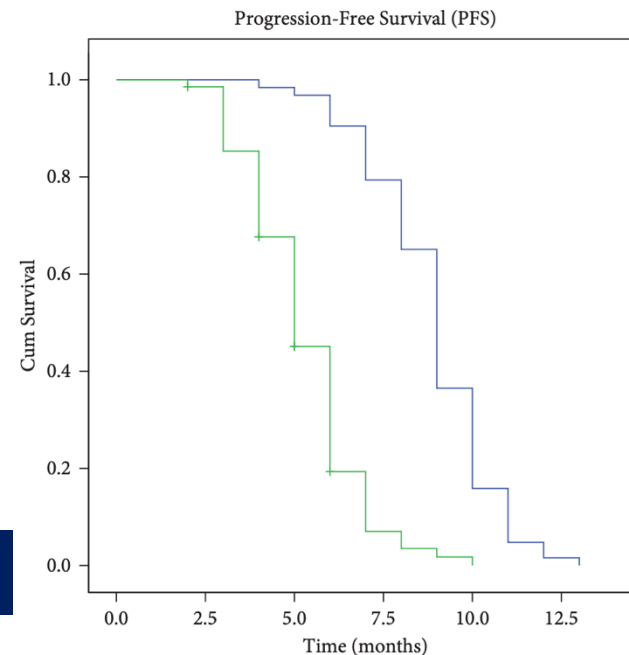
Research Article

Efficacy and Safety of TACE Combined with Regorafenib versus TACE in the Third-Line Treatment of Colorectal Liver Metastases



(1) TACE+Regorafenib
Median OS: 18.2 months
95% CI: 17.1-19.2 months
(2) TACE
Median OS: 11.3 months
95% CI: 10.5-12.1 months
 $\chi^2=74.963, P<0.001$

p < 0.001



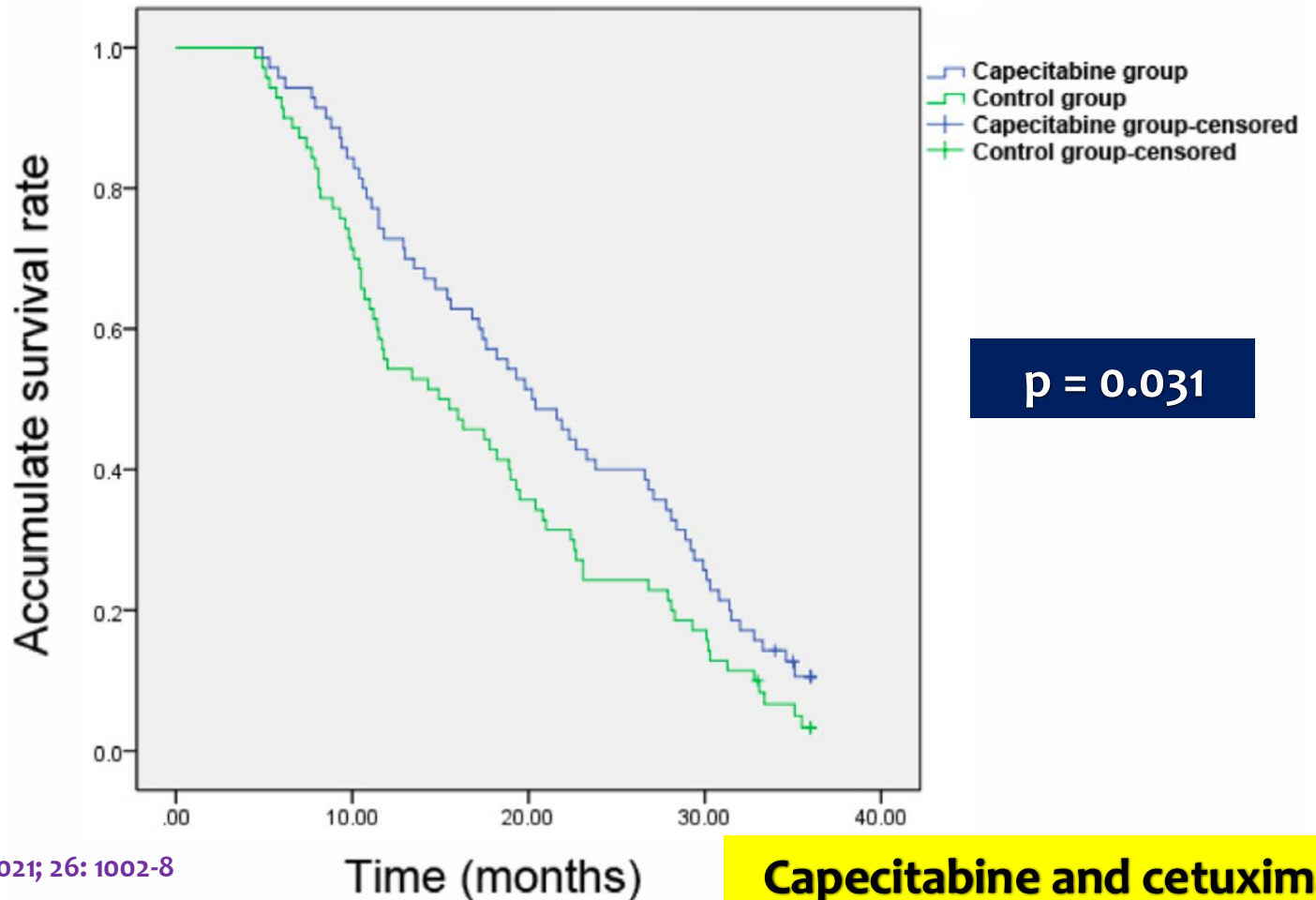
(1) TACE+Regorafenib
Median PFS: 8.9 months
95% CI: 8.5-9.3 months
(2) TACE
Median PFS: 5.3 months
95% CI: 4.9-5.7 months
 $\chi^2=82.549, P<0.001$

Group
— TACE+Regorafenib + TACE+Regorafenib-censored
— TACE + TACE-censored

Group
— TACE+Regorafenib + TACE+Regorafenib-censored
— TACE + TACE-censored

ORIGINAL ARTICLE

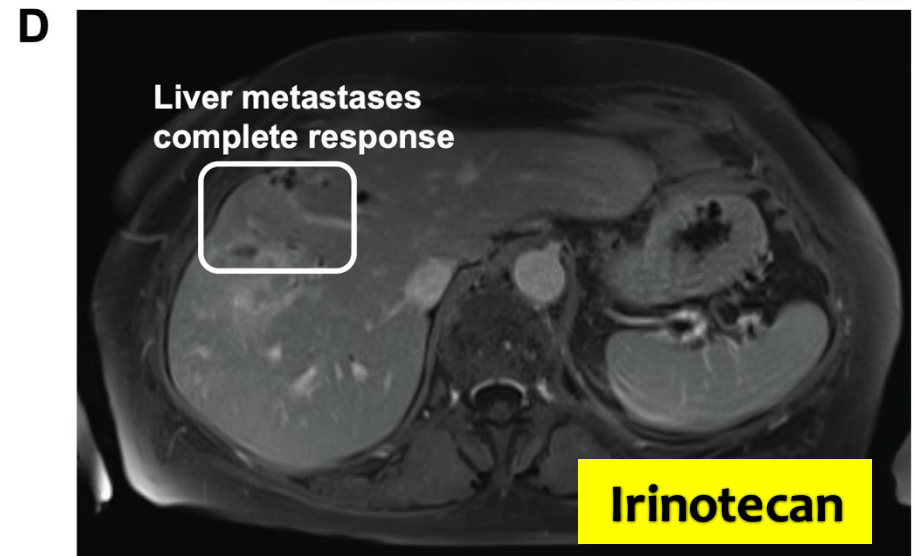
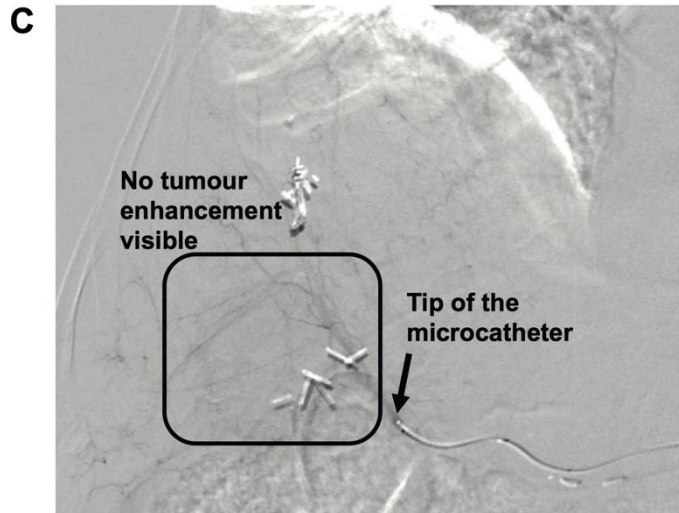
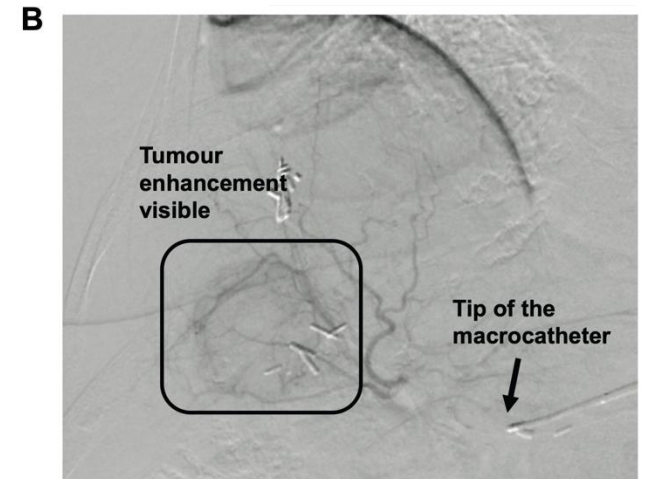
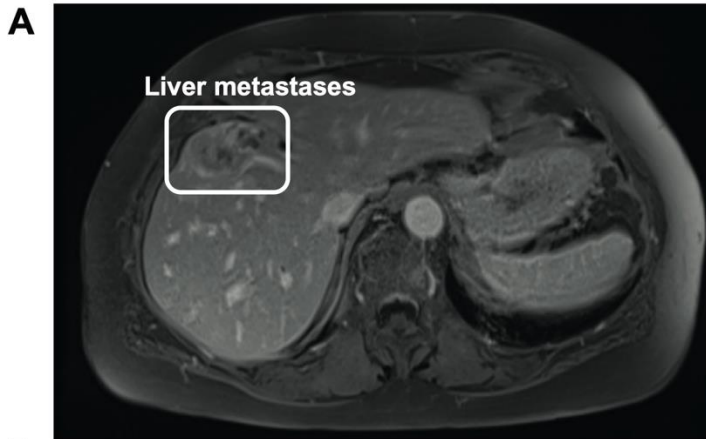
Efficacy of transcatheter arterial chemoembolization combined with capecitabine and cetuximab in the treatment of colorectal cancer with liver metastasis



ORIGINAL ARTICLE

TACE in CRLM

Transarterial chemoembolisation with irinotecan (irinotecan-TACE) as salvage or post-inductive therapy for colorectal cancer liver metastases: effectiveness results from the CIREL study

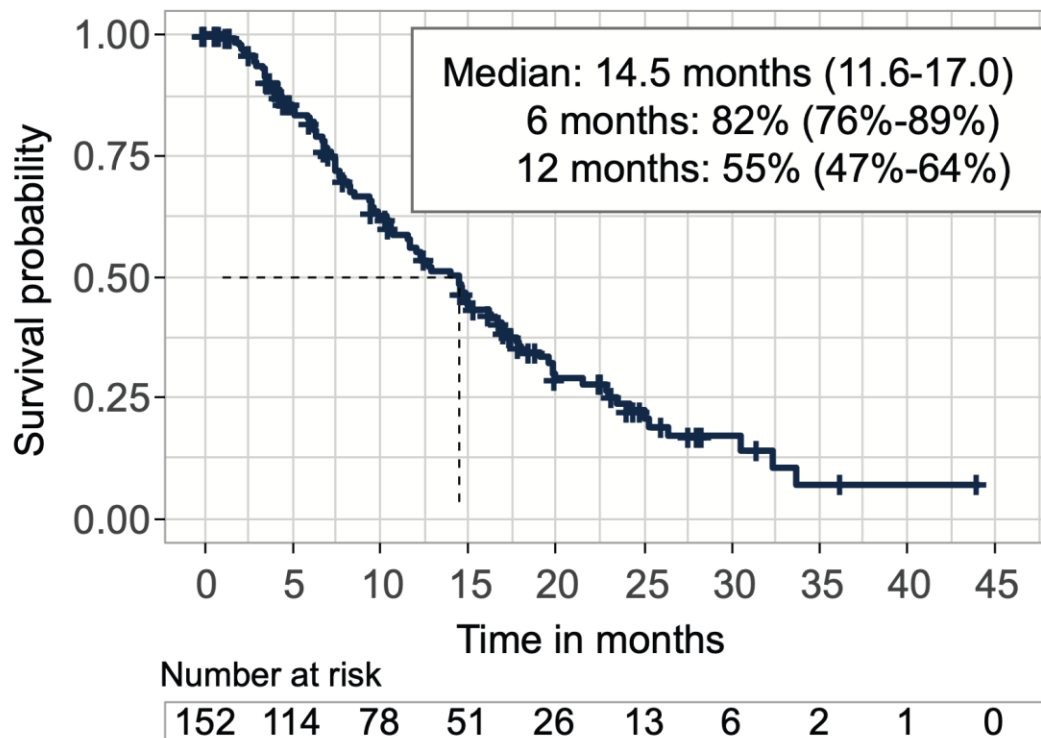


ORIGINAL ARTICLE

TACE in CRLM

Transarterial chemoembolisation with irinotecan (irinotecan-TACE) as salvage or post-inductive therapy for colorectal cancer liver metastases: effectiveness results from the CIREL study

E Overall survival



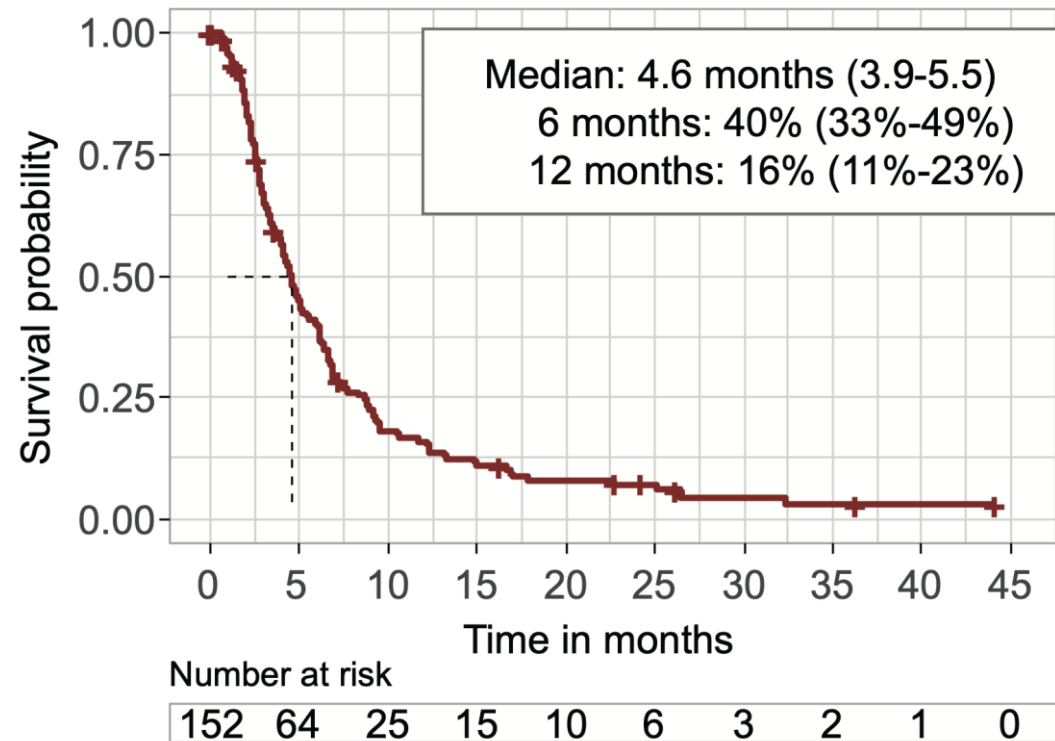
Irinotecan

ORIGINAL ARTICLE

Transarterial chemoembolisation with irinotecan (irinotecan-TACE) as salvage or post-inductive therapy for colorectal cancer liver metastases: effectiveness results from the CIREL study

TACE in CRLM

F Progression-free survival

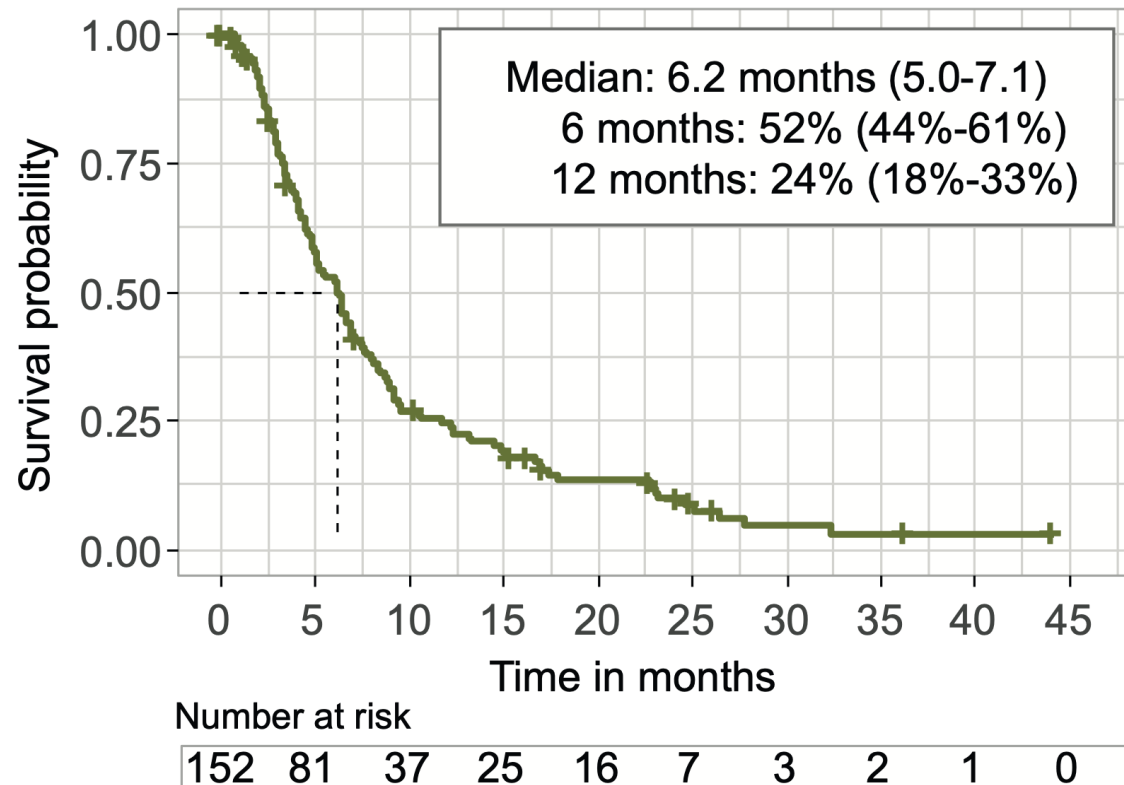


ORIGINAL ARTICLE

TACE in CRLM

Transarterial chemoembolisation with irinotecan (irinotecan-TACE) as salvage or post-inductive therapy for colorectal cancer liver metastases: effectiveness results from the CIREL study

G Hepatic progression-free survival



Irinotecan

Drug-eluting bead transarterial chemoembolization (DEB-TACE) VS Conventional transarterial chemoembolization (cTACE)

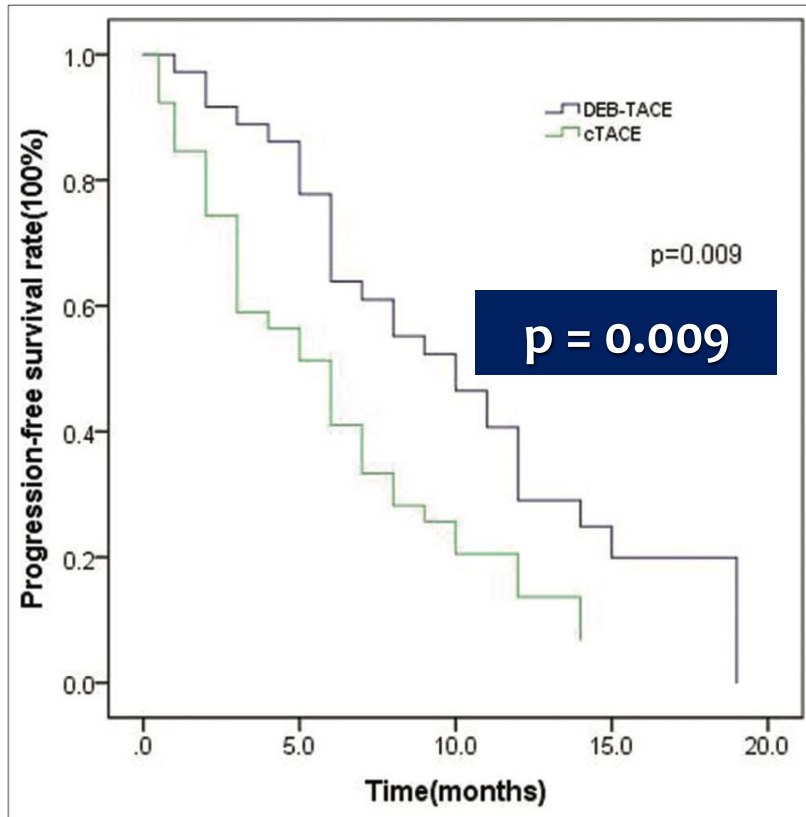


Figure 1: Progression-free survival of patients in the DEB-TACE and cTACE groups

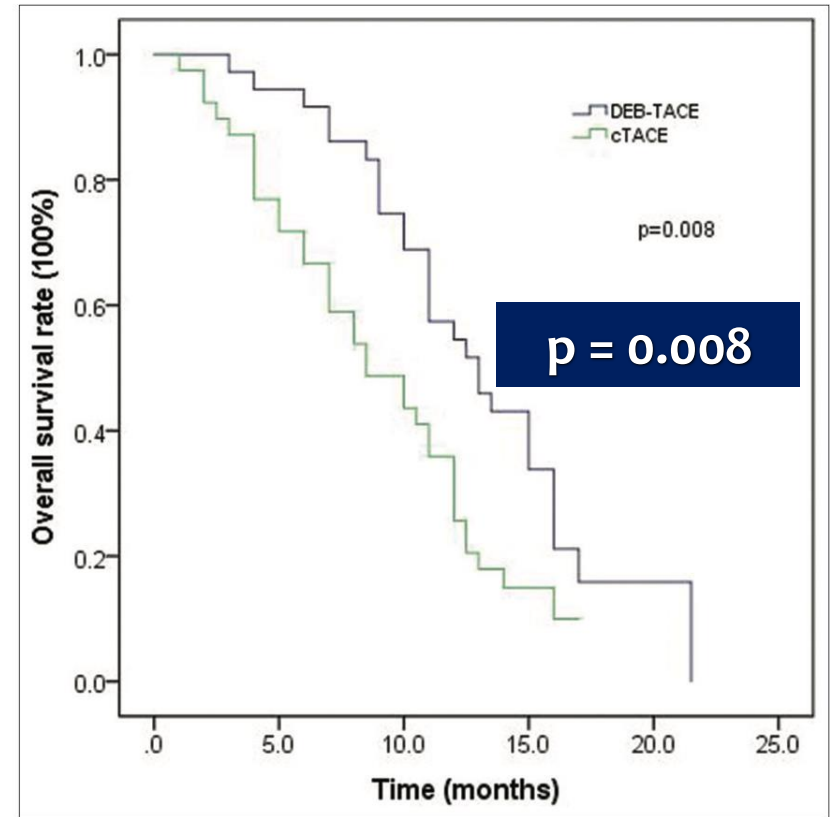
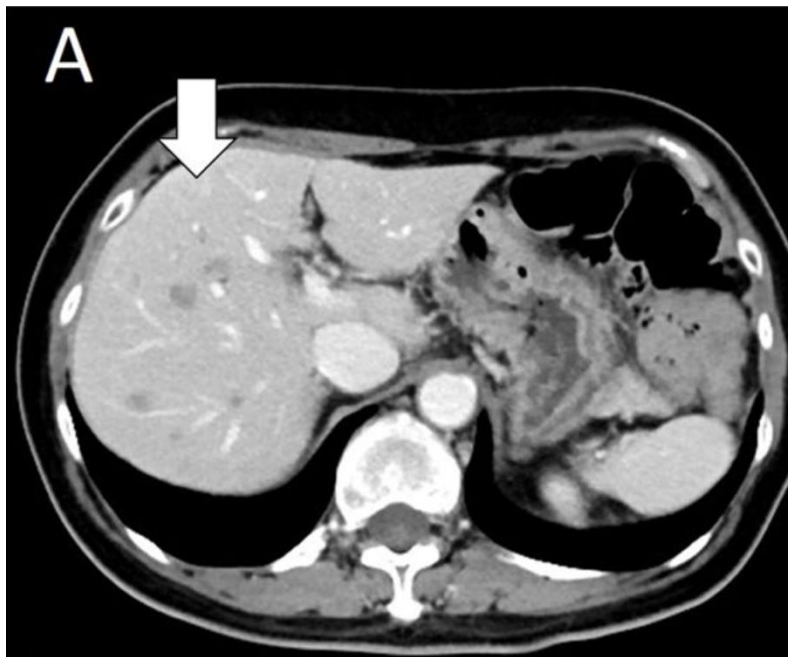


Figure 2: Overall survival of patients in the DEB-TACE and cTACE groups

DEB-TACE

DEB-TACE VS TACE



(drug-eluting beads-TACE)

Outcomes of repeat conventional transarterial chemoembolization in patients with liver metastases

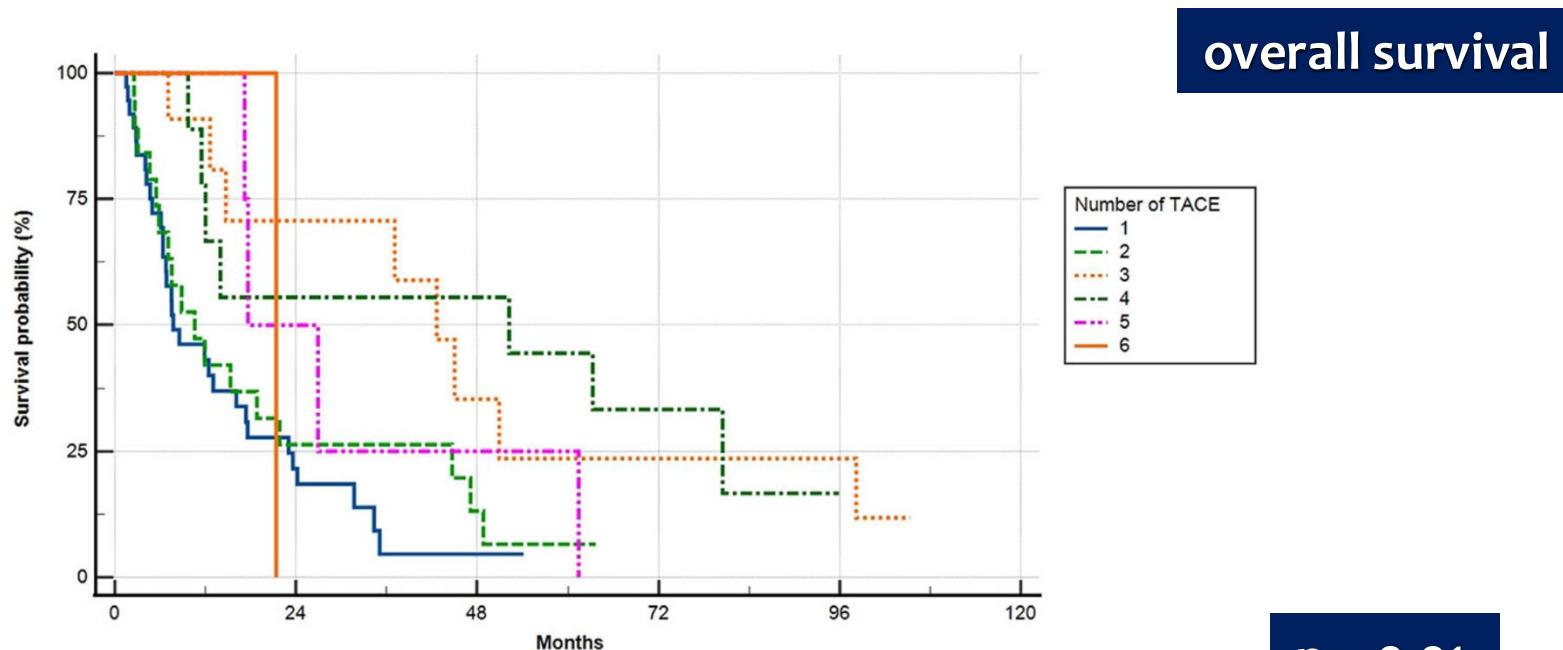
Conventional TACE (cTACE): doxorubicin (50mg) + mitomycin (10mg)

Rates of radiologic response in nonresponders to previous cTACE session for the entire cohort and each tumor type subgroup.

		Total	Nonresponder	Responder	P-value
CRC	Number of lesions	37	25	12	–
	Enhancing tumor volume (cm ³), median (IQR)	60.5 (13.3–133.4)	40.7 (11.4–108.0)	123.4 (16.8–196.9)	0.25
	Responder after		–	–	–
	1st cTACE	9/37 (24.3 %)			
	2nd cTACE	4/11 (36.3 %)			
	3rd cTACE	0/3 (0 %)			
	4th cTACE	0/3 (0 %)			
	5th cTACE	0/1 (0 %)			

Repeat TACE

Outcomes of repeat conventional transarterial chemoembolization in patients with liver metastases

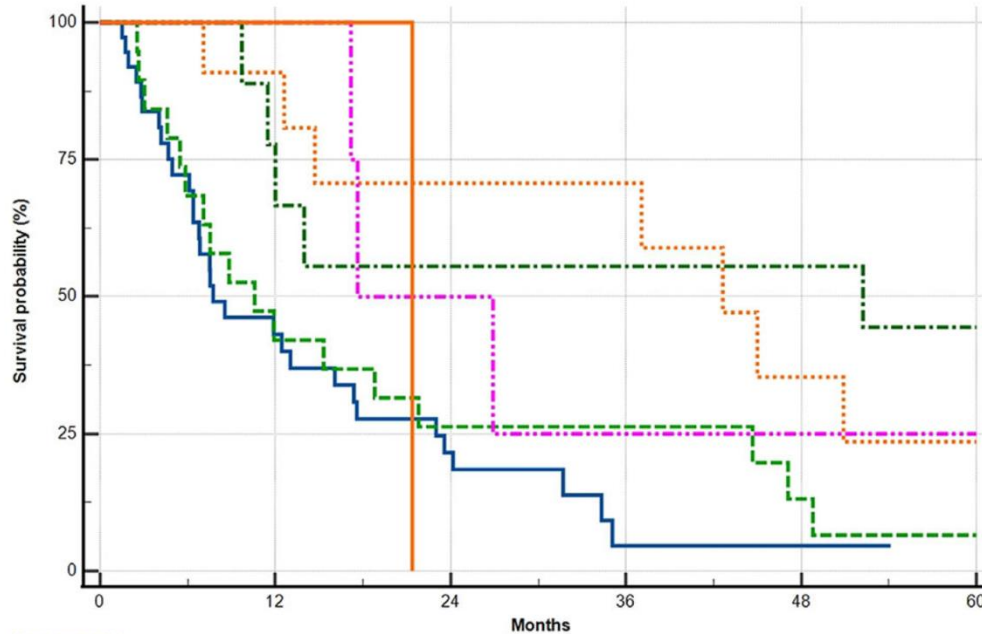


Number at risk		Months					
	0	24	48	72	96	120	
1	38	7	1	0	0	0	
2	21	5	2	0	0	0	
3	11	6	3	2	2	0	
4	9	5	5	2	0	0	
5	4	2	1	0	0	0	
6	1	0	0	0	0	0	

p = 0.01

Repeat TACE

Outcomes of repeat conventional transarterial chemoembolization in patients with liver metastases



5-year survival

p = 0.01

Number at risk	0	12	24	36	48	60
1	38	14	7	1	1	0
2	21	8	5	4	2	1
3	11	9	6	6	3	2
4	9	6	5	5	5	4
5	4	4	2	1	1	1
6	1	1	0	0	0	0

Repeat TACE

Article

Interventional Treatments of Liver Metastases from Colorectal Cancer: Prognostic Factors and Subgroup Analyses

TACE followed by MWA

Table 2. Prognostic factors for OS (Group A).

Prognostic Factors	<i>p</i> -Value	Hazard Ratio	95% Confidence Interval: Lower	95% Confidence Interval: Upper
Age	0.856	0.998	0.981	1.016
Sex	0.265	1.265	0.837	1.913
Number of metastases	0.717	1.026	0.893	1.179
Recurrence	0.984	0.995	0.617	1.604
Diameter of the largest metastasis	0.09	0.988	0.974	1.002
Volume of the largest metastasis	0.091	0.989	0.977	1.002
Complete ablation status	0.348	0.672	0.293	1.541
Number of TACE before MWA treatment	0.137	1.051	0.984	1.123

TACE

Article

Interventional Treatments of Liver Metastases from Colorectal Cancer: Prognostic Factors and Subgroup Analyses

MWA alone

Table 3. Prognostic factors for OS (Group B).

Prognostic Factors	<i>p</i> -Value	Hazard Ratio	95% Confidence Interval: Lower	95% Confidence Interval: Upper
Age	0.292	0.983	0.951	1.015
Sex	0.917	1.037	0.520	2.067
Number of metastases	0.618	1.039	0.894	1.207
Recurrence	0.126	0.498	0.204	1.217
Diameter of the largest metastasis	0.819	0.998	0.979	1.017
Volume of the largest metastasis	0.564	1.005	0.989	1.021
Complete ablation status	0.228	0.415	0.099	1.736

Article

Interventional Treatments of Liver Metastases from Colorectal Cancer: Prognostic Factors and Subgroup Analyses

Entire cohort

Table 4. Prognostic factors for OS (Group C).

Prognostic Factors	<i>p</i> -Value	Hazard Ratio	95% Confidence Interval: Lower	95% Confidence Interval: Upper
Age	0.468	0.994	0.979	1.010
Sex	0.28	1.215	0.853	1.729
Number of metastases	0.629	1.025	0.927	1.133
Recurrence	0.524	0.873	0.574	1.327
Diameter of the largest metastasis	0.126	0.991	0.980	1.002
Volume of the largest metastasis	0.141	0.993	0.984	1.002
Complete ablation status	0.159	0.597	0.292	1.224

TACE

TACE followed by MWA and MWA alone

Article

Interventional Treatments of Liver Metastases from Colorectal Cancer: Prognostic Factors and Subgroup Analyses

Entire cohort

Table 7. Prognostic factors for hPFS (Group C).

Prognostic Factors	<i>p</i> -Value	Hazard Ratio	95% Confidence Interval: Lower	95% Confidence Interval: Upper
Age	0.824	0.999	0.987	1.011
Sex	0.905	0.983	0.746	1.296
Number of metastases	0.034	1.103	1.008	1.207
Diameter of the largest metastasis	0.908	1.000	0.992	1.009
Volume of the largest metastasis	0.635	1.001	0.996	1.006
Complete ablation status	0.464	1.199	0.738	1.950

hPFS: hepatic progression free survival

TACE followed by MWA and MWA alone

CONCLUSION

- ❑ The role of percutaneous ablation or arterial embolization in the management of CRLM as a bridge for liver transplant is still under debate.
- ❑ Arterial embolization seems to be better than ablation.

Thanks!

Gracias!

Obrigado!

