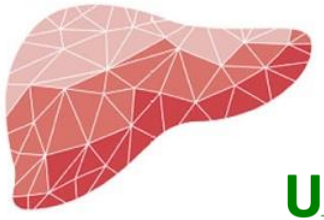


MÁSTER EN HEPATOLOGÍA

UAM Universidad Autónoma de Madrid

Universidad de Alcalá

Asignatura 7 : HEPATOCARCINOMA

“Tratamiento del paciente en estadio intermedio. TARE y expectativas del tratamiento combinado”

Prof. Mercedes Iñarrairaegui

Clínica Universidad de Navarra

Objetivos de aprendizaje

Recordar el fundamento y la técnica de los tratamientos intraarteriales empleados en HCC en estadio intermedio.

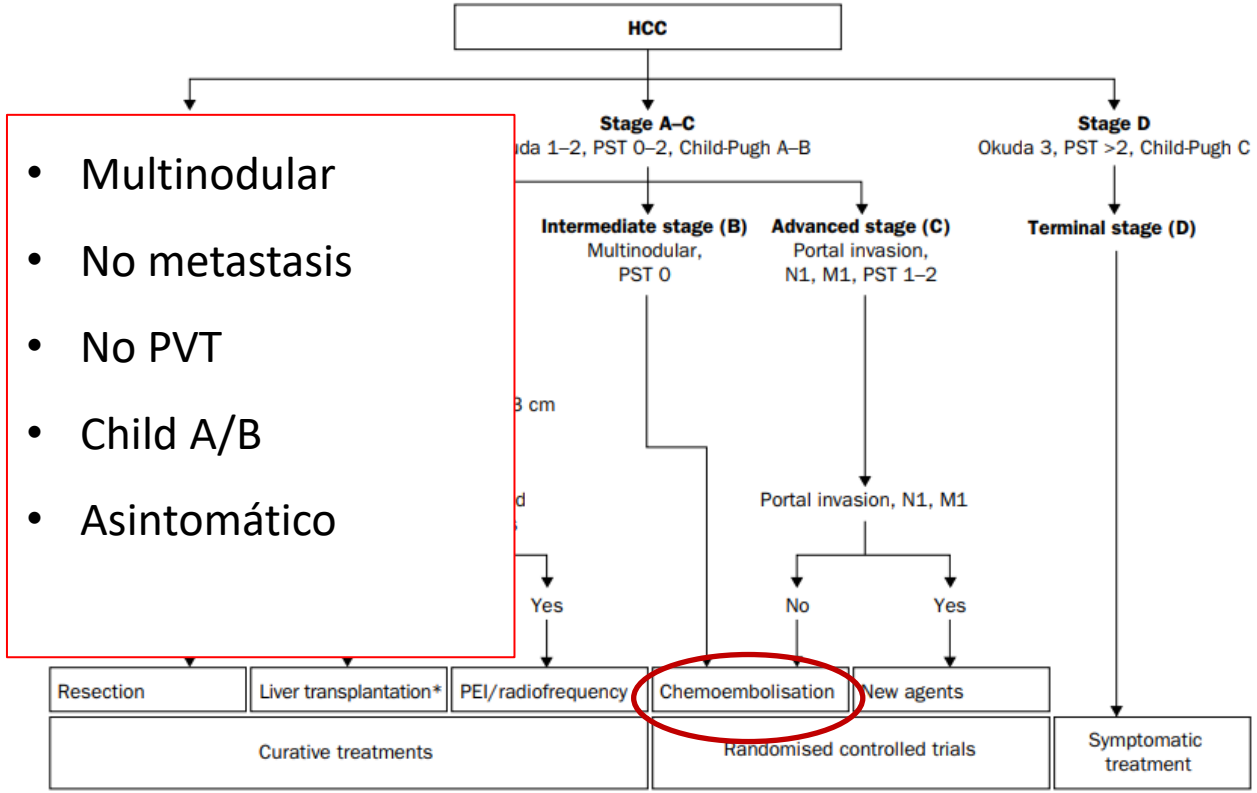
Contrastar los resultados de los tratamientos locorregionales en HCC intermedio

Conocer las novedades del tratamiento con RE en HCC

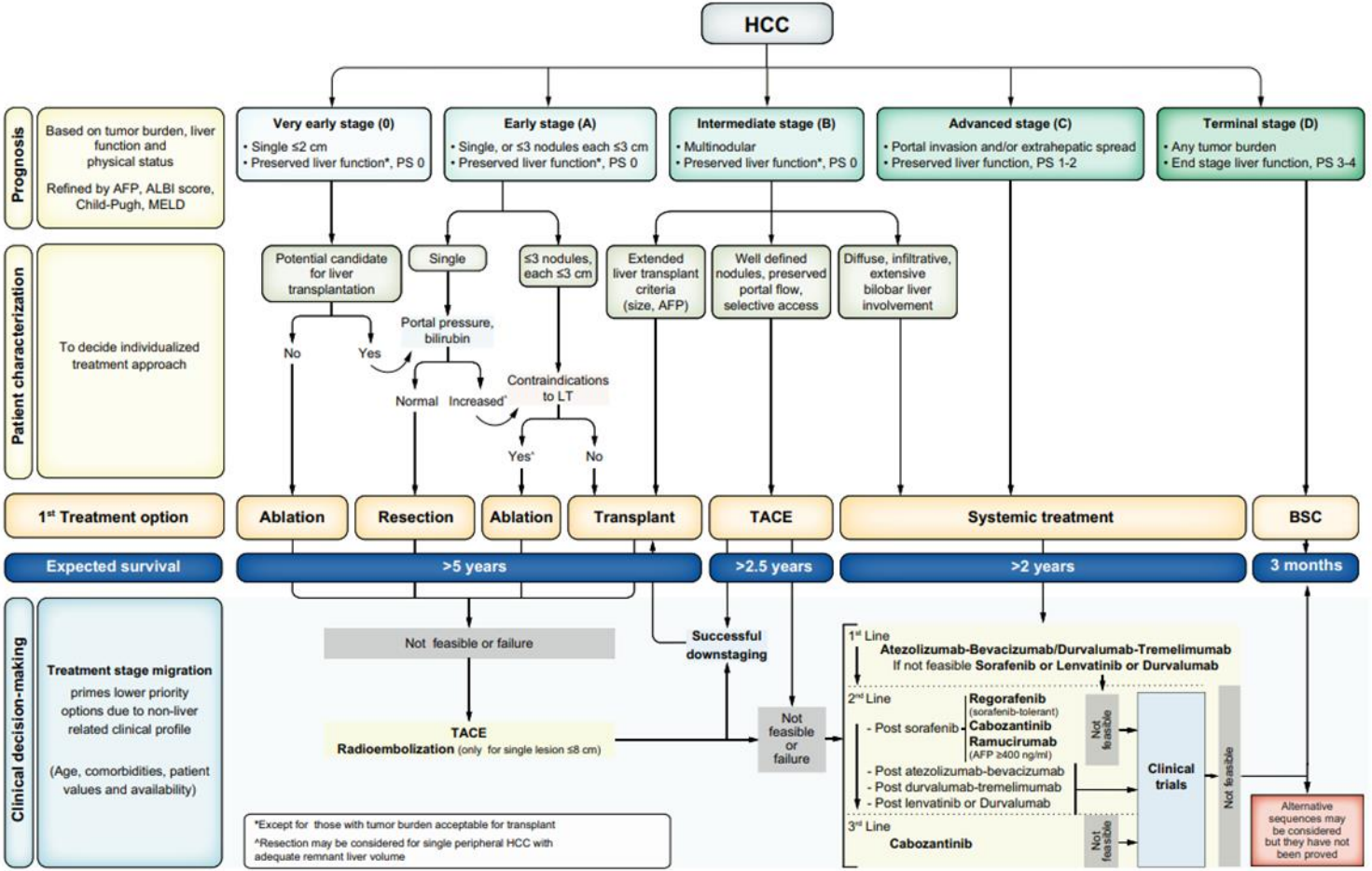
Analizar las tendencias futuras del tratamiento combinado en estadio intermedio

Estadio intermedio. Terapias intraarteriales.

- Multinodular
- No metastasis
- No PVT
- Child A/B
- Asintomático

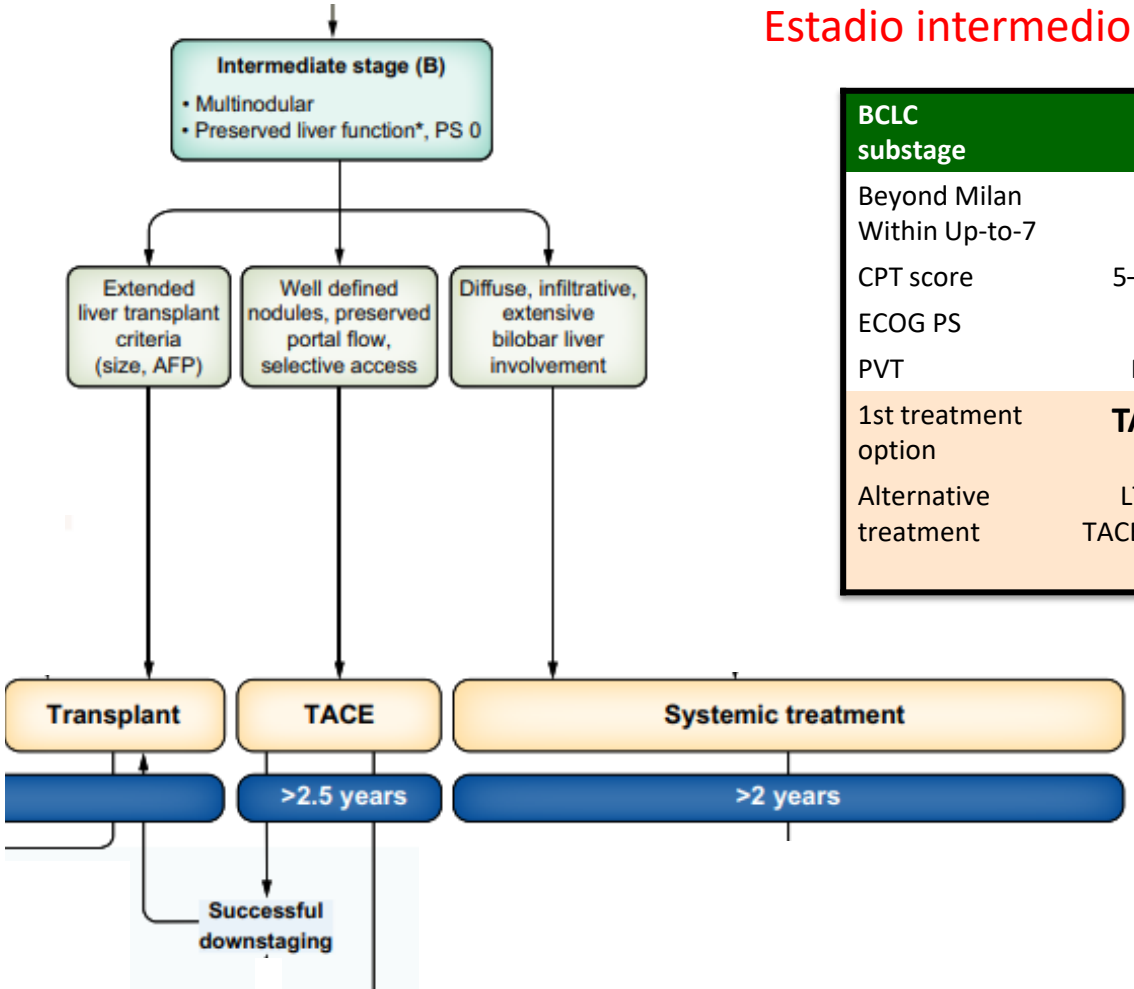


Llovet, Lancet 2003



Reig, J Hepatol 2021

Estadio intermedio: **GRUPO HETEROGÉNEO**

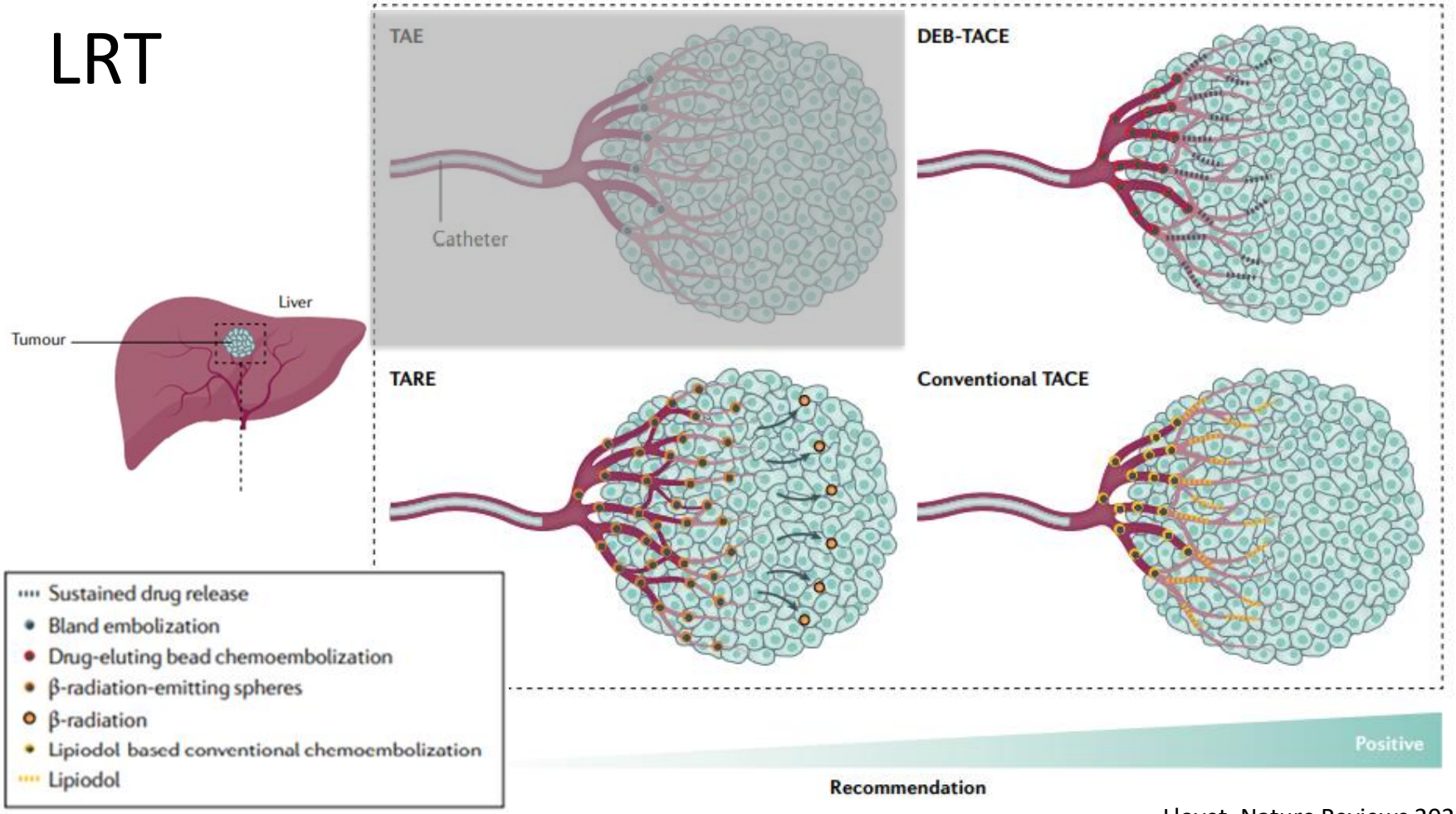


BCLC substage	B1	B2	B3	B4
Beyond Milan Within Up-to-7	IN	OUT	OUT	ANY
CPT score	5–6–7	5–6	7	8–9*
ECOG PS	0	0	0	0–1
PVT	NO	NO	NO	NO
1st treatment option	**TACE**	TACE or TARE		**BSC**
Alternative treatment	LT or TACE + ABL	SOR	Research or TACE	LT**

Reig, J Hepatol 2021

Bolondi, Semin Liv Dis 2012

LRT

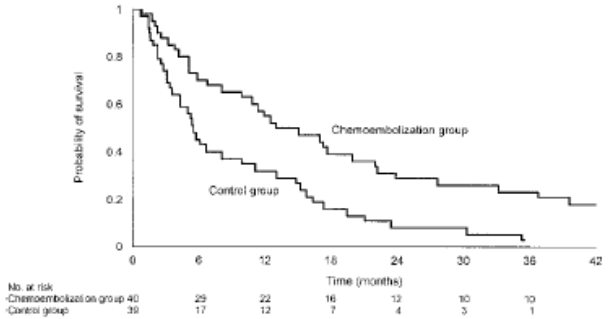


Llovet, Nature Reviews 2021

RCTs supporting the use of TACE

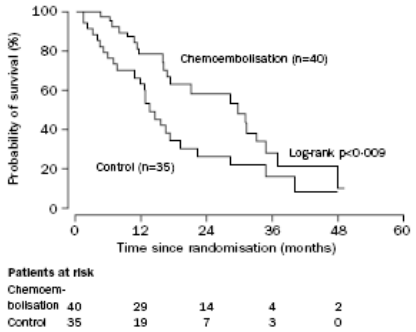
Randomized Controlled Trial of Transarterial Lipiodol Chemoembolization for Unresectable Hepatocellular Carcinoma

Chung-Mau Lo, Henry Ngan, Wai-Kuen Tso, Chi-Leung Liu, Chi-Ming Lam, Ronnie Tung-Ping Poon, Sheung-Tat Fan, and John Wong



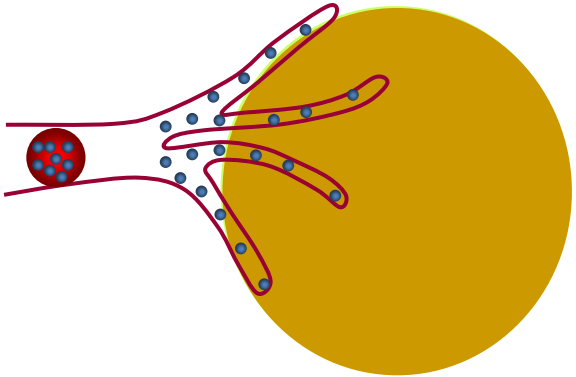
Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial

*Josep M Llovet, Maria Isabel Real, Xavier Montaña, Ramon Planas, Susana Coll, John Aponte, Carmen Ayuso, Margarita Sala, Jordi Muchart, Ricard Solà, Joan Rodés, Jordi Bruix, for the Barcelona Clínic Liver Cancer Group**



Lo, Hepatology 2022
Llovet, Lancet 2002

TACE with Drug-Eluting Beads



DC-Bead® (100-300; 300-500; 500-700 µm)
DC-Bead M1 ® (75-150 µm)
HepaSphere® (30-60; 50-100; 100-150; 150-200 µm)

Embozene TANDEM®
LifePearl®

Tamaño: 40-900 µm

Review

CrossMark

EASL JOURNAL OF HEPATOLOGY

Transarterial chemoembolization: Modalities, indica patient selection

Wolfgang Sieghart*, Florian Hucke, Markus Peck-Radosavljevi

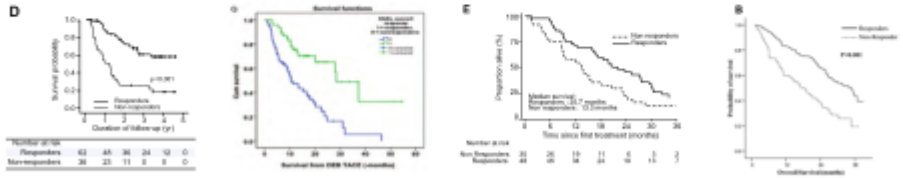
Key Points

- Conventional TACE is the standard of care for intermediate stage HCC
- DEB-TACE is equally effective as cTACE, but may provide a better safety profile due to less systemic absorption of chemotherapy
- Early radiologic response according to mRECIST after TACE-1 correlates with overall survival
- Patient selection for initial TACE and retreatment with TACE is key for optimal survival outcomes and may be guided by recently developed clinical scoring system

Early response to TACE predicts survival

Reference	Jung,	Prajapati	Gillmore	Kim
Type	cTACE	DEB-TACE	cTACE/TAE	cTACE
Time post 1st TACE	1–2 sessions	6 weeks	Median 64 days	4 weeks
Patients	98	120	83	292
mRECIST ORR	63%	63%	57%	72%

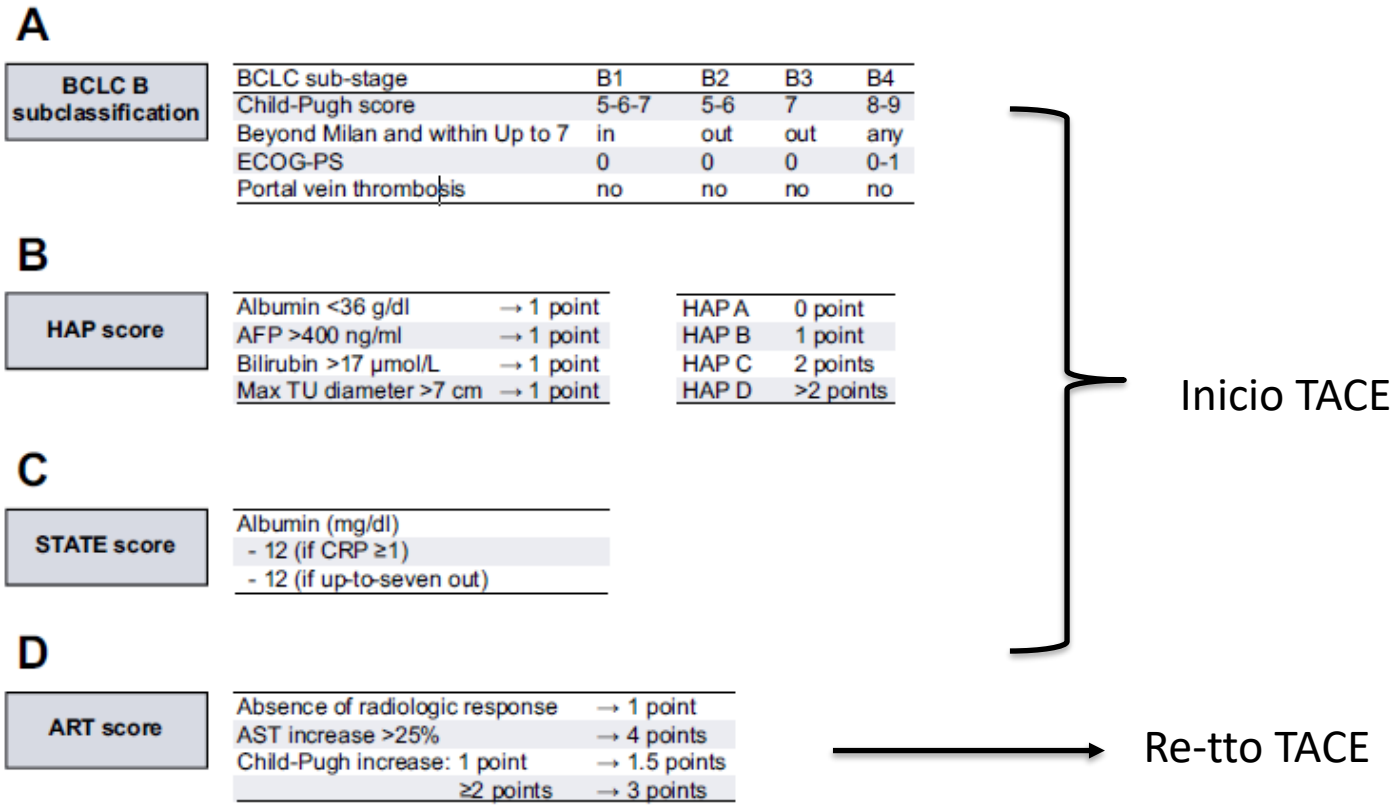
On demand TACE in all series



Jung ES, et al. J Hepatol. 2013. doi: j.jhep.2013.01.039. Prajapati HJ, et al. Ann Oncol. 2013;24:965-73. Gillmore R, et al. J Hepatol. 2011;55:1309-16. Kim BY, et al. Eur J Cancer. 2013;49:826-34.

Sieghart, Hepatology 2015

Descripción general de los nuevos sistemas de puntuación clínica para mejorar la selección para TACE.



Sieghart, Hepatology 2015

Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevier.com/locate/ctrv

Anti-Tumour Treatment

Updated use of TACE for hepatocellular carcinoma treatment: How and when to use it based on clinical evidence

Jean-Luc Raoul[a,*], Alejandro Forner[b,c], Luigi Bolondi[d], Tan To Cheung[e], Roman Kloeckner[f], Thierry de Baere[g]

Key points

No diferencias entre cTACE y DEB-TACE en eficacia (respuesta tumoral y supervivencia)

No se han podido validar scores de tratamiento y retratamiento

Tratamiento combinado

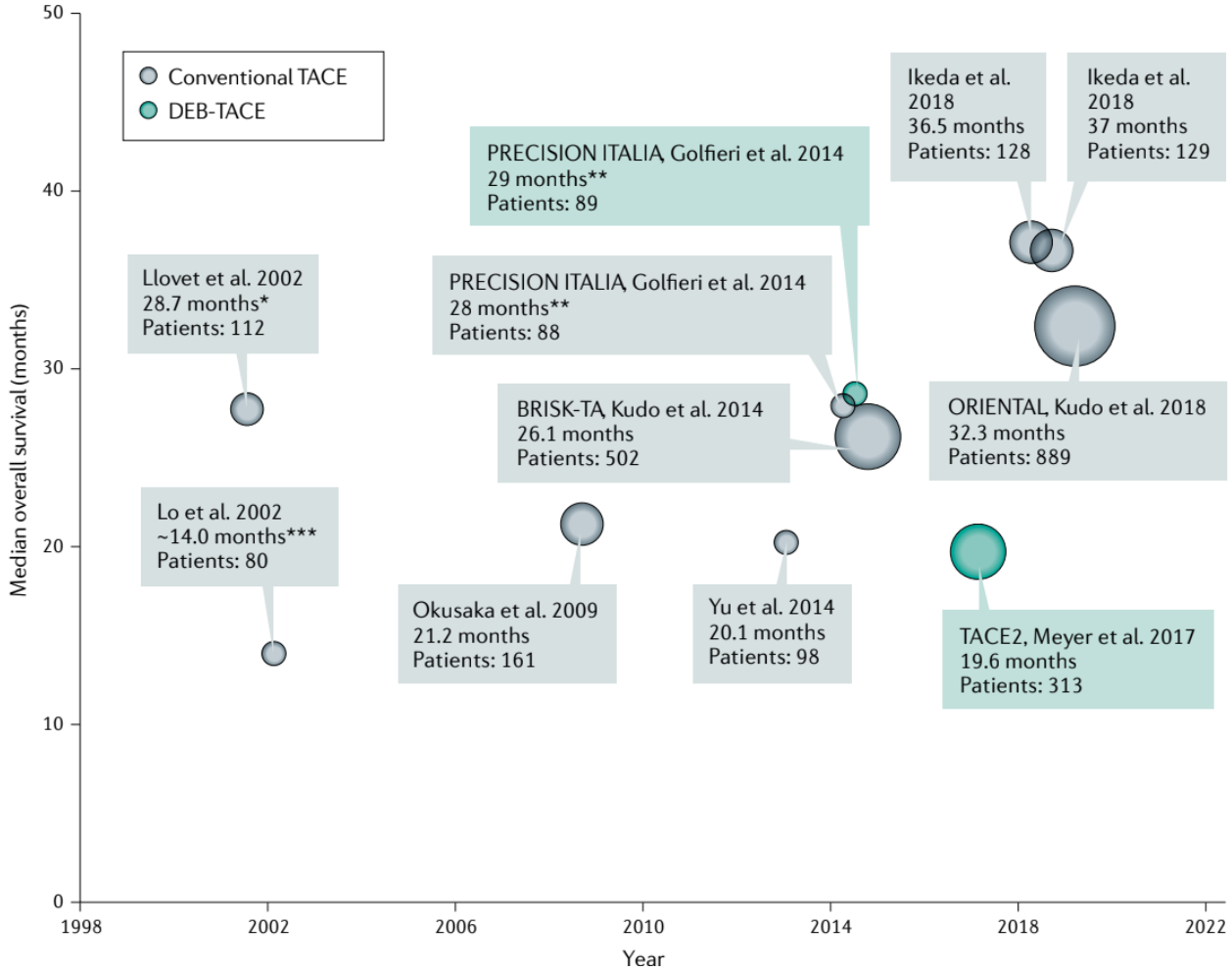
Raoul, Cancer Treat Rev 2019

Table 1
Summary of technical recommendations from experts on how to perform reproducible cTACE. Adapted from de Baere et al. [22].

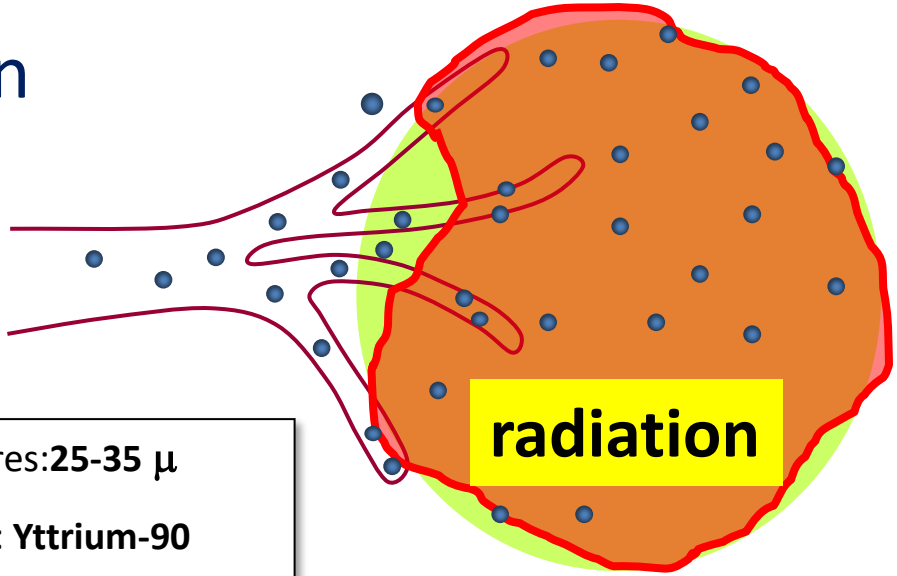
Item	Recommendations for reproducible cTACE
Patient selection	Pay particular attention to underlying liver disease and Performance Status (PS)
Pre-procedure imaging	Perform multiphasic computed tomography (CT) or dynamic contrast-enhanced-magnetic resonance imaging (MRI) of the liver before treatment allocation
Patient preparation	Discuss systematic antiemetic treatment, intravenous hydration, and pain killer use as well as antibiotic prophylaxis according to the risk of liver abscess
Per-procedure imaging	Use cone beam (CB)-CT for tumor visualization, targeting, and assessment of treatment completion
Chemotherapy	Use doxorubicin 50–75 mg/m^2 body surface area or cisplatin 50–100 mg/m^2
Lipiodol emulsion	Prepare water-in-oil emulsion (aqueous chemotherapy droplets in internal phase and Lipiodol in continuous external phase) to improve tumor deposit. The water-in-oil emulsion is obtained by mixing one volume of drug solution with two to three volumes of Lipiodol by pushing the drug syringe into the syringe containing Lipiodol
Embolizing agent	Gelatin sponge is commonly used. If used, the size of calibrated microspheres should be 100–300 μm in order to ensure distal occlusion with preservation of feeding segmental arteries
Selectivity	Superselective cTACE, using microcatheter when treating a single tumor or low number of tumors
Endpoint	Lipiodol opacification of the small arterioportal sinusoids should be used as a predictive factor for tumor response, tumor necrosis, and local recurrence
Response evaluation	Assess tumor viability using the mRECIST criteria
cTACE regimen	Perform at least two cTACE procedures 2–8 weeks apart before stopping due to a lack of response

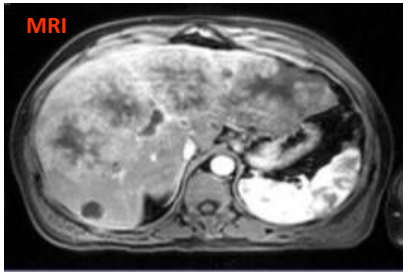
Raoul, Cancer Treat Rev 2019

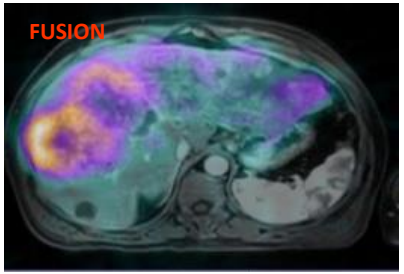
RCTs


Conventional TACE
DEB-TACE
Median overall survival (months)
Year
50
40
30
20
10
0
1998
2002
2006
2010
2014
2018
2022
Llovet et al. 2002
28.7 months*
Patients: 112
Lo et al. 2002
~14.0 months***
Patients: 80
PRECISION ITALIA, Golfieri et al. 2014
29 months**
Patients: 89
PRECISION ITALIA, Golfieri et al. 2014
28 months**
Patients: 88
BRISK-TA, Kudo et al. 2014
26.1 months
Patients: 502
Okusaka et al. 2009
21.2 months
Patients: 161
Yu et al. 2014
20.1 months
Patients: 98
Ikeda et al.
2018
36.5 months
Patients: 128
Ikeda et al.
2018
37 months
Patients: 129
ORIENTAL, Kudo et al. 2018
32.3 months
Patients: 889
TACE2, Meyer et al. 2017
19.6 months
Patients: 313

Y90 Radioembolization







Resin or glass spheres:**25-35 μ**

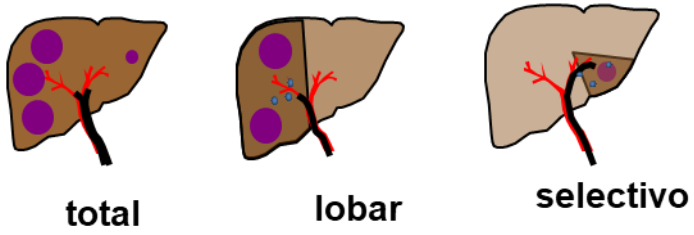
Source of radiation: **Yttrium-90**

Pure **beta** emitter

Mean **penetration: 2.5 mm**

Half-life: 64.2 h

- **95% of dose delivered by d 11**



Procedimiento

Paciente candidato a RE

- Evaluación multidisciplinar
- Diseño del tratamiento

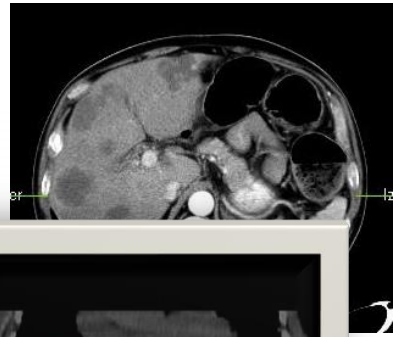


Image	Right lung	Left lung
Thorax ant	22788.00	16558.00
Thorax post	24984.00	16990.00

^{90}Y → ^{99m}Tc

Microesferas → MAA

Gammagrafía y SPECT/TAC MAA

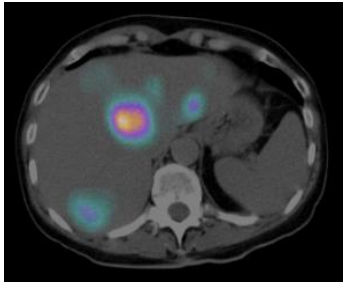
- Cálculo SHP
- Detección de comunicaciones extrahepáticas
- Distribución intrahepática MAA
- Cálculo T/N

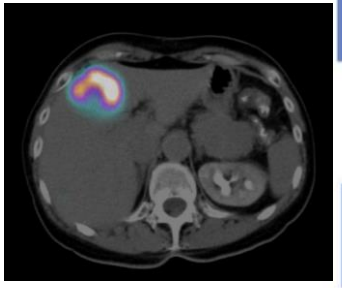
SHP > 20%, comunicación arterial no ocluible, mala correlación tumoral

Rodríguez-Fraile M Rev Esp Med Nucl 2015

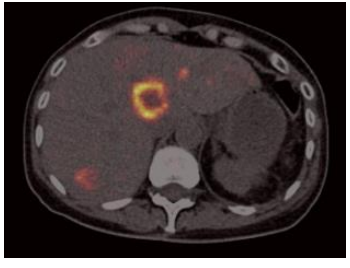
Procedimiento

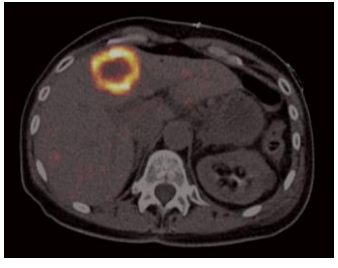
SPECT/CT ^{99m}Tc-MAA





PET/CT ^{90}Y-microesferas





Es posible administrar la RE

Cálculo de la actividad a administrar (dosimetría)

Administración de ^{90}Y-microesferas

A través de una arteriografía hepática

Evaluación de la distribución de ^{90}Y-microesferas

· SPECT/TAC de Bremsstrahlung
· ^{90}Y-microesferas PET/TAC

Evaluación de la respuesta a la RE

TAC, RM ó PET-FDG

Contraindicaciones

Contraindicaciones absolutas

- Shunt hepatopulmonar elevado(>20%)
- Imposibilidad para prevenir la embolización de microesferas en el TGI.
- Irradiación hepática externa previa.
- Deterioro de la función hepática Child-Pugh >B8

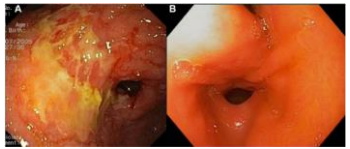
Contraindicaciones relativas:

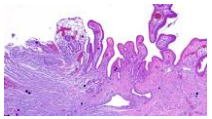
- Función pulmonar comprometida.

Complicaciones

Ulcera gastrointestinal

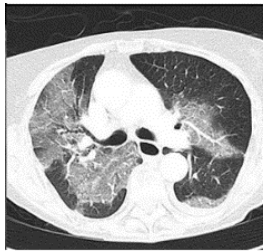
- Incidencia: 1.9-3.2%

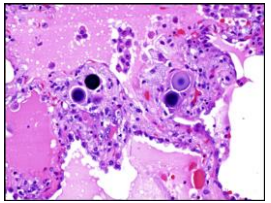




Pneumonitis por radiación

- Incidencia: <1%
- Potencialmente muy grave.





Enfermedad hepática inducida por radiación (REILD)*

- Incidencia: 5.3%

Otras potenciales complicaciones:

- Habitualmente leves y de escasa duración
- Dolor abdominal (13-39%), Fiebre (2-12%), Nauseas y vómitos (17-32%)

Sangro B, Hepatology 2017

RE en HCC

Radioembolization with Yttrium-90 Glass Microspheres in Hepatocellular Carcinoma: European Experience on Safety and Long-Term Survival

Philip Hilgard,[1] Monia Hamami,[2] Amr El Fouly,[1] André Scherag,[3] Stefan Müller,[2] Judith Ertle,[1] Till Heusner,[4] Vito R. Cicinnati,[1] Andreas Paul,[5] Andreas Bockisch,[2] Guido Gerken,[1] and Gerald Antoch[4]

Radioembolization for Hepatocellular Carcinoma Using Yttrium-90 Microspheres: A Comprehensive Report of Long-term Outcomes

RIAD SALEM,*,‡,§ ROBERT J. LEWANDOWSKI,* MARY F. MULCAHY,‡ AHSUN RIAZ,* ROBERT K. RYU,* SAAD IBRAHIM,* BASSEL ATASSI,* TALIA BAKER,§ VANESSA GATES,* FRANK H. MILLER,* KENT T. SATO,* ED WANG,§ RAMONA GUPTA,* AL B. BENSON,‡ STEVEN B. NEWMAN,‡ REED A. OMARY,* MICHAEL ABECASSIS,‡ and LAURA KULIK‖

Survival After Yttrium-90 Resin Microsphere Radioembolization of Hepatocellular Carcinoma Across Barcelona Clinic Liver Cancer Stages: A European Evaluation

Bruno Sangro,[1] Livio Carpanese,[2] Roberto Cianni,[3] Rita Golfieri,[4] Daniele Gasparini,[5] Samer Ezziddin,[6] Philipp M. Paprottka,[7] Francesco Fiore,[8] Mark Van Buskirk,[9] Jose Ignacio Bilbao,[10] Giuseppe Maria Ettorre,[11] Rita Salvatori,[12] Emanuela Giampalma,[4] Onelio Geatti,[13] Kai Wilhelm,[14] Ralf Thorsten Hoffmann,[7] Francesco Izzo,[15] Mercedes Iñarrairaegui,[1] Carlo Ludovico Maini,[16] Carlo Urigo,[3] Alberta Cappelli,[17] Alessandro Vit,[5] Hojjat Ahmadzadehfar,[6] Tobias Franz Jakobs,[7] and Secondo Lastoria,[18] on behalf of the European Network on Radioembolization with Yttrium-90 Resin Microspheres (ENRY)

HEPATOBILIARY MALIGNANCIES

Yttrium-90 Radioembolization for Intermediate-Advanced Hepatocellular Carcinoma: A Phase 2 Study

Vincenzo Mazzaferro,[1] Carlo Sposito,[1] Sherrie Bhoori,[1] Raffaele Romito,[1] Carlo Chiesa,[2] Carlo Morosi,[3] Marco Maccauro,[2] Alfonso Marchianò,[3] Marco Bongini,[1] Rodolfo Lanocita,[3] Enrico Civelli,[3] Emilio Bombardieri,[2] Tiziana Camerini,[4] and Carlo Spreafico[3]

January 2010 Volume 138 • Number 1
Gastroenterology
www.gastrojournal.org

HEPATOLOGY
Official Journal of the American Association for the Study of Liver Diseases
AASLD

Hilgard P. Hepatology 2010
Salem R. Gastroenterology 2010
Sangro B. Hepatology 2011
Mazzaferro V. Hepatology 2013

RE en HCC. Series retrospectivas

Table 1. Summary of Large Series Reporting On Long-Term Outcome After ^{90}Y Radioembolization

		Intermediate Stage		Branch PVT		Main PVT		Branch or Main PVT	
Reference	Child-Pugh	N	OS* (95% CI)	N	OS (95% CI)	N	OS (95% CI)	N	OS (95% CI)
Hilgard et al.[27] (N = 108)	A/B	51	16.4 (12.1-NC)					33	10 (6-NC)
Salem et al.[3] (N = 291)	A	48	17.3 (13.7-32.5)	19	16.6 (8.8-24)	16	7.7 (3.3-13.2)	35	10.4 (7.2-16.6)
	B	35	13.5 (6.4-25.4)	27	6.5 (5-8.5)	30	4.5 (2.9-6.6)	57	5.6 (4.5-6.7)
Sangro et al.[7] (N = 325)†	A	82	18.4 (13.6-23.2)	44	10.7 (8.3-17.1)	32	9.7 (4.8-11.8)	76	10.2 (7.7-11.8)
	B	5	3.6 (2.4-10.8)						
Mazzaferro et al.[33] (N = 51)	A	15	18 (13-38)	23	17 (13-21)	5	9 (4-NC)		
	B	2	–	6	8 (5-10)	1	5		

95% CI, 95% confidence interval; NC, not calculable.

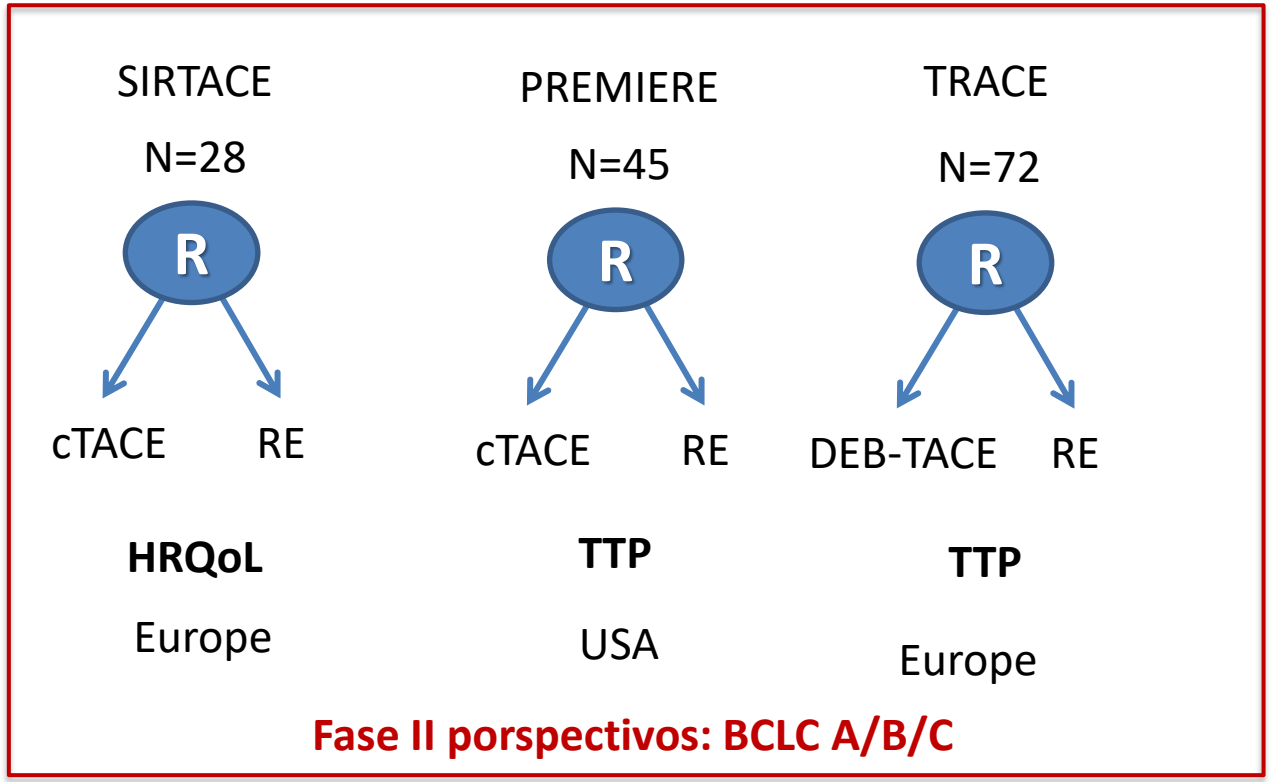
*Months.

†Unpublished data for branch and main PVT cohorts provided by authors.

Hilgard P. Hepatology 2010
Salem R. Gastroenterology 2010
Sangro B. Hepatology 2011
Mazzaferro V. Hepatology 2013

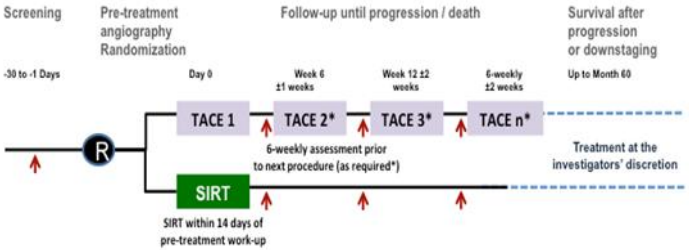
Salem R. Hepatology 2013

RE en HCC. Ensayos clínicos randomizados



RE en HCC. Ensayos clínicos randomizados

SIRTACE 28 pacientes



Basal characteristic	cTACE N=13	Y90 N=15
Age	66	65
Child A (%)	86	92
BCLC A/**B**/C (%)	27/**53**/20	38/**38**/23
Bilobar (%)	33	29
Multifocal (%)	48	46
ECOG PS = 1 (%)	20	23
AFP ng/dL mean	2624	636

Objetivo primario QoL

No se hallaron diferencias en:

Calidad de vida

Severidad de efectos adversos

Kolligs, Liver Int 2015

RE en HCC. Ensayos clínicos randomizados

PREMIERE n=45 TRACE n= 72

Basal characteristic	cTACE N=21	Y90 N=24	DEB-TACE N=33	Y90 N=38
Age	64	62	68	67
Alcohol (%)	5	17	70	71
Child A (%)	76	42	85	95
ALBI 1/2/3 (%)	5/81/14	0/71/29		
Prior therapy (%)	nr	13	18	10
BCLC A/B (%)	81/19	75/25	12/88	18/82
Bilobar (%)	33	29	50	53
Multifocal (%)	48	46	79	88
AFP > 200 ng/mL (%) AFP> 400 ng/mL (%)*	12	12	15*	10*

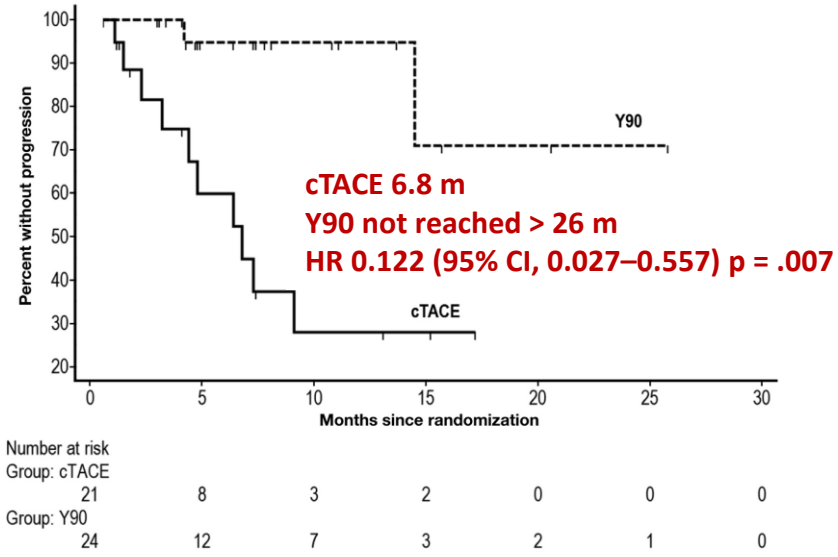
Salem R. Gastroenterology 2016

Dhondt. Radiology 2022

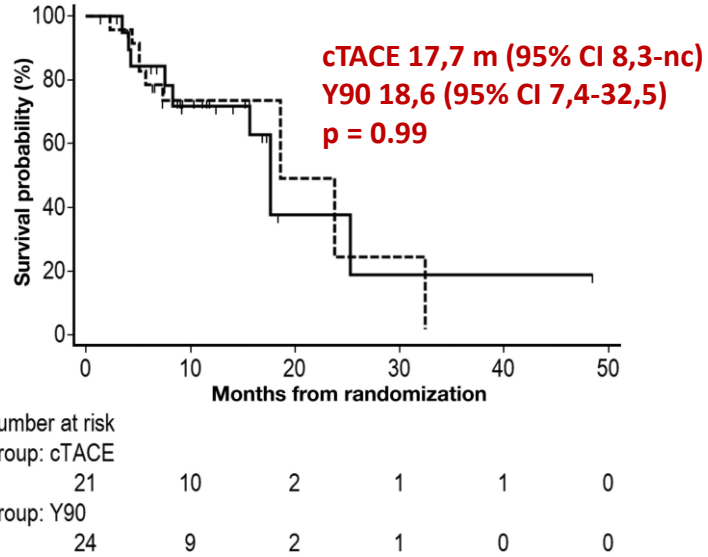
RE en HCC. Ensayos clínicos randomizados

PREMIERE

Tiempo a progresión



Supervivencia

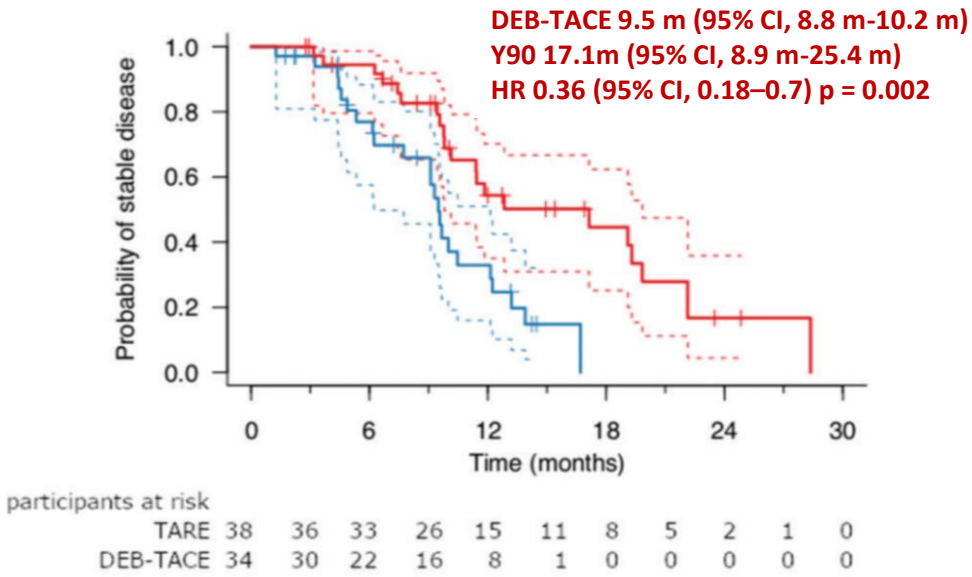


Salem, et al. Gastroenterology 2016

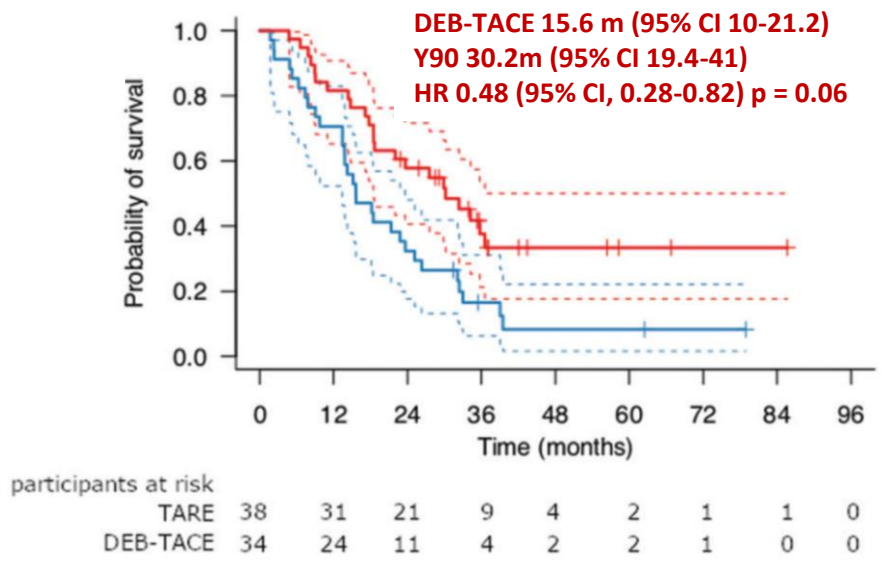
RE en HCC. Ensayos clínicos randomizados

TRACE

Tiempo a progresión



Supervivencia



Dhondt. Radiology 2022

RE en HCC. Novedades

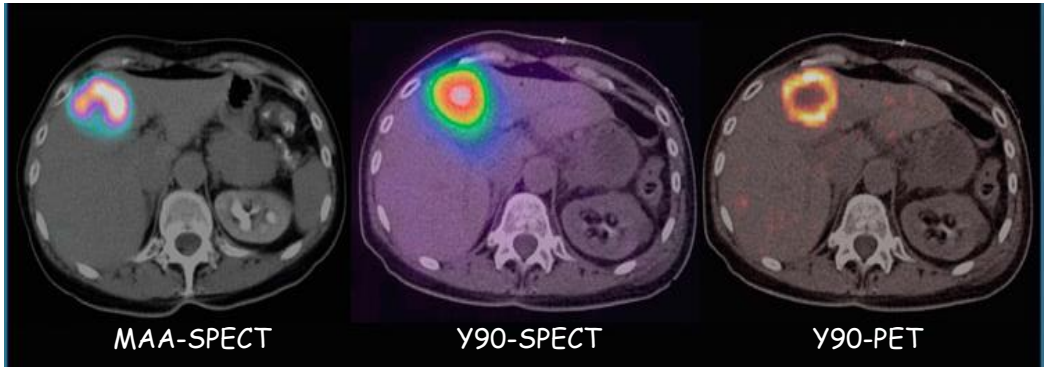
Puede usarse en tumores precoces con intención curativa:
Segmentectomía rádica

Tumores intermedios/avanzados, infraestadificar para tratamientos radicales: estrategia downstaging.

Dosimetría personalizada

RE en HCC.

Segmentectomía rádica



- 84 patients with BCLC A (32%), B (30%) or C (37) tumors, 50% of which were in Child B class
- EASL response: 81%.
- Median dose to the tumor supposing a nonuniform distribution: 1279 Gy (resp) vs. 1118 Gy (non-resp), (p = 0.51).

Riaz A, et al. IJROBP 2011.

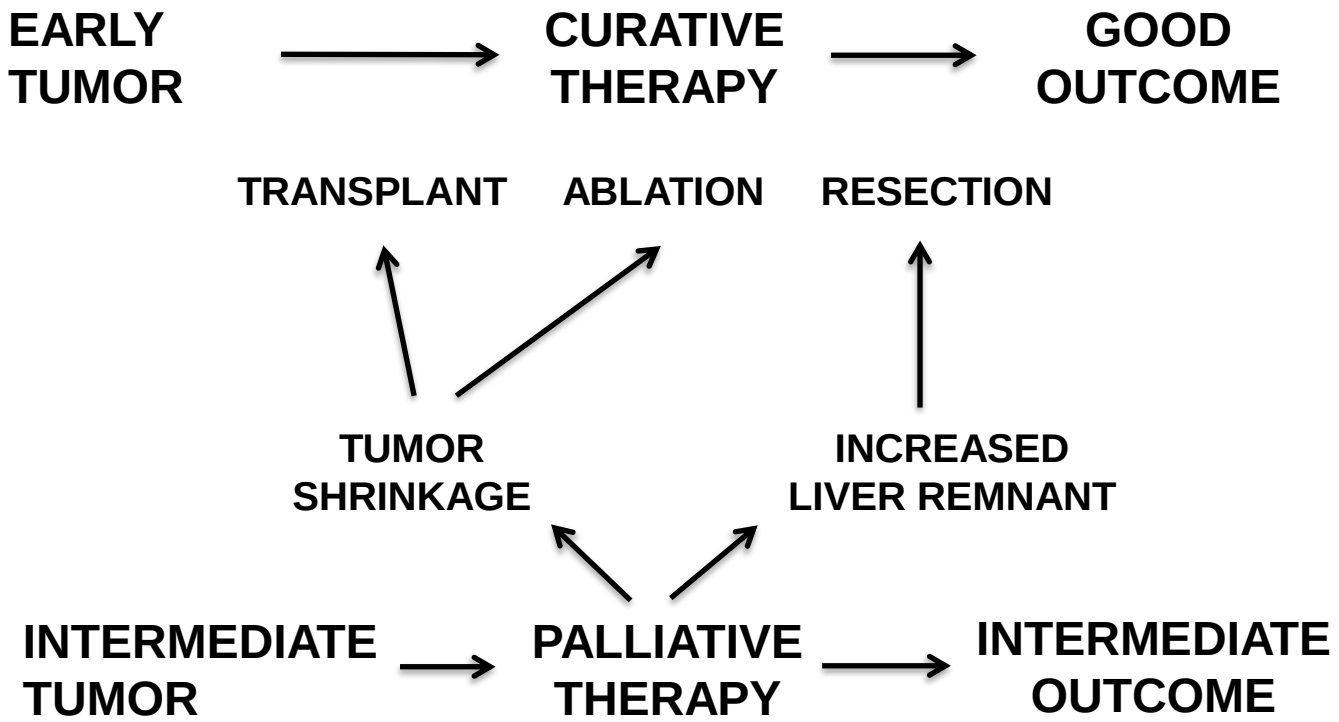
35 patients submitted to LT after ^{90}Y-RE

Pre-treatment size		1–2.9 cm	3–5 cm	> 5 cm
No. of nodules		9	17	12
Necrosis	100%	89%	65%	33%
	> 50%	11%	12%	50%
	< 50%	0%	23%	17%

Riaz A, et al. Hepatology. 2009.

RE en HCC.

Downstaging



Cedida por Sangro B. Personal communication.

RE en HCC.

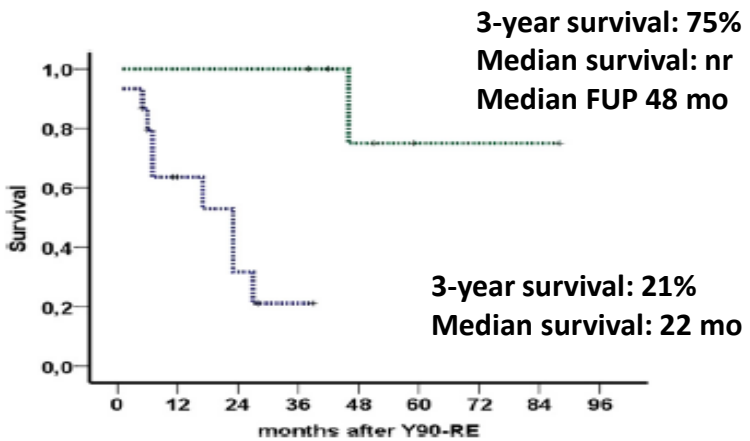
Downstaging

21 UNOS T3 HCC patients treated by RE

RADICAL therapy (6 patients: 28%)

No radical therapy (15 patients: 72%)

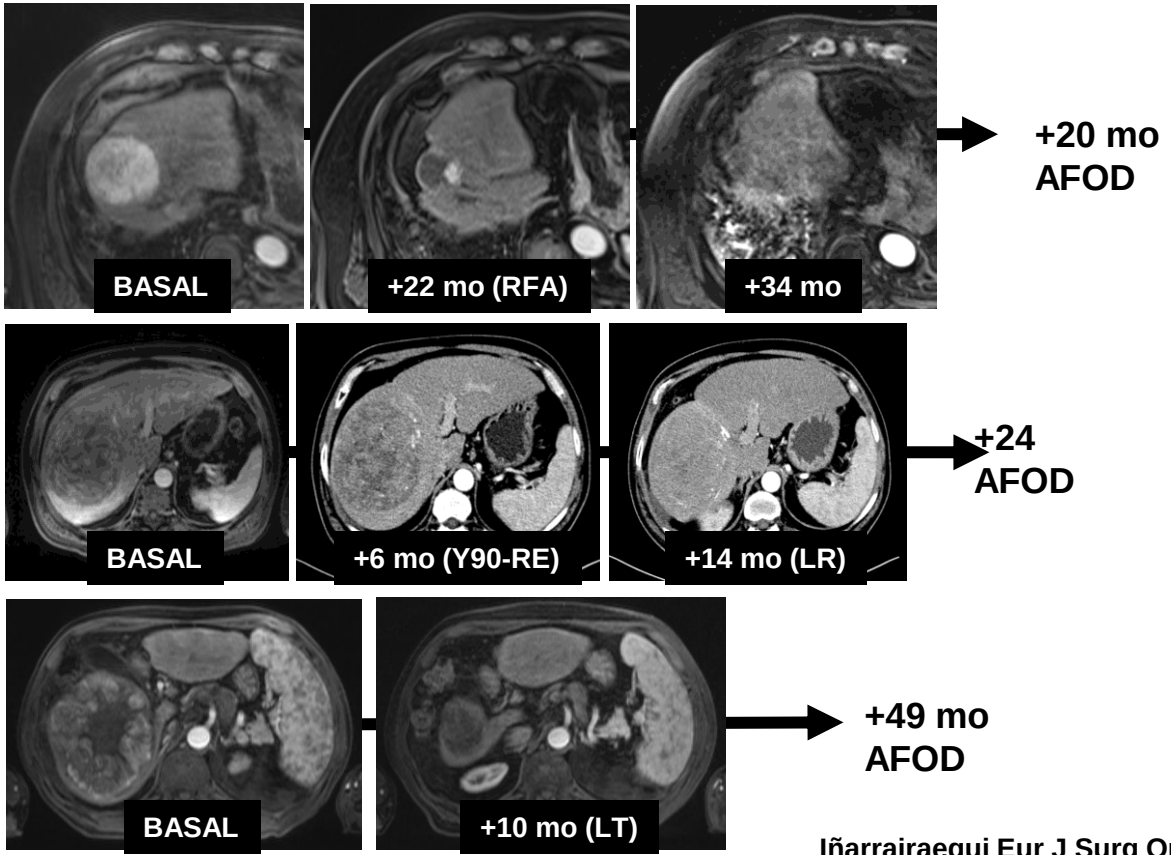
Pt	Cirrhosis	T Bili (mg/dL)	# nodules	**Size (cm)**
1	Yes	0.94	1	**8.4**
2	Yes	1.20	1	**14.2**
3	Yes	1.28	2	**5.5**
4	No	0.88	1	**11.5**
5	Yes	1.03	1	**13.0**
6	No	0.94	1	**11.0**



Iñarrairaegui M. Eur J Surg Oncol 2012.

RE en HCC.

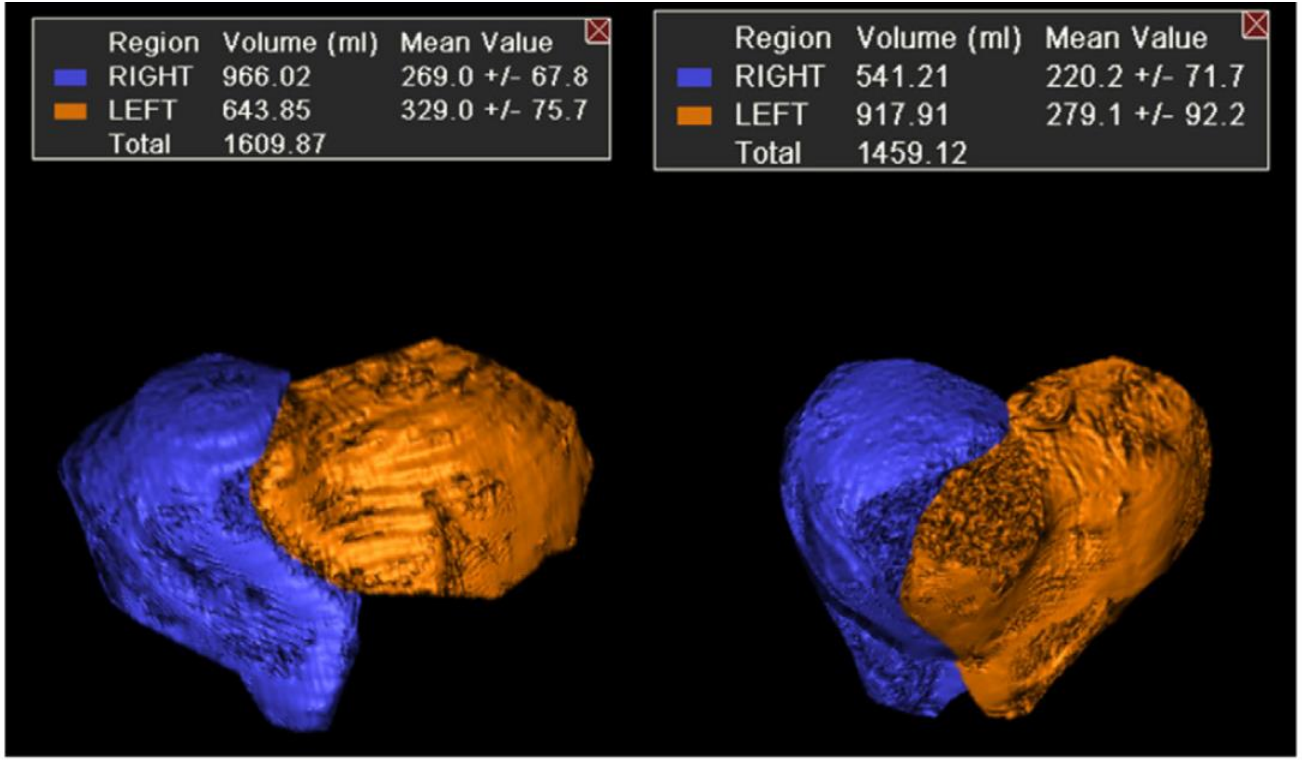
Downstaging



Iñarrairaegui Eur J Surg Oncol 2012

RE en HCC.

Proceso atrofia-hipertrofia tras RE

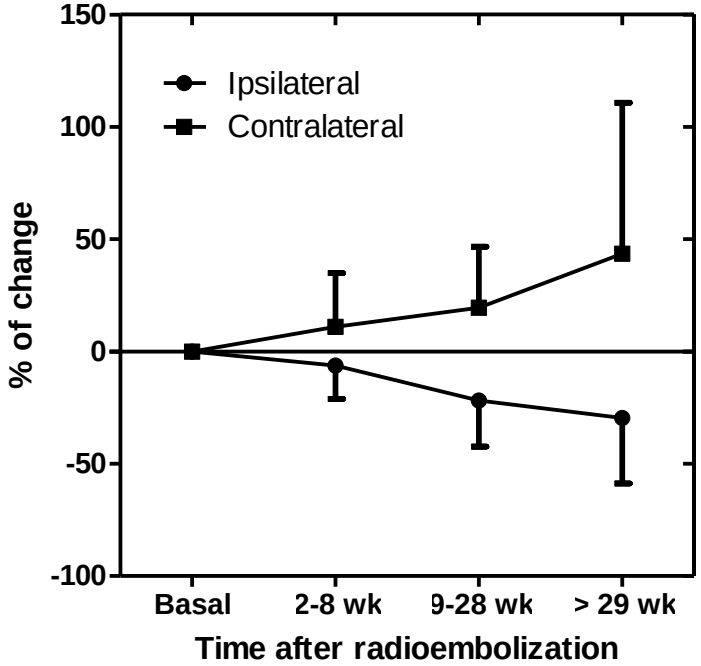


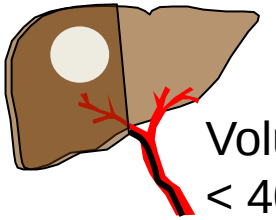
Vouche J Hepatol 2013

RE en HCC.

Proceso atrofia-hipertrofia tras RE

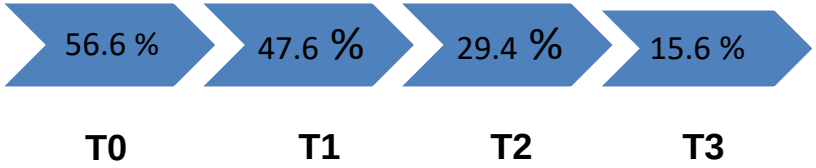
Changes in lobe volume in 82 patients after lobar or sublobar 90Y-RE





Volumen no tratado/volumen total < 40 %

Proporción de pacientes

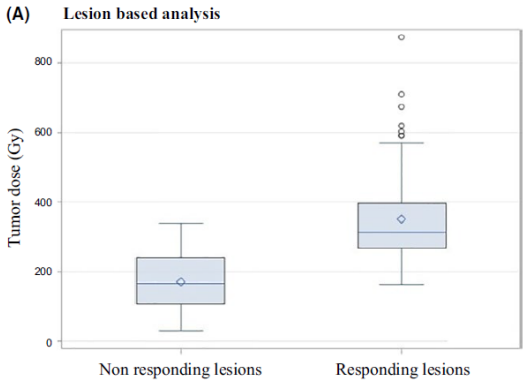


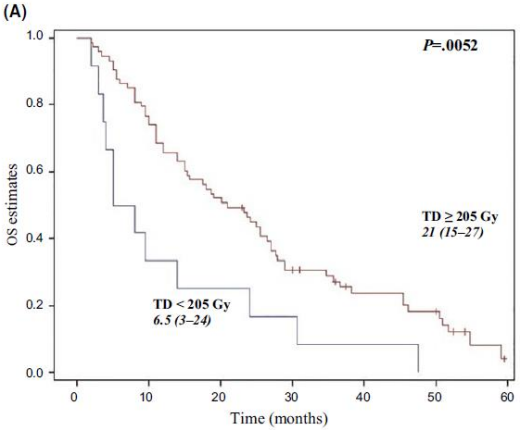
Fernández-Ros HBP 2013

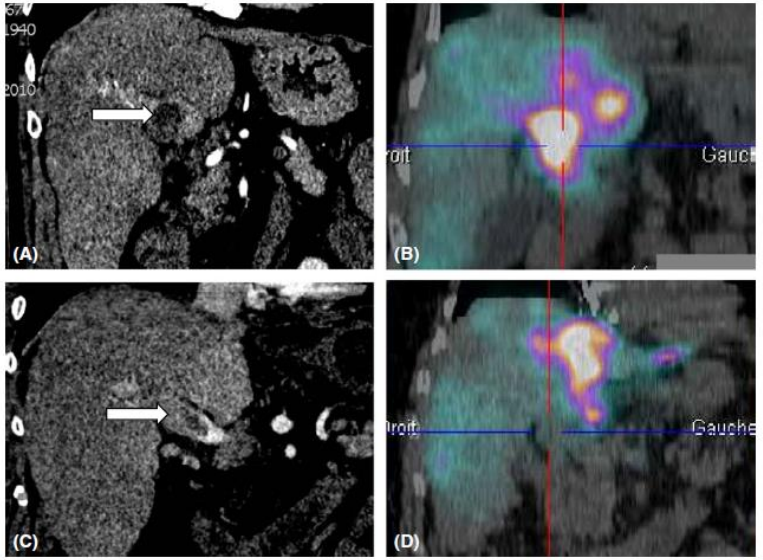
RE en HCC. Novedades

RE personalizada: Dosimetría

Respuesta tumoral y supervivencia







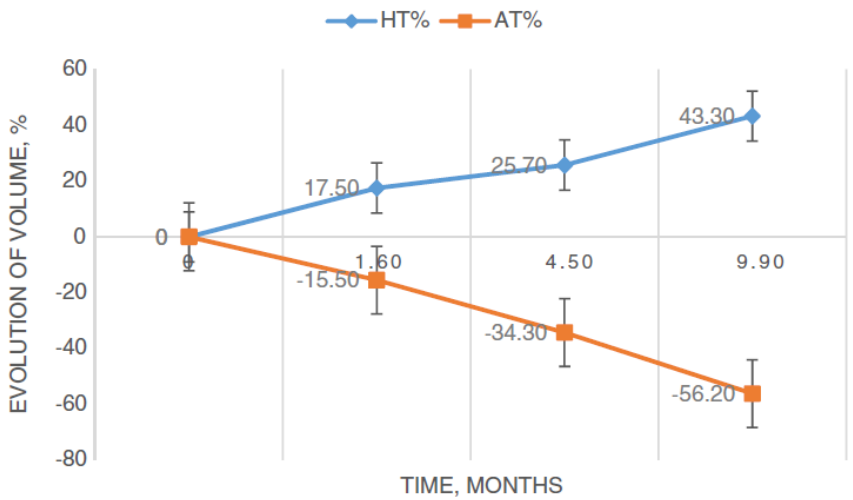
Garin Liver Int 2017

RE en HCC. Novedades

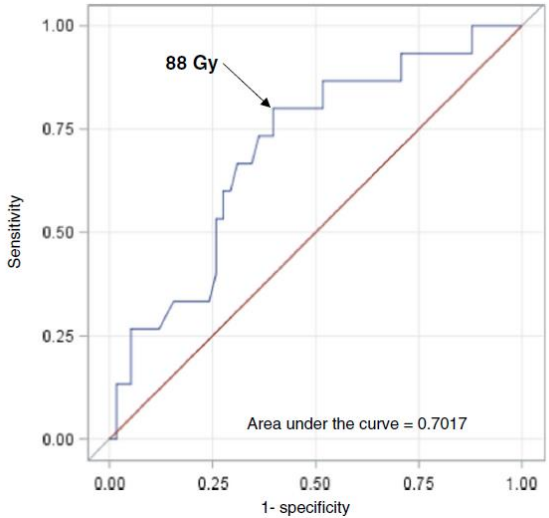
RE personalizada: Dosimetría

Hipertrofia contralateral

73 pac; RE lobar



	HILD > 88 Gy	HILD < 88 Gy
MHT >10%	92,2%	65,7%



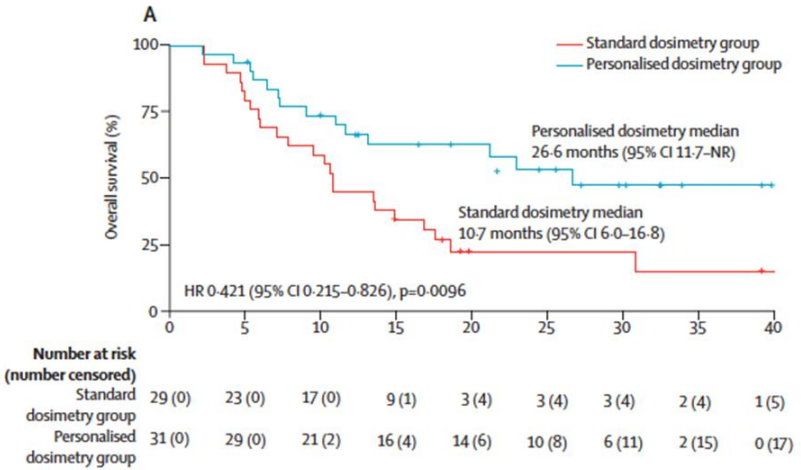
MHT: máxima hipertrofia
HILD: dosis a hígado sano

Palard EJNMMI 2018

RE en HCC. Novedades

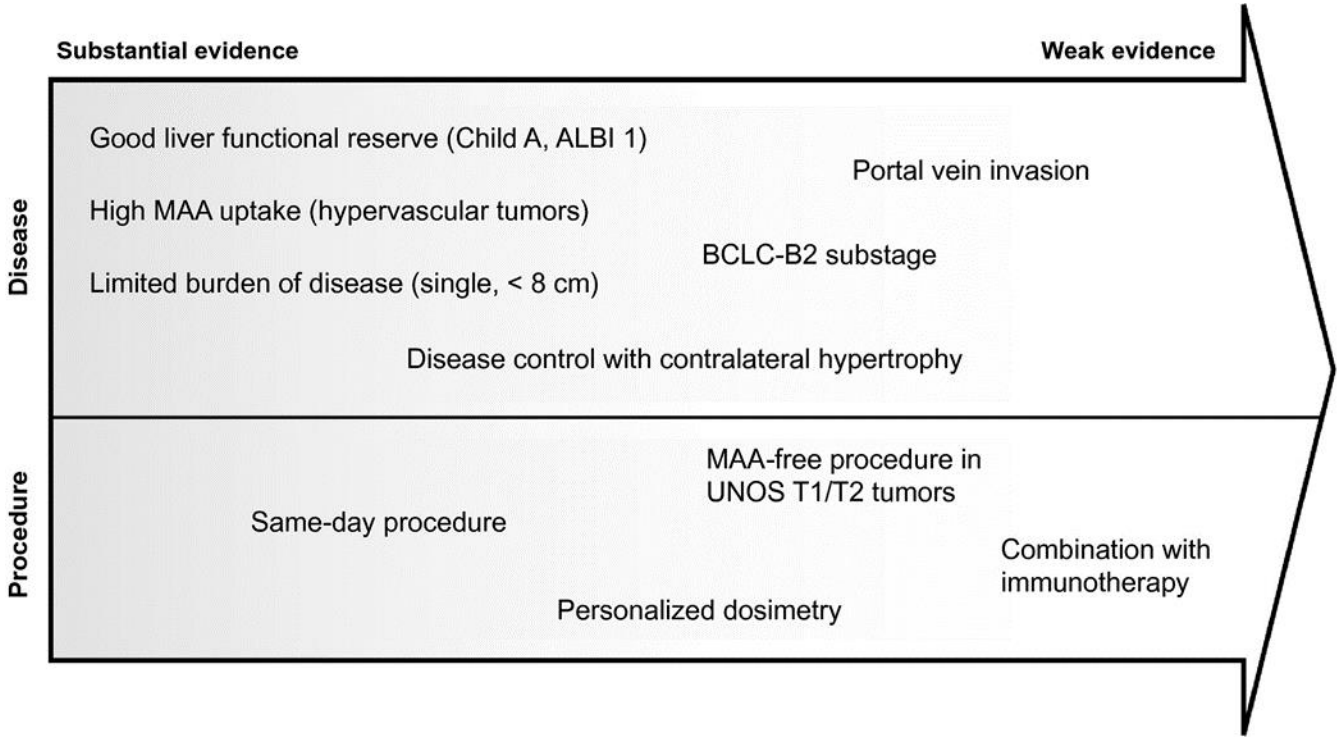
RE personalizada: Dosimetría

	Investigator evaluation		
	Personalised dosimetry group (n=28)	Standard dosimetry group (n=28)	p value
Objective response	20 (71%)	10 (36%)	--
Complete response	6 (21%)	3 (11%)	--
Partial response	14 (50%)	7 (25%)	--
No response	8 (29%)		
Stable disease	4 (14%)		
Progressive disease	1 (4%)		
Other	3 (11%)*		
Objective response rate (95% CI)	71% (51–8		



Garin E. Lancet Gastroenterol Hepatol 2021

Supporting Evidence for Y90 in HCC



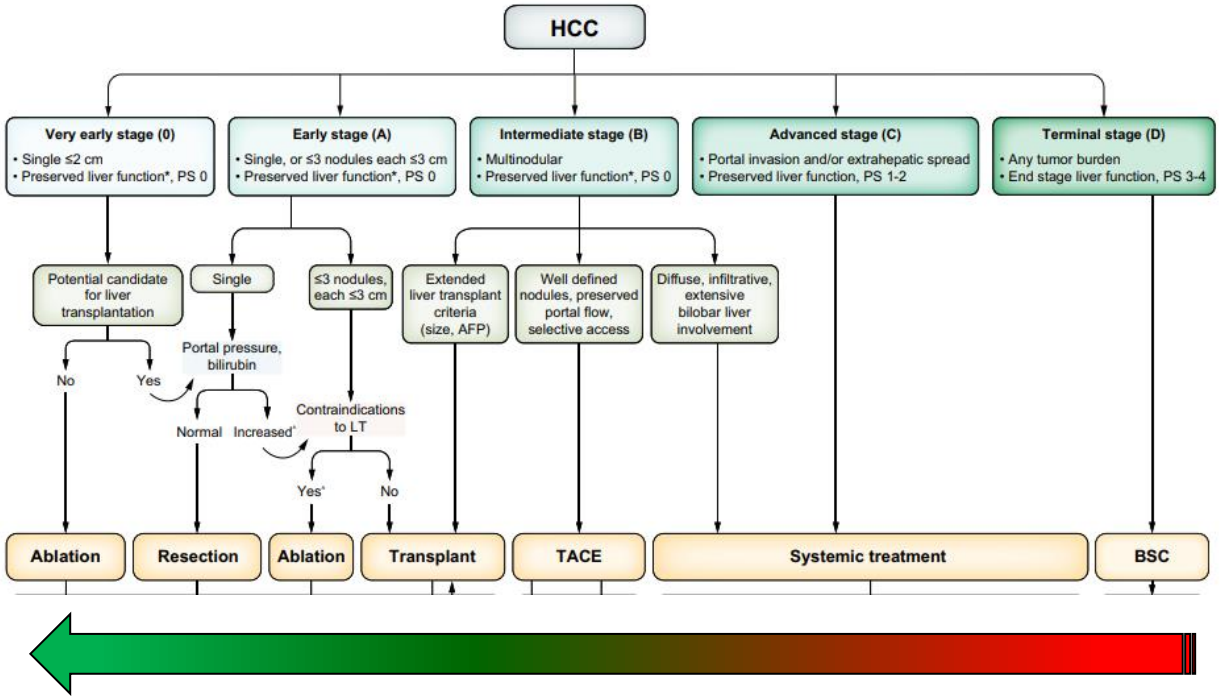
Iñarrairaegui M, Hepatology 2021

Cardiovasc Intervent Radiol (2022) 45:1599–1607
https://doi.org/10.1007/s00270-022-03072-8

REVIEW

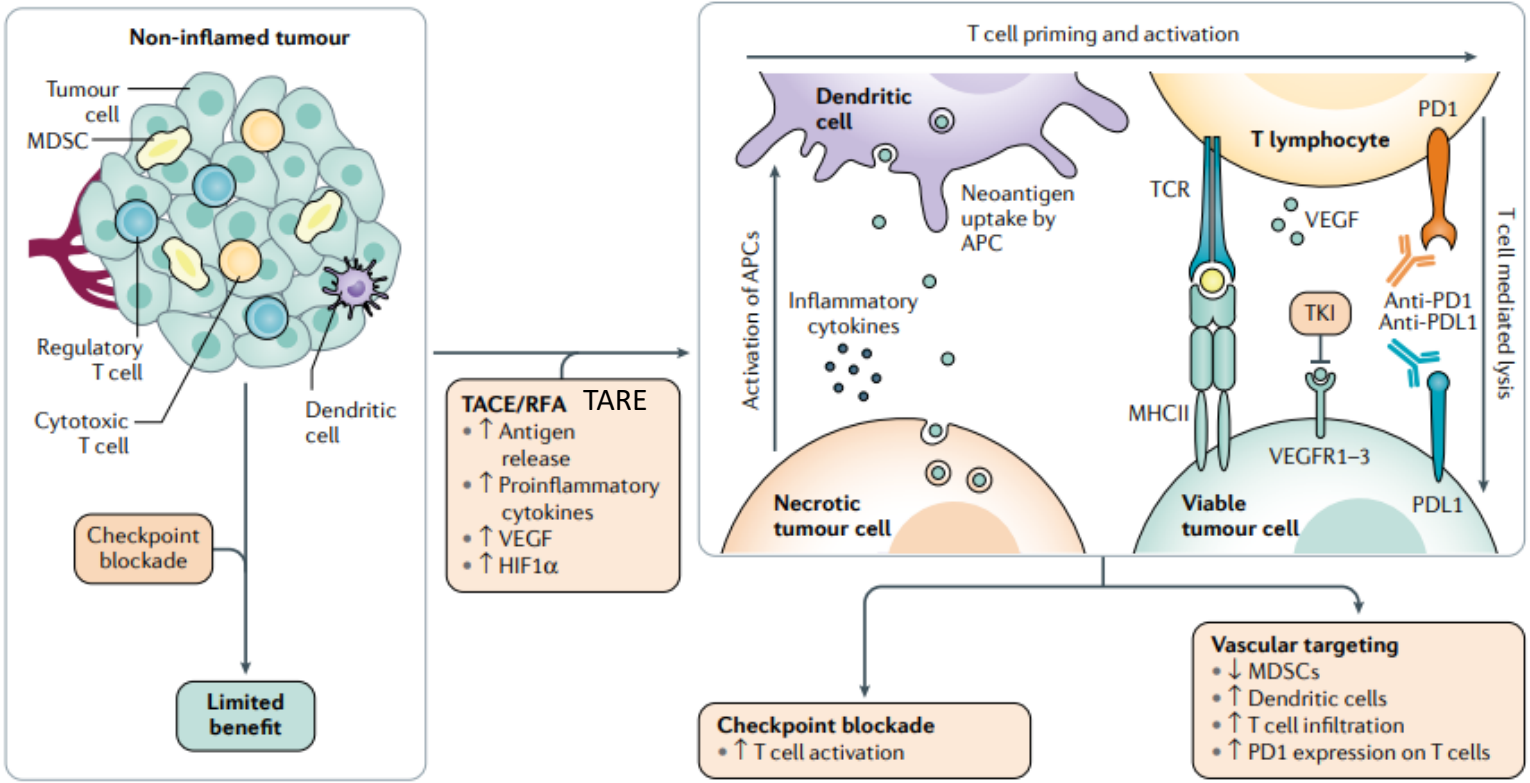
TARE in Hepatocellular Carcinoma: From the Right to the Left of BCLC

Boris Guiu[1] · **Etienne Garin**[2] · **Carole Allima**
Riad Salem[4]



Guiu, CVIR 2022

Tratamientos combinados



Llovet, Nature Reviews 2021

Tratamientos combinados. TACE + TKI

Table 1. Clinical trials of TACE combined with molecular targeted agents

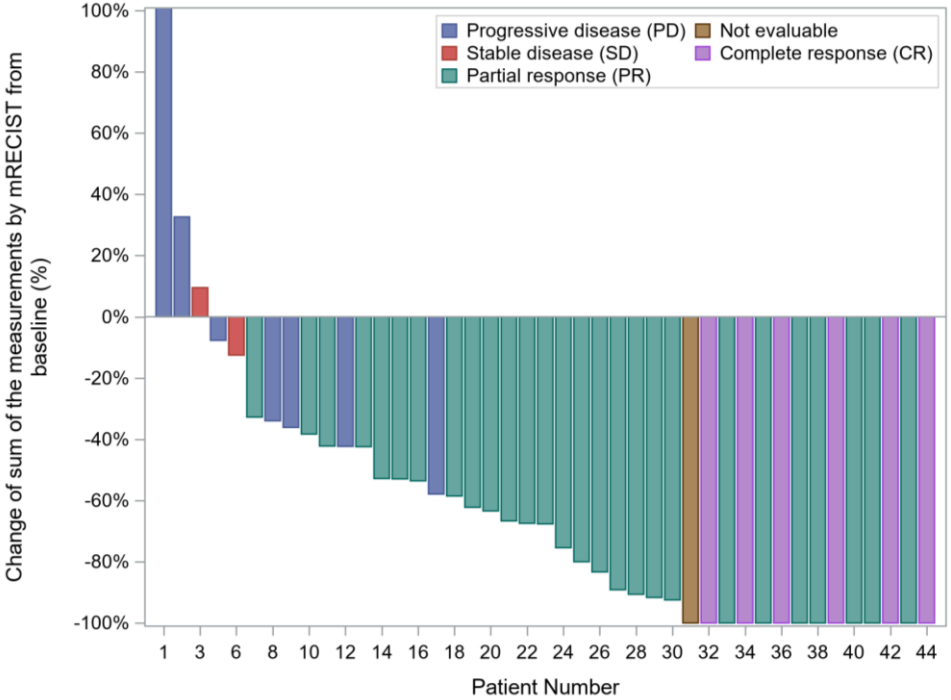
	Post-TACE (n = 458)		BRISK-TA (n = 502)		SPACE (n = 307)		ORIENTAL (n = 888)		TACE-2 (n = 313)		TACTICS (n=156)
	sorafenib (n = 229)	placebo (n = 227)	brivanib (n = 249)	placebo (n = 253)	sorafenib (n = 154)	placebo (n = 153)	orantinib (n = 444)	placebo (n = 444)	sorafenib (n = 157)	placebo (n = 156)	Sorafenib+TACE N=80 / TACE N=76
Phase	III		III (immature/ terminated)		II		III (terminated due to interim analysis)		III (terminated due to interim analysis)		II
mOS, months	29.7	NR	26.4	26.1	NR	NR	31.1	32.3	21.1	19.7	36,2 / 30,8
HR (95% CI)	1.06 (0.69 – 1.64)		0.90 (0.66 – 1.23)		0.898 (0.606 – 1.330)		1.090 (0.878 – 1.352)		0.91 (0.67 – 1.24)		0,861 (0,607-1,223)
p value	0.79		0.528		0.295		0.435		0.57		0,4
mTTP, months	5.4	3.7	8.4	4.9	5.6	5.5	ND	ND	7.9[a]	7.8[a]	25,2 * 13,5
HR (95% CI)	0.87 (0.70 – 1.09)		0.61 (0.48 – 0.77)		0.797 (0.588 – 1.080)		ND		0.99 (0.77 – 1.27)		0,59 (0,41-0,87)
p value	0.252		<0.0001		0.072		ND		0.94		0,006
Primary endpoint	TTP		OS		TTP		OS		PFS		OS; mPFS
Definition of progression	RECICLE		mRECIST		mRECIST		TACE discontinuation criteria		RECIST 1.1		RECICL
Median DOT of study drug	17 weeks		24.0 weeks		21.0 weeks		43.6 weeks		17.1 weeks		64

* modification of PFS: time to unTACEtable progression

No hay diferencias significativas en respuesta, supervivencia, ni seguridad de TACE combinado con antiangiogenicos

Kudo, Eur J Cancer 2017
Kudo, Hepatology 2014
Lencioni, J Hepatol 2016
Kudo, Lancet Gastroenterol Hepatol 2018
Meyer, Lancet Gastroenterol Hepatol 2017
Kudo Liver Cancer 2022

DEB-TACE + Immunotherapy (IMMUTACE)



ORR according to mRECIST

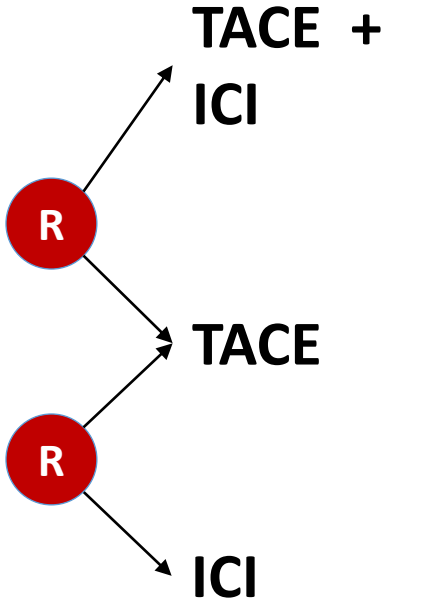
Variable	Analysis (n=49)
ORR, % (95% CI)	71.4 (56.8, 83.4)
Best OR, n (%)	
CR	8 (16.3)
PR	27 (55.1)
SD	2 (4.1)
PD	7 (14.3)
Not evaluable	5 (10.2)

% change not available in 5 patients

Vogel A, *et al*. ESMO 2021; abstract LBA37. Courtesy of Prof A. Vogel.

Tratamientos combinados. TACE + immunotherapy

Ensayos Fase 3 ongoing Estadio intermedio



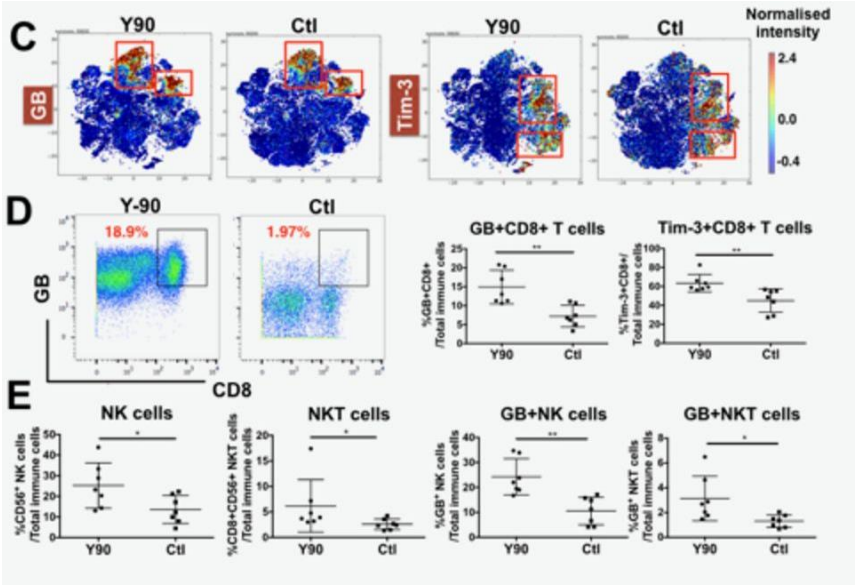
Durvalumab + Bevacizumab or Durvalumab	EMERALD-1
STRIDE + Lenvatinib or STRIDE	EMERALD-3
Pembrolizumab + Lenvatinib	LEAP-012
Nivolumab	TACE-3
Atezolizumab + Bevacizumab	ML42612

Atezolizumab + Bevacizumab	ABC-HCC
Nivolumab + Regorafenib	RENOTACE

TARE +IMUNOTHERAPY. Activación SI tras RE

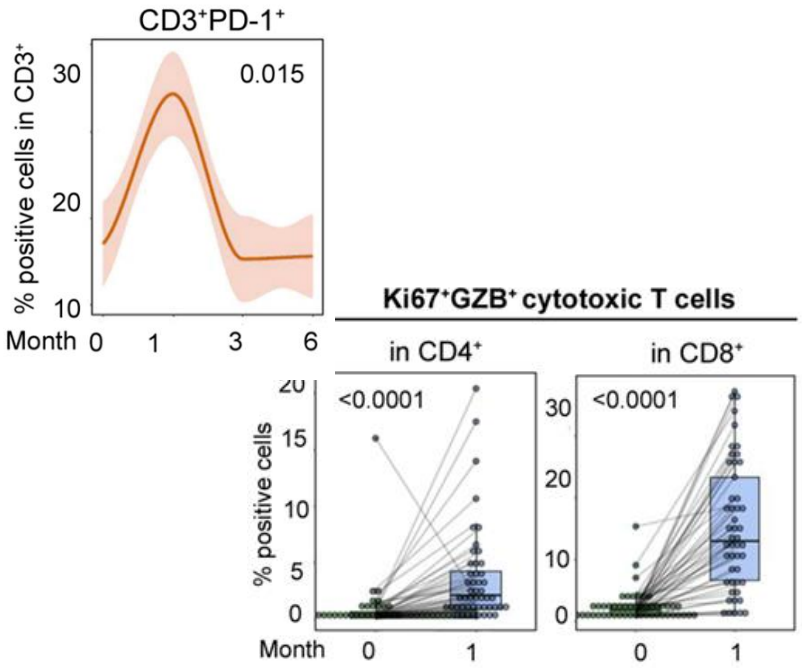
Tumor tissue and blood samples 41 patients

- TILs from 14 resected patients
- PBMCs from 31 patients (4 also resected)



Chew V, Gut 2018

49 patients receiving SIRT as 1L



Rivoltini L. Gut 2022

Tratamientos combinados. TARE + immunotherapy

Ensayos Fase 2 ongoing

Trial	Active Arm	Comparator	Primary EP	ID number
CA209-678	SIRT+ Nivolumab		ORR	NCT03033446
NASIR-HCC	SIRT + Nivolumab	--	Safety	NCT03383458
IMMUWIN	SIRT + STRIDE	TACE + STRIDE	ORR	NCT03847428
ROWAN	SIRT + STRIDE	SIRT	ORR DoR	NCT04102098
ZUGSPITZE	Personalized SIRT + STRIDE STRIDE + On-demand SIRT	SIRT	RFS	NCT03859128

TARE+ Immunotherapy

Patient characteristics	NASIR (%)	CA209-678 (%)
Number of patients	42	36
Age in years, median (range)	65	64
Males, (%)	85.7	78
Prior therapies, (%) Local (Resection, RFA, TACE) Systemic	 52% 12%	 39% 11%
BCLC, (%) A B C	7% 59 % 33 %	3% 30% 66,7%
Vascular invasión Extrahepatic spread	26% 0	44% 36%
AFP > 400 ng/mL (%)	29%	50%

De la Torre et al. JITC 2022
Tai D. Lancet Gastroenterol Hepatol 2021

TARE+ Immunotherapy.Safety

Safety	Patients with adverse events, No (%)*			
	NASIR N= 42		CA209-678 N =36	
	Any grade	Grade 3-4	Any grade	Grade 3-4
All causality AEs	98%	19%		
Treatment-related AEs	79%	19%	81%	17%
Related to SIRT	50 %	5 %	50%	8%
Related to Nivolumab (irAEs)	64 %	14 %	69%	9%
All causality SAEs	50 %	26%		
Treatment-related SAEs		12%		14%
Related to SIRT		2 %		9%
Related to Nivolumab (irAEs)		9%		6%
Reasons for Nivolumab discontinuation (%)				
Tumor progression		40.5%		64%
Toxicity		12%		10%

De la Torre et al. JITC 2022
Tai D. Lancet Gastroenterol Hepatol 2021

TARE+ Immunotherapy. Efficacy

Best overall response RECIST 1.1	NASIR N=42	CA209-678 N=36
Complete response	**12%**	**3%**
Partial response	**26%**	**28%**
Stable disease	43%	31%
Progressive disease	6 (14.3%)	31%
Not evaluable	4.8%	8%
Objective Response Rate (95%CI)	**41.5% (26.3-57.9)**	**30.6% (16.4-48.1)**
Disease Control Rate (95%CI)	**92.7% (80.1-98.5)**	**61.1% (43.5 -76.9)**
Resection or trasplantation, n (%)	9%	6%
Median OS, (95% CI)	20.9 months (17.7-24.1)	16.9 months (8.1–27.6) 20.2 months (11.4–32.1)
2 year survival rate	41%	38%

De la Torre et al. JITC 2022
Tai D. Lancet Gastroenterol Hepatol 2021

El estadio intermedio constituye un grupo heterogéneo de pacientes.

Las terapias intraarteriales son, **por el momento**, el tratamiento de elección para los pacientes con hepatocarcinoma en estadio intermedio. (TACE evidencia de primer nivel y RE en evidencia de segundo nivel).

El papel de la RE está migrando hacia estadios mas precoces.
La dosimetría personalizada permite mejorar la respuesta al tratamiento.

No hay diferencias en seguridad y eficacia entre cTACE y DEB-TACE
La combinación de TACE con TKI no ha demostrado beneficio clínico.

La combinación de TRL con inmunoterapia tiene un buen perfil de seguridad y resultados prometedores en ensayos en fase II.

Se ha abierto un gran campo de investigación y nos esperan grandes novedades.