PRACTICAL RADIOEMBOLIZATION

Y90 for HCC: Year in Review

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Disclosures

Consultant/Advisory Board

- Boston Scientific
- Cook
- Bard
- Genentech
- Astrazeneca
- Eisai
- Exelixis
- Sirtex

Grant/Research Support

- Boston Scientific

Themes

- Transplantation
- IO combination
- Portal Vein Thrombosis
- Eliminating MAA
- Resection
- FDA Approval-PMA
- Threshold dose RAD-SEG >400 Gy
- Network Graph
- Costs
- Up-to-7
- COVID

VALIDATION

Safety and Efficacy of Locoregional Treatment during Immunotherapy with Nivolumab for Hepatocellular Carcinoma: A Retrospective Study of 41 Interventions in 29 Patients

Brett Marinelli, MD, MSCR, Mario Cedillo, MD, Sara D. Pasik, BA, Dudley Charles, BA, Shashi Murthy, MD, Rahul S. Patel, MD, FSIR, Aaron Fischman, MD, FSIR, Monda Ranade, MD, Vivian Bishay, MD, Scott Nowakowski, MD, Max Sung, MD, Thomas Marron, MD, PhD, Robert Lookstein, MD, MHCDL, FAHA, FSVM, FSIR, Myron Schwartz, MD, and Edward Kim, MD, FSIR

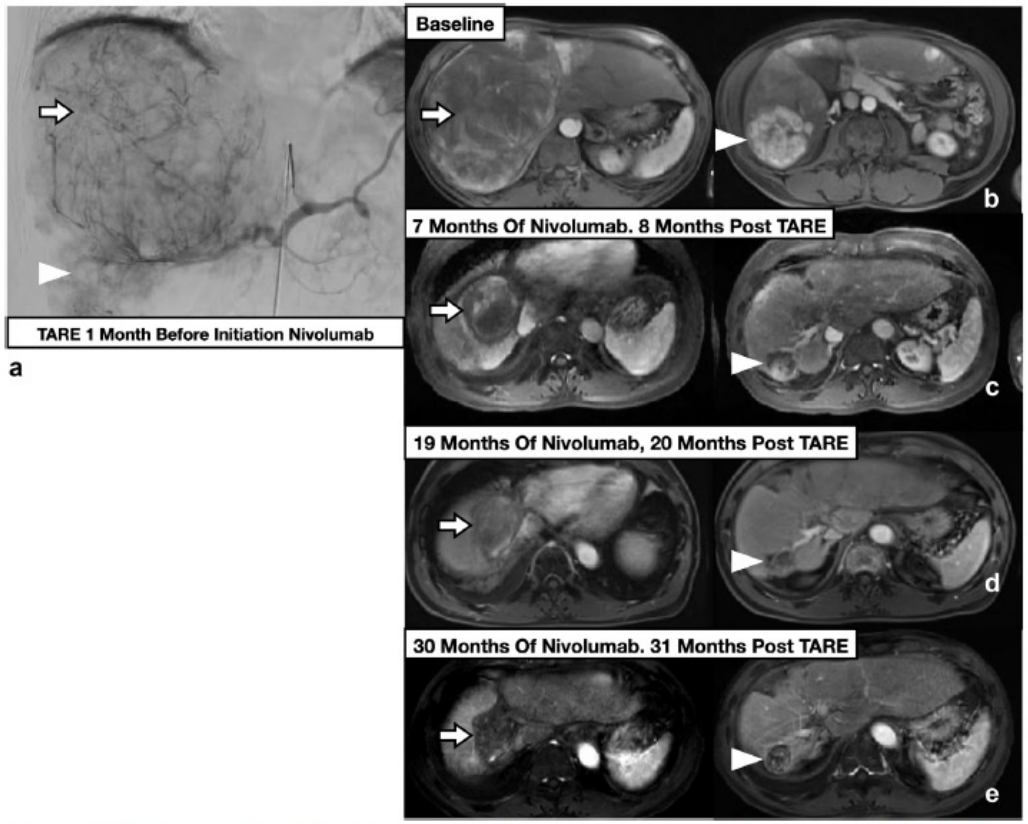


Figure 5. Longitudinal imaging in patient undergoing nivolumab and transarterial radioembolization. **(a)** Celiac digital subtraction angiography demonstrates multiple large right hepatic lobe masses at transarterial radioembolization treatment. Nivolumab therapy was initiated 2 months later. Pre-transarterial radioembolization **(b)** and follow-up imaging at **(c)** 8, **(d)** 20, and **(e)** 31 months later demonstrate response of segment 7/8 (long white arrow) and segment 6 (white arrowhead) tumors over time.

Marinelli et al. JVIR 2020

Liver Transplantation Following Yttrium-90 Radioembolization: 15-Year Experience in 207-Patient Cohort

Ahmed Gabr ,[1] Laura Kulik,[2] Samdeep Mouli,[1] Ahsun Riaz,[1] Rehan Ali,[1] Kush Desai,[1] Ronald A. Mora,[1] Daniel Ganger,[2] Haripriya Maddur,[1] Steven Flamm,[2] Justin Boike ,[2] Christopher Moore,[2] Bartley Thornburg,[1] Ali Alasadi,[1] Talia Baker,[3] Daniel Borja-Cacho,[4] Nitin Katariya,[4] Daniela P. Ladner,[4] Juan Carlos Caicedo,[4] Robert J. Lewandowski,[1,4] and Riad Salem [1,4]

- 207 patients were bridged or downstaged to transplant, median OS 12.5 years, 10-year survival rate =60%, & median RFS: 10-years

- Univariate Predictors of
  - OS: only age
  - RFS: age and tumor necrosis
  - Time dependent recurrence rate: tumor necrosis, AFP & tumor stage within Milan criteria.
  - Disease specific mortality rate: tumor necrosis, AFP and Milan criteria
- Multivariate predictors of
  - OS: only age
  - RFS: age, Tumor necrosis, and AFP

Gabr et al. Hepatology 2020

Y90: Personalization Matters

DOSISPHERE-01

RCT Phase II; 4 centers

93 patients screened

74 patients screened

Key Eligibility
- Unresectable HCC
- ≥ 1 tumor ≥ 7cm
- BCLC A, B or C
- Hepatic reserve after 1st SIRT ≥30%
- Written consent

Pre-Treatment
- Arteriogram
- ^{99m}Tc-MAA using SPECT/CT

Exclusion Criteria
- LSF >30Gy
- Risk of GI exposure
- Poor tumor or PVT perfusion

R 1:1

ITT population: PDA: n=31; SDA: n=29

Treatment

Standard Dosimetry (mITT n=28):
Dosimetry goal: 120±20 Gy to the perfused liver

Personalized Dosimetry (mITT n=28):
Dosimetry goal*: ≥ 205 Gy to the index lesion; 250-300 Gy if possible. Limit non-tumor tissue dose to no more than 120 Gy with hepatic reserve ≥30%.

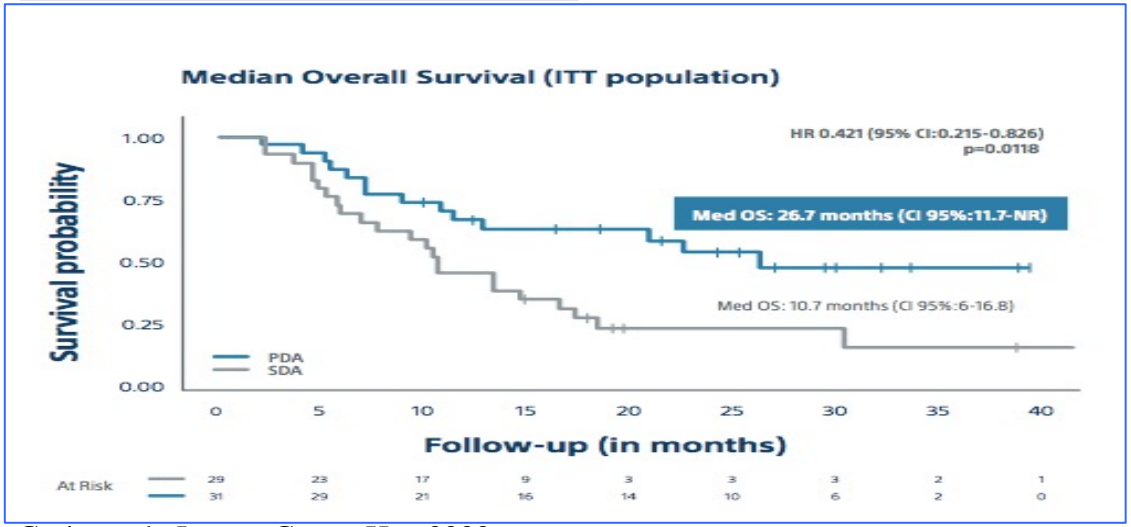
Follow-Up Assessments (efficacy, safety)

Post-Treatment Dosimetry — 6-8w — 3M — 6M — 12M

PATIENT DEMOGRAPHICS (mITT population)

Parameter	PDA (n=28)	SDA (n=28)
Age (median±SD)	64.8±10.1	62.5±13.1
Male (%)	92.9	92.9
Underlying cirrhosis (%)	85.7	85.7
Child-Pugh Status (%)	CP A5: 78.6 CP A6: 21.4 CP B7: 0	CP A5: 78.6 CP A6: 21.4 CP B7: 0
Mean Total Bilirubin (µM/L±SD)	14.63±6.43	13.63±5.78
ECOG (%)	0: 57.1 1: 42.9	0: 46.4 1: 53.6
PVT present (%)	67.9	75.0
Index lesion (mean, cm)	10.36±2.44	10.67±2.79
Tumoral involvement (mean±SD)	23.01±13.95	23.97±14.2

*No significant difference in baseline characteristics between groups



Garin et al. Lancet Gastro Hep 2020

The safety of hepatectomy after transarterial radioembolization: Single institution experience and review of the literature

Christopher Noda BS[1] | Gregory A. Williams BS, MA[1] | Gretchen Foltz MD[2] | Hyun Kim MD[3] | Dominic E. Sanford MD, MPHS[1] | Chet W. Hammill MD, MCR, FACS[1] | Ryan C. Fields MD, FACS[1]

- 12 patients were treated with a TARE followed by a hepatectomy (nine
- with ≥4 segments resected).

- Diagnoses: six HCC, four CC, one NET, one mCRC. There were no 90-day post-hepatectomy mortalities and the overall morbidity was 66% (16% severe ≥MAGS 3). Hepatectomy-specific complications after hepatectomy included two **(16%) bile leaks and no post-hepatectomy liver failures**. The median recurrence free survival was 26 months. Overall survival at 1-year was 78% and at 3 years was 47%.

- Our results support the safety of hepatectomy in select patients after TARE. Additional comparison to patients who receive hepatectomy as a first-line treatment for liver cancers should be investigated.

Marinelli et a JVIR 2020

Streamlining radioembolization in UNOS T1/T2 hepatocellular carcinoma by eliminating lung shunt estimation

Ahmed Gabr[1], Srirajkumar Ranganathan[1], Samdeep K. Mouli[1], Ahsun Riaz[1], Vanessa L. Gates[1], Laura Kulik[2], Daniel Ganger[2], Haripriya Maddur[2], Christopher Moore[2], Elias Hohlastos[1], Nitin Katariya[3], Juan Carlos Caicedo[3], Aparna Kalyan[4], Robert J. Lewandowski[1,3], Riad Salem[1,3,4,*]

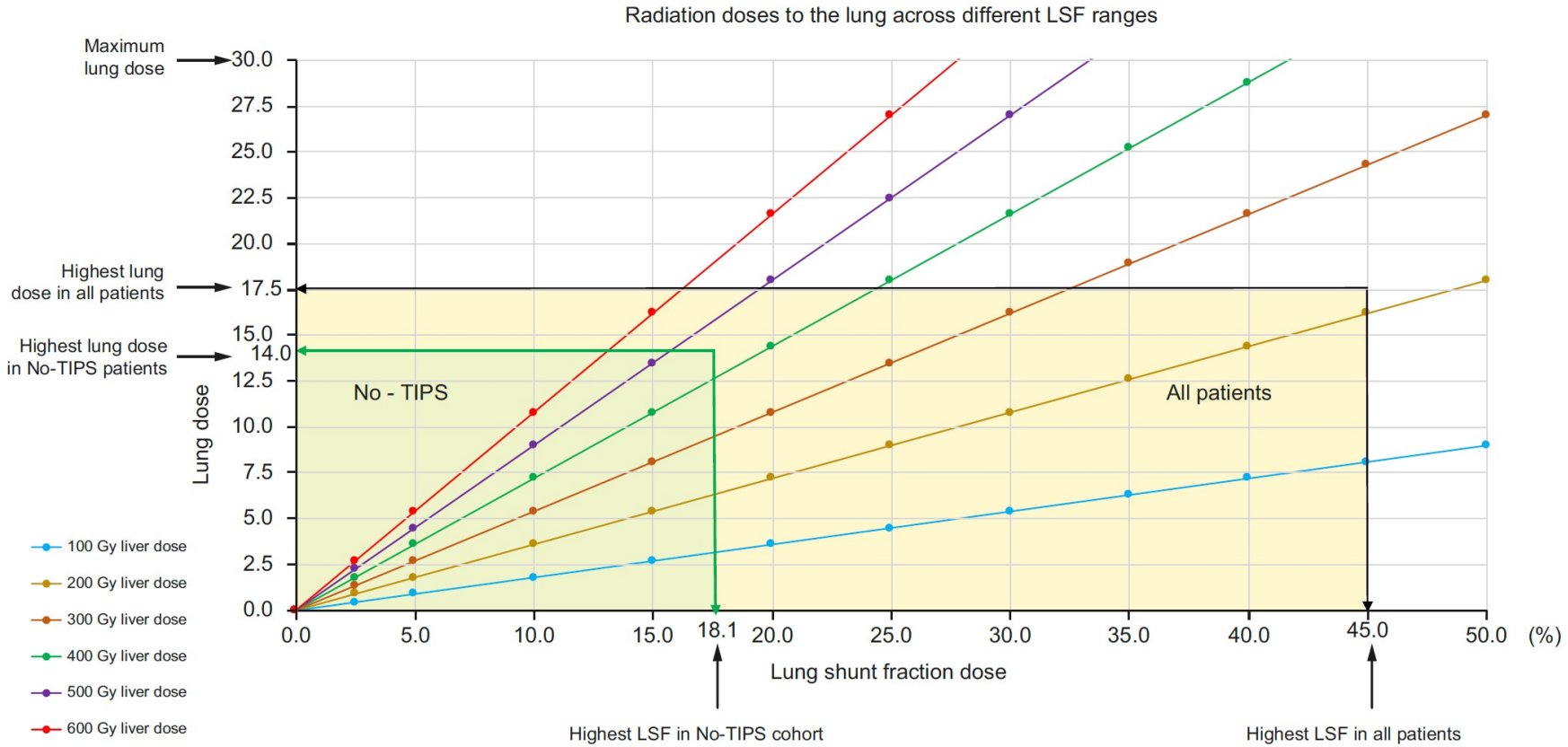


Fig. 2. Mathematical model of radiation doses to the lung across different LSF ranges as prescribed dose of liver tissue is increased from 100 to 600 Gy assuming median perfused mass of 0.18 kg. LSF, lung shunt fraction. (This figure appears in color on the web.)

Yttrium-90 Radioembolization for the Treatment of Solitary, Unresectable HCC: The LEGACY Study

Riad Salem ,[1] Guy E. Johnson,[2] Edward Kim,[3] Ahsun Riaz,[1] Vivian Bishay,[3] Eveline Boucher,[4] Kirk Fowers,[4] Robert Lewandowski,[1] and Siddharth A. Padia [5]

Yttrium-90 Radioembolization for the Treatment of Solitary, Unresectable Hepatocellular Carcinoma: The LEGACY Study

Riad Salem, MD, Guy E. Johnson, MD, PharmD, Edward Kim, MD, Ahsun Riaz, MBBS, Vivian Bishay, MD, Eveline Boucher, MD, Kirk Fowers, PhD, Robert Lewandowski, MD, Siddharth A. Padia, MD

Salem et al HEPATOLOGY 2021

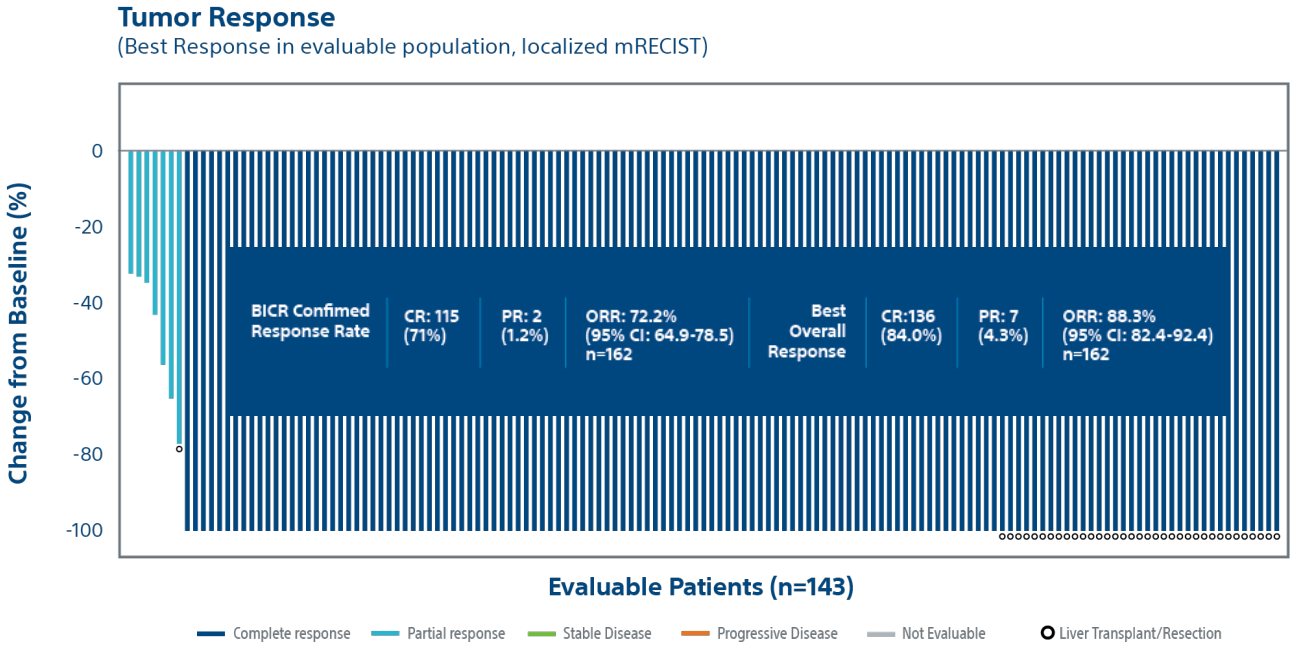
Baseline Characteristics

Median age (range), years	66 (21-90)
≥ 18 to < 65	69 (42.6)
≥ 65 to < 75	64 (39.5)
≥ 75	29 (17.9)
Gender, male	123 (75.9)
HCC Etiology	
HCV	112 (69.1)
Alcohol	48 (29.6)
NASH	23 (14.2)
HBV	15 (9.3)
Other/unknown	5 (3.1)
ECOG Status	
0	98 (60.5)
1	64 (39.5)
BCLC Status	
A	98 (60.5)
C	64 (39.5)
AFP ≥ 200 ng/mL	24 (14.8)

Treatment Characteristics	Treated Population (N=162) N (%)
Median Tumor Size (range), cm	2.6 (0.9-8.1)
Initial Y-90 Treatment Goal	
Radiation segmentectomy	104 (64.2)
Radiation lobectomy	8 (5.0)
Bridge to liver transplantation	36 (22.2)
Other	1 (0.6)
Unknown	13 (8.0)
Type of Infusion	
Selective	155 (95.7)
Lobar	3 (1.9)
Mixed	4 (2.5)
Absorbed dose to perfused liver volume (Gy), median, (IQR)	410.1 (199.7, 797.7)
Number of TheraSphere Treatments	
1	130 (80.2)
≥2	32 (19.8)

Primary Efficacy Outcome: Tumor Response

Best Response in Evaluable population, localized mRECIST



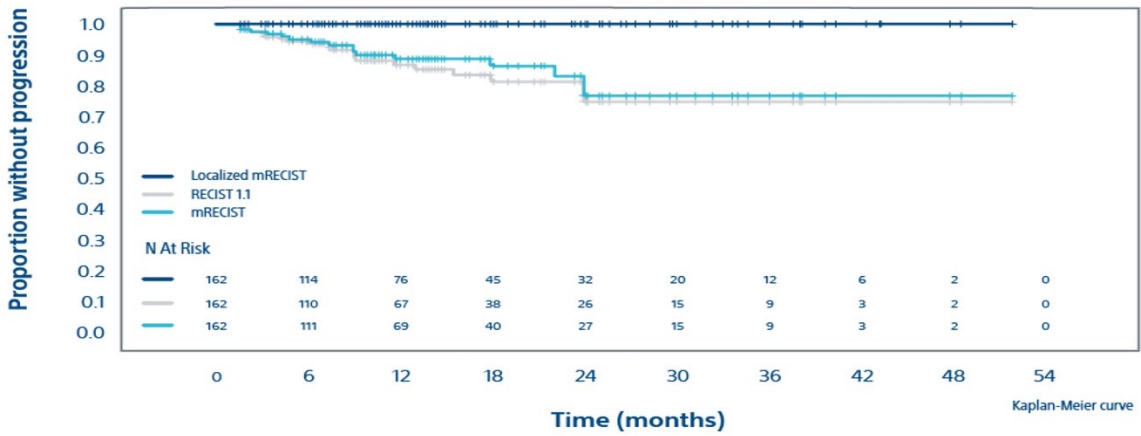
NOTE: Of the 162 patients in the total cohort, 45 were transplanted. Confirmed response at a subsequent visit >4 weeks (30 days) after the date of the first occurrence of CR or PR

Salem R et al. "3020.2: Yttrium-90 Glass Microspheres in the Treatment of Hepatocellular Carcinoma: The LEGACY Study," CIRSE 2020 Virtual Summit, September 12-15, 2020

LEGACY Results

KM Analyses

a.



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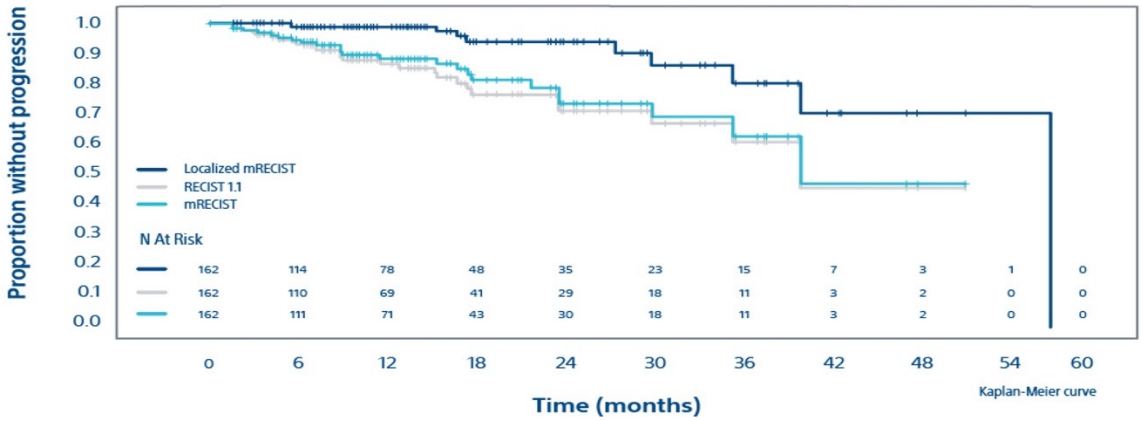
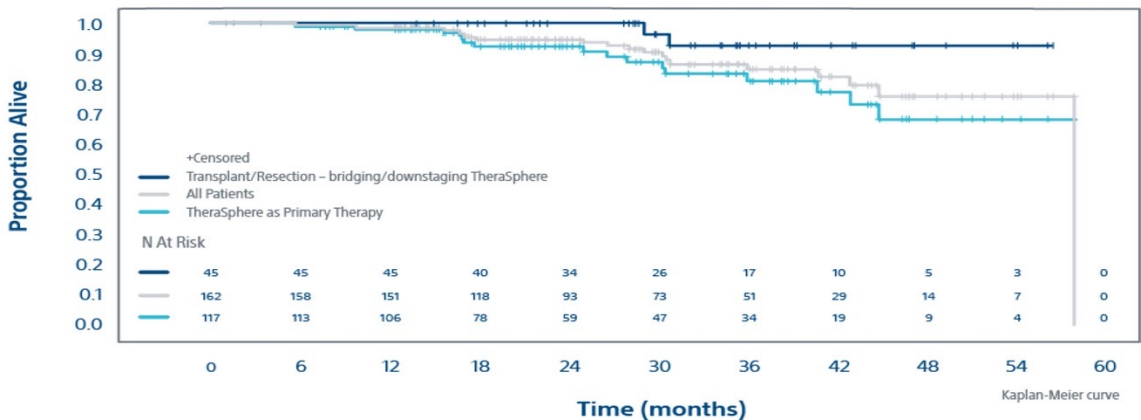
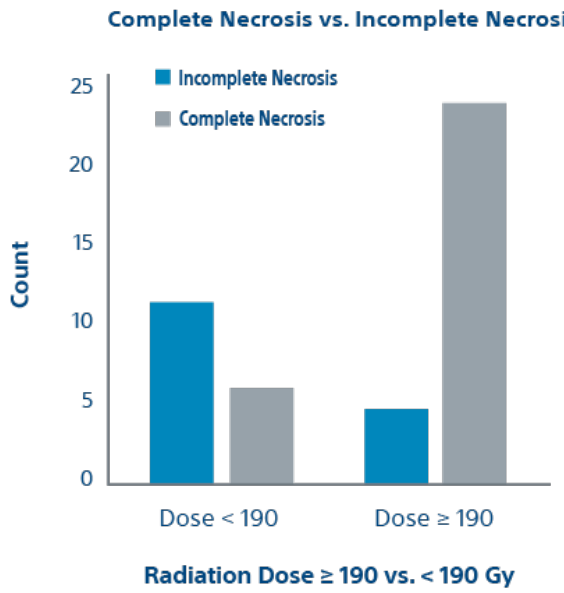


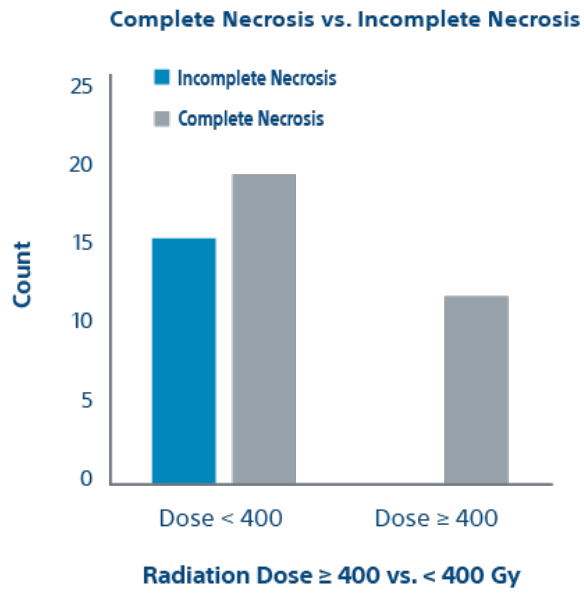
c.



Histopathology Correlation with Absorbed Dose

- Post-explant tumors from 45 LEGACY patients underwent histopathology analysis
- Complete pathologic necrosis was higher in tumors treated with ≥ 400 Gy vs < 400 Gy

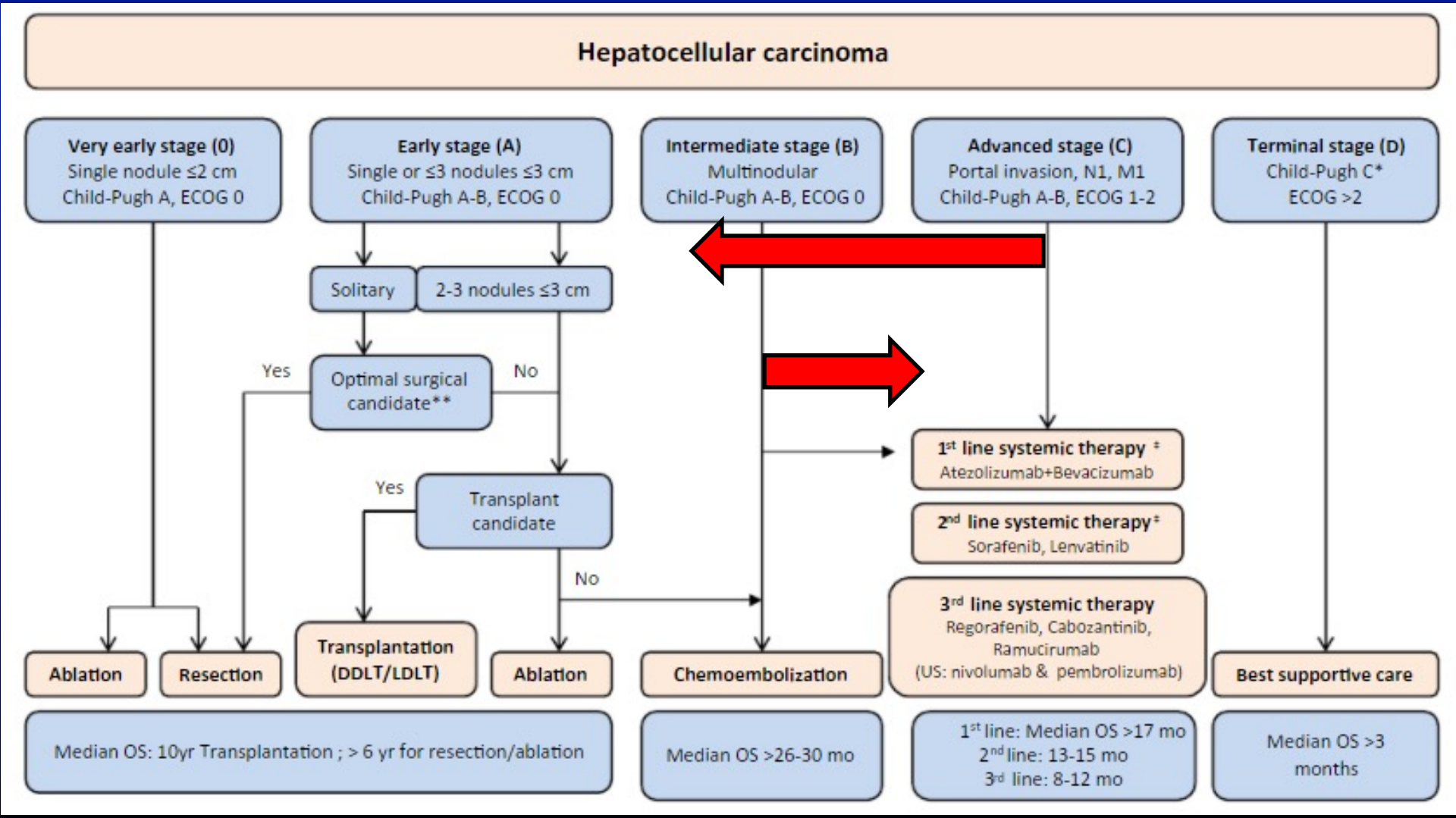




>400 Gy is the new >190 Gy!

Gabr et al. EJNMMI 2020 Aug 4l doi.org/10.1007/s00259-020-04976-8

AASLD Consensus Conference 2021



BCLC 2021

Llovet et al HEP 2021

Comparing Real World, Personalized, Multidisciplinary Tumor Board Recommendations with BCLC Algorithm: 321-Patient Analysis

Monica M. Matsumoto[1,2] · Samdeep Mouli[1] · Priyali Saxena[1] · Ahmed Gabr[1] · Ahsun Riaz[1] · Laura Kulik[3] · Daniel Ganger[3] · Haripriya Maddur[3] · Justin Boike[3] · Steven Flamm[3] · Christopher Moore[3] · Aparna Kalyan[4] · Kush Desai[1] · Bartley Thornburg[1] · Michael Abecassis[5] · Ryan Hickey[6] · Juan Caicedo[7] · Karen Grace[1] · Robert J. Lewandowski[1,4,7] · Riad Salem[1,4,7]

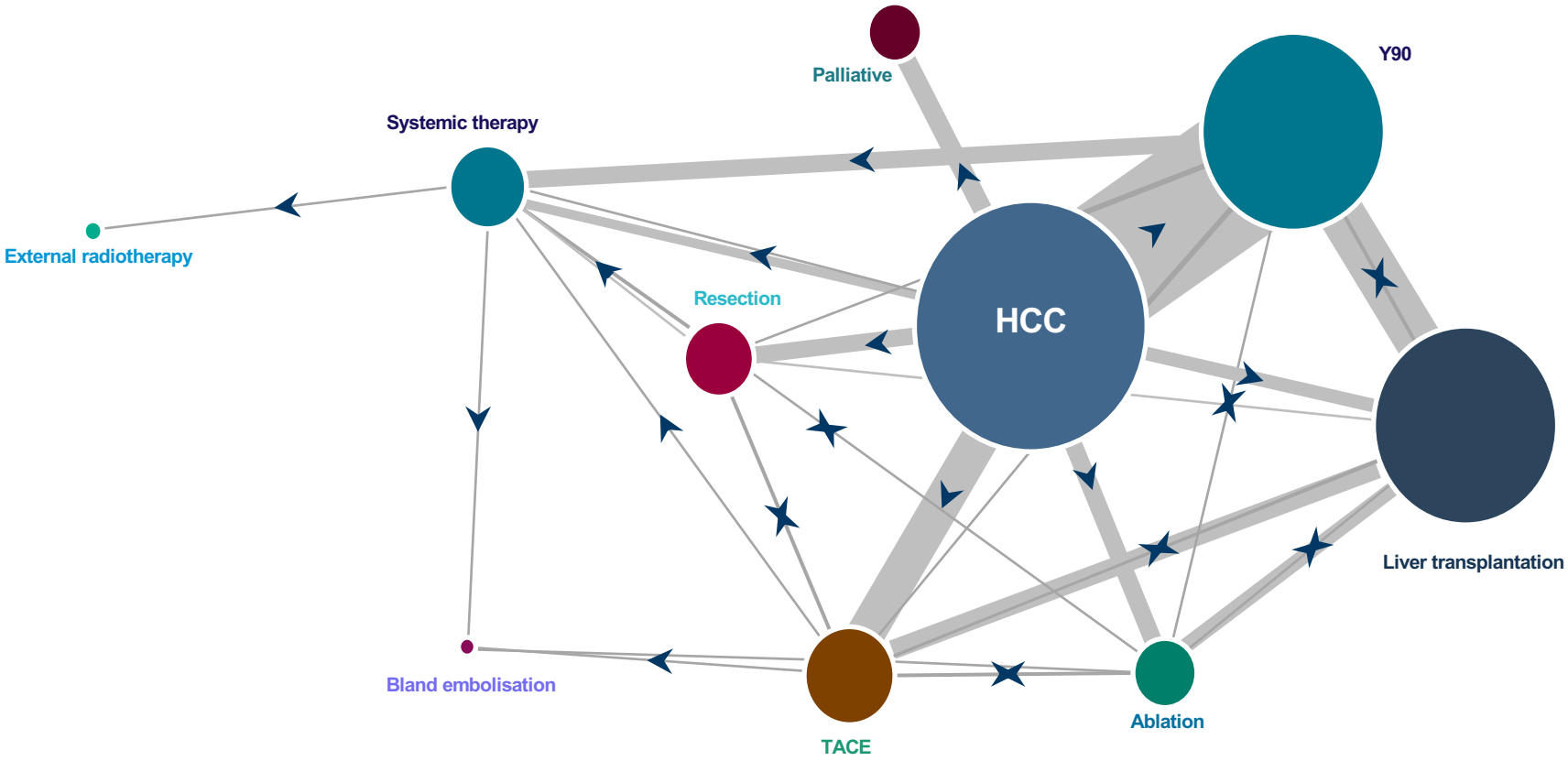
- Studied MDT 2010-2013
- Looked at discordance to BCLC first-treatment recommendation
- Follow-up all patients > 8 years
- Looked at all post-progression treatments→ **Network Graph**
- N=321

BCLC Stage		Number	%	
A (n=142)	Discordant	94	66%	*
	Concordant	48	34%	
B (n=28)	Discordant	21	75%	*
	Concordant	7	25%	
C (n=100)	Discordant	96	96%	*
	Concordant	4	4%	
D (n=51)	Discordant	33	65%	*
	Concordant	18	35%	

Matsumoto, Salem et al CVIR 2021

A patient's treatment journey can be viewed as a network rather than a linear pathway

Northwestern Medicine HCC treatment network graph (N=321)



- The size of the node is commensurate with the number of patients (N=321)
  The thickness of the link is commensurate with the frequency of the interaction

Matsumoto…Salem et al. Cardiovasc Intervent Radiol 2021

OS Comparison to Guideline Expectations

Comparing Real World, Personalized, Multidisciplinary Tumor Board Recommendations with BCLC Algorithm: 321-Patient Analysis

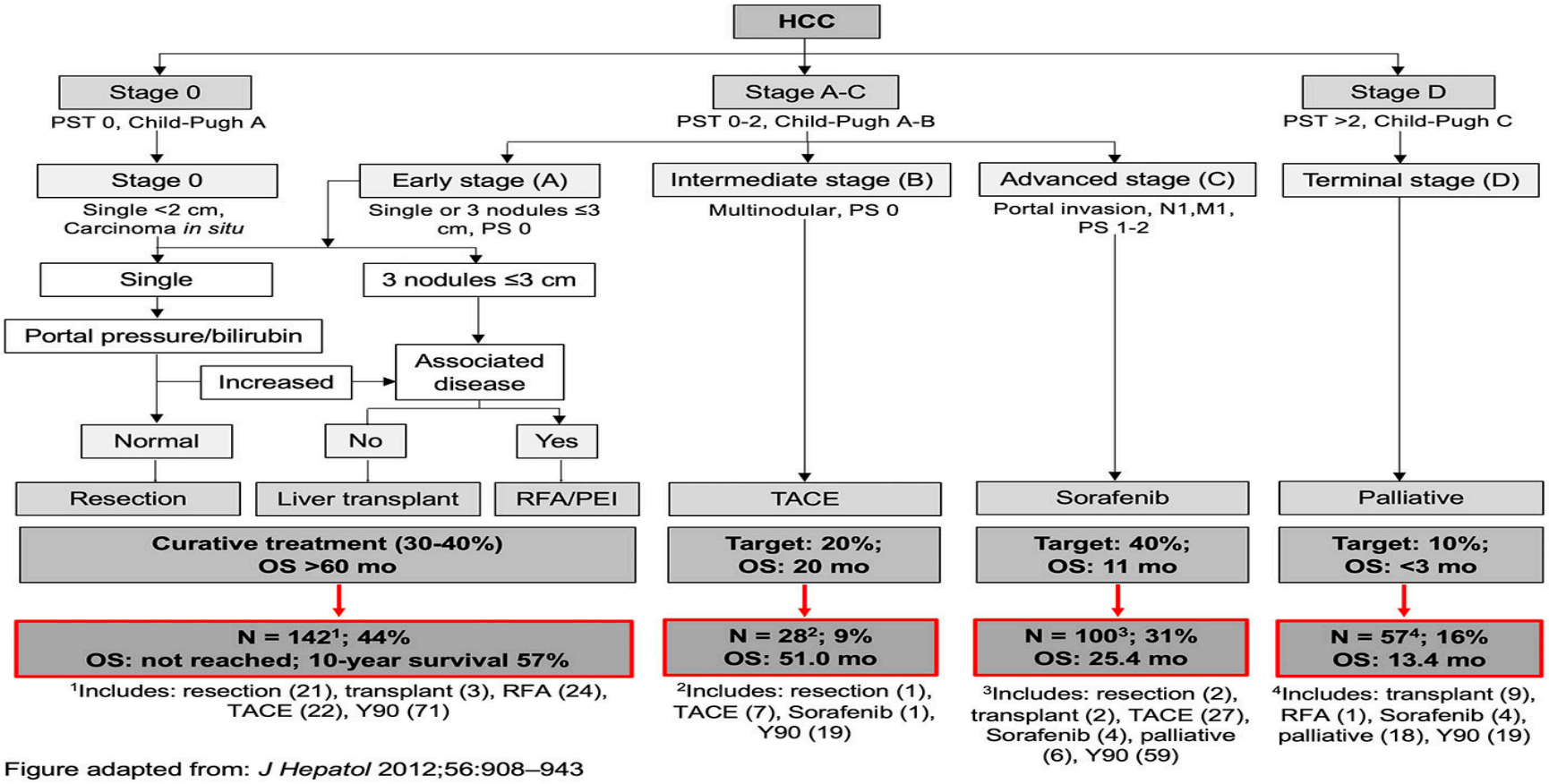


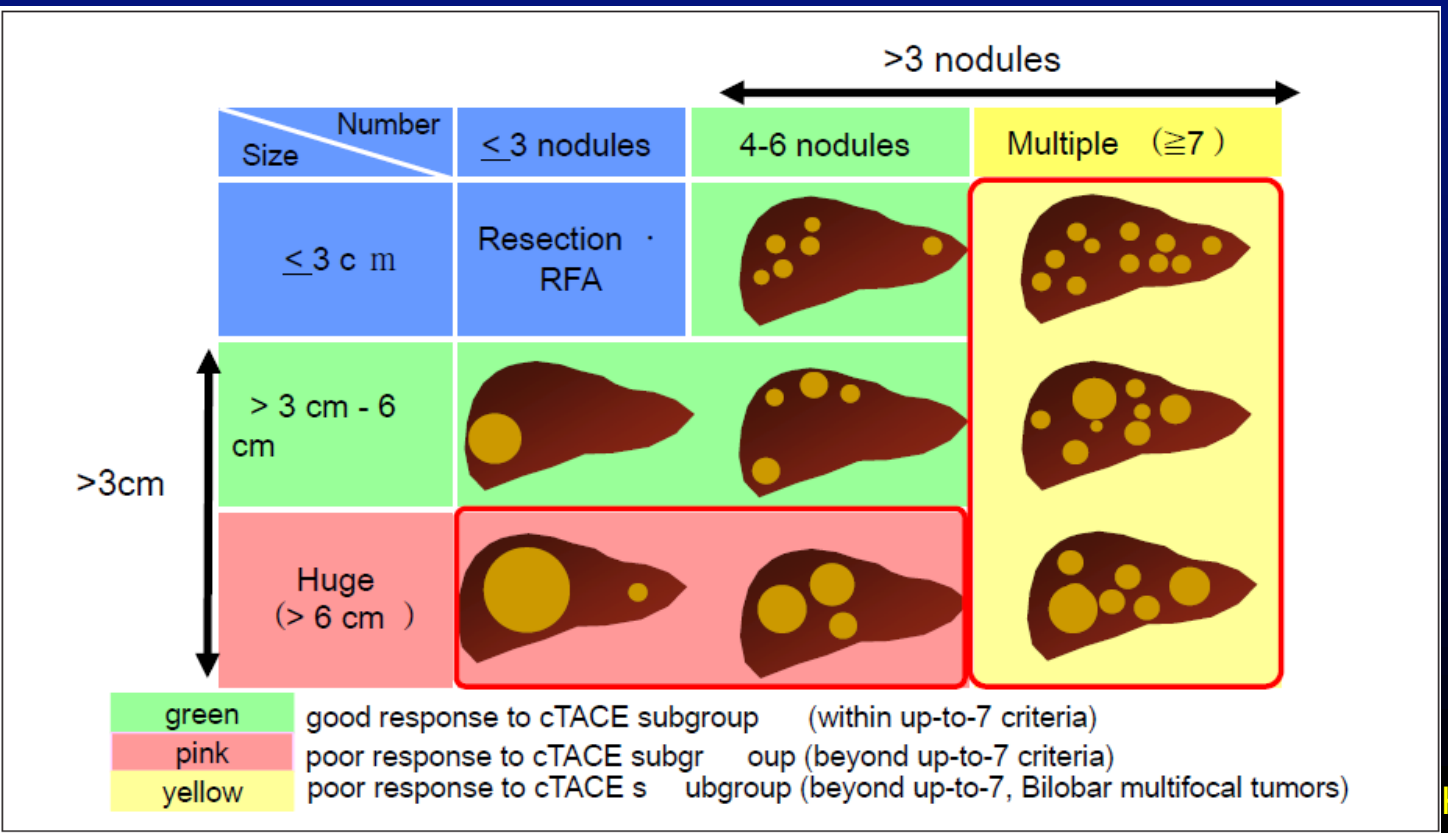
Figure adapted from: *J Hepatol* 2012;56:908–943

Matsumoto, Salem et al CVIR 2021

A Changing Paradigm for the Treatment of Intermediate-Stage Hepatocellular Carcinoma: Asia-Pacific Primary Liver Cancer Expert Consensus Statements

Masatoshi Kudo[a] Kwang-Hyub Han[b] Sheng-Long Ye[c] Jian Zhou[d] Yi-Hsiang Huang[e, f] Shi-Ming Lin[g, h] Chung-Kwe Wang[i] Masafumi Ikeda[j] Stephen Lam Chan[k] Su Pin Choo[l] Shiro Miyayama[m] Ann Lii Cheng[n–p] on behalf of the APPLE Association

tumors + sum of largest tumor ≤ 7 = up-to-7 criteria



Kudo et al Liver Cancer 2020

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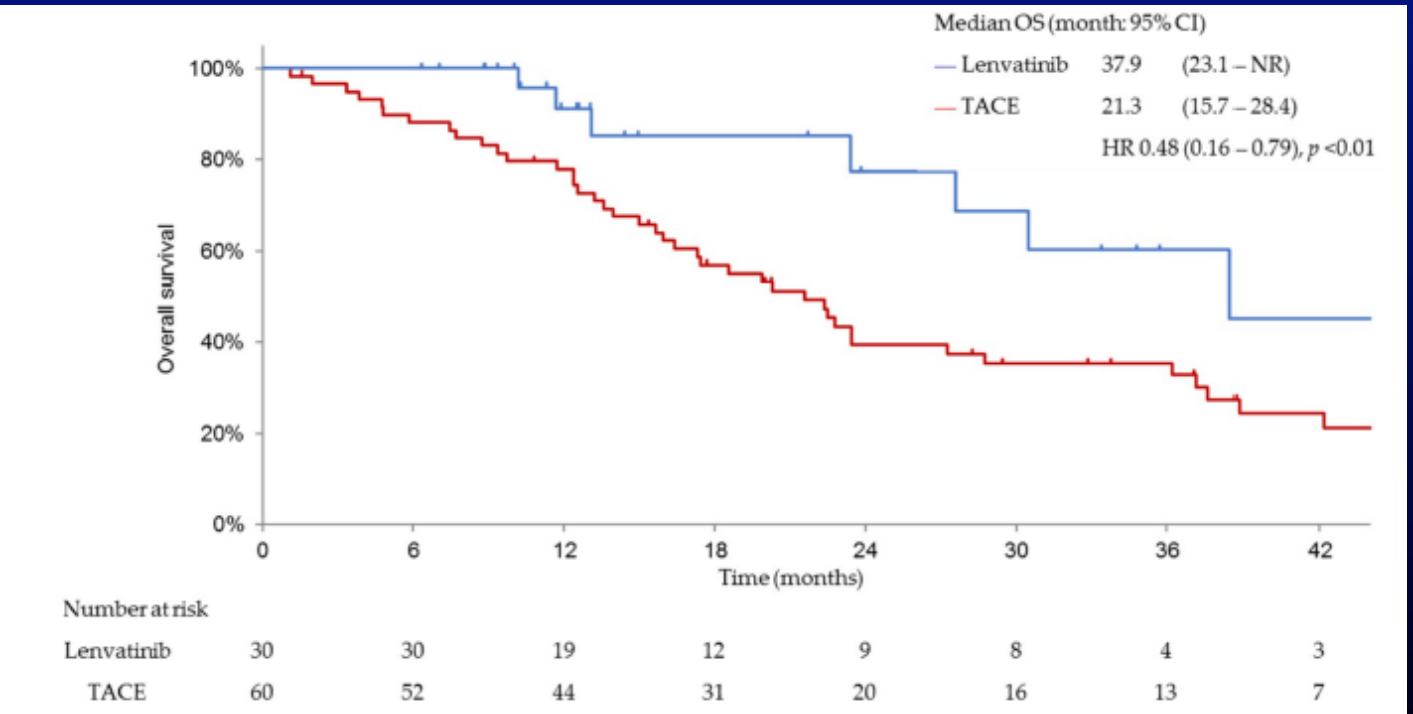

Figure 4. Overall survival (OS) in both groups after propensity score matching. OS in the lenvatinib-treated group was significantly better than that in the TACE-treated group (37.9 months vs. 21.3 months; hazard ratio (HR)0.48, $p < 0.01$). NR; not reached

Kudo et al Liver Cancer 2020

Cost-Effectiveness Analysis of Selective Interna Radiotherapy With Yttrium-90 Versus Sorafenib in Locally Advanced Hepatocellular Carcinoma

Kathryn E. Marqueen, MD[1]; Edward Kim, MD[2]; Celina Ang, MD[3]; Madhu Mazumdar, PhD[4]; Michael Buckstein, MD, PhD[1]; and Bart S. Ferket, MD, PhD[4]

-costs were $78,859 v $58,397 (difference $20,462; 95% uncertainty interval $14,444 to 27,205) and QALYs were 0.88 v 0.87 (difference 0.02, 20.02 to 0.05) for sorafenib versus SIRT, respectively. The incremental cost-effectiveness ratio (ICER) of sorafenib was $1,280,224/QALY. The likelihood that sorafenib would be cost effective did not exceed 1%, assuming cost-effectiveness thresholds up to $200k/QALY. If the monthly price of sorafenib decreased from $16,390 to below $7,000, the ICER of sorafenib fell below $200k/QALY, and an ICER , $100k/QALY was reached if the monthly price fell below $6,600.

CONCLUSION: Sorafenib unlikely to provide a gain in quality-adjusted survival compared with SIRT at an acceptable cost for the US healthcare sector.

Only if the current price decreased by more than 50% would sorafenib be considered economically attractive.

Marqueen et al JCO Onc Pract 2020

Article

Management of Liver Tumors during the COVID-19 Pandemic: The Added Value of Selective Internal Radiation Therapy (SIRT)

Irene Bargellini [1,*], Giuseppe Boni [2], Antonio Claudio Traino [3], Elena Bozzi [1], Giulia Lorenzoni [1], Francesca Bianchi [2], Rosa Cervelli [1], Tommaso Depalo [2], Laura Crocetti [1], Duccio Volterrani [2] and Roberto Cioni [1]

- During COVID, LRTs → minimally invasive tools → Y90
- present Y90 during COVID-19 pandemic and overview of the indications and challenges of SIRT in this scenario.
- analyzed MDT in 2020 and compared it to 2019
-
- 27.5% ▼ patients referred to MDT, and 28.3% ▼ RFA; TACE were stable, while Y90 ▲ 64%. Most were HCC (75%). ORR → 56.7%; DCR → 72.2%.
- Conclusion: COVID-19 was characterized by ▲ demand for Y90
  - safe, flexible, effective, with simplified workflow and personalized dosimetry

Bargellini et al. JCM 2020

Year in Review in Y90 Radioembolization: Metastatic Disease

Daniel B. Brown, MD FSIR
Professor of Radiology and Biomedical Engineering
Vice-Chair, Innovation and Clinical Research
Director, Interventional Oncology
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Disclosures

- Research Support: Sirtex, Guerbet
- Speaker: Cook Medical
- Consulting: BD/Bard, Astra-Zeneca

VANDERBILT UNIVERSITY
MEDICAL CENTER

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

Mary F. Mulcahy, MD[1]; Armeen Mahvash, MD[2]; Marc Pracht, MD[3]; Amir H. Montazeri, MD[4]; Steve Bandula, MD, PhD[5]; Robert C. G. Martin II, MD[6]; Ken Herrmann, MD[7]; Ewan Brown, MD[8]; Darryl Zuckerman, MD[9]; Gregory Wilson, MD[10]; Tae-You Kim, MD[11]; Andrew Weaver, MD[12]; Paul Ross, MD[13]; William P. Harris, MD[14]; Janet Graham, MD[15]; Jamie Mills, MD[16]; Alfonso Yubero Esteban, MD[17]; Matthew S. Johnson, MD[18]; Constantinos T. Sofocleous, MD[19]; Siddharth A. Padia, MD[20]; Robert J. Lewandowski, MD[21]; Etienne Garin, MD[22]; Philip Sinclair, PhD[23]; and Riad Salem, MD, MBA[21]; for the EPOCH Investigators

Co-Primary Endpoints:
1. PFS
2. HPFS

Secondary Endpoints:
1. OS
2. ORR/DCR

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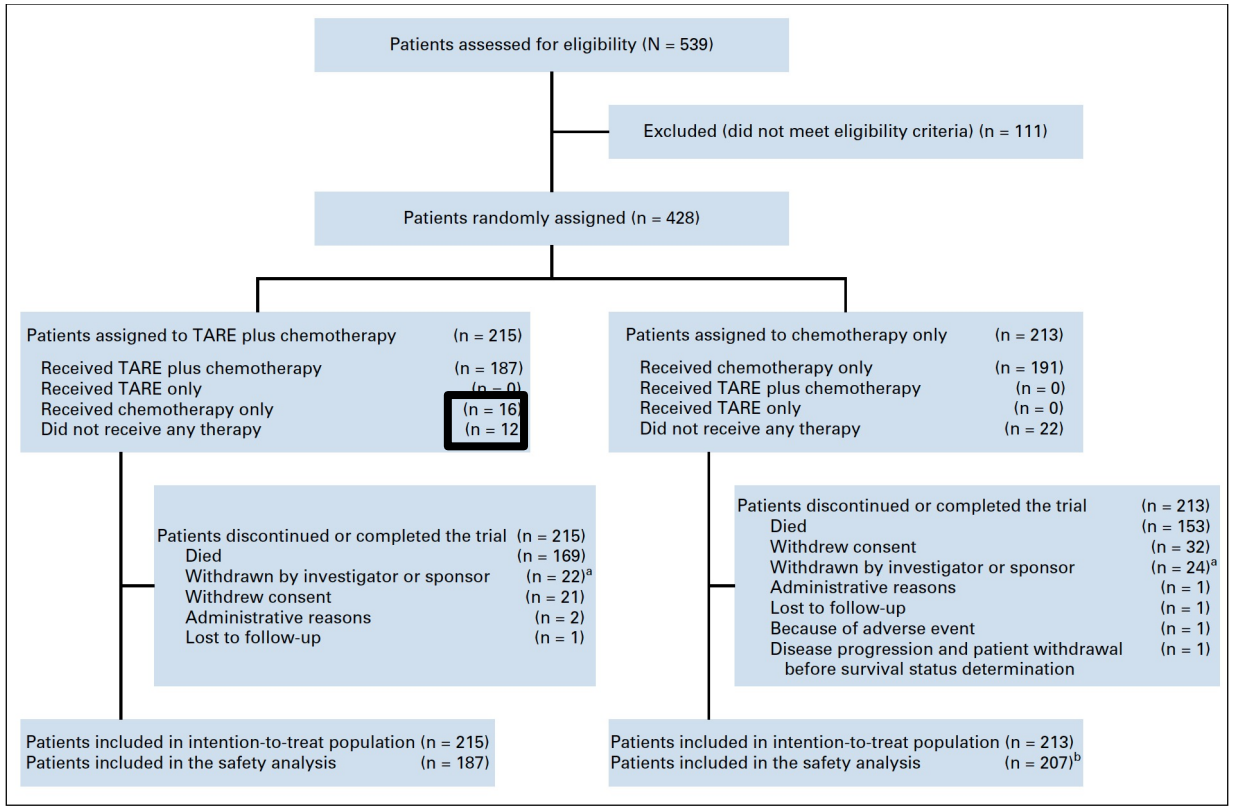
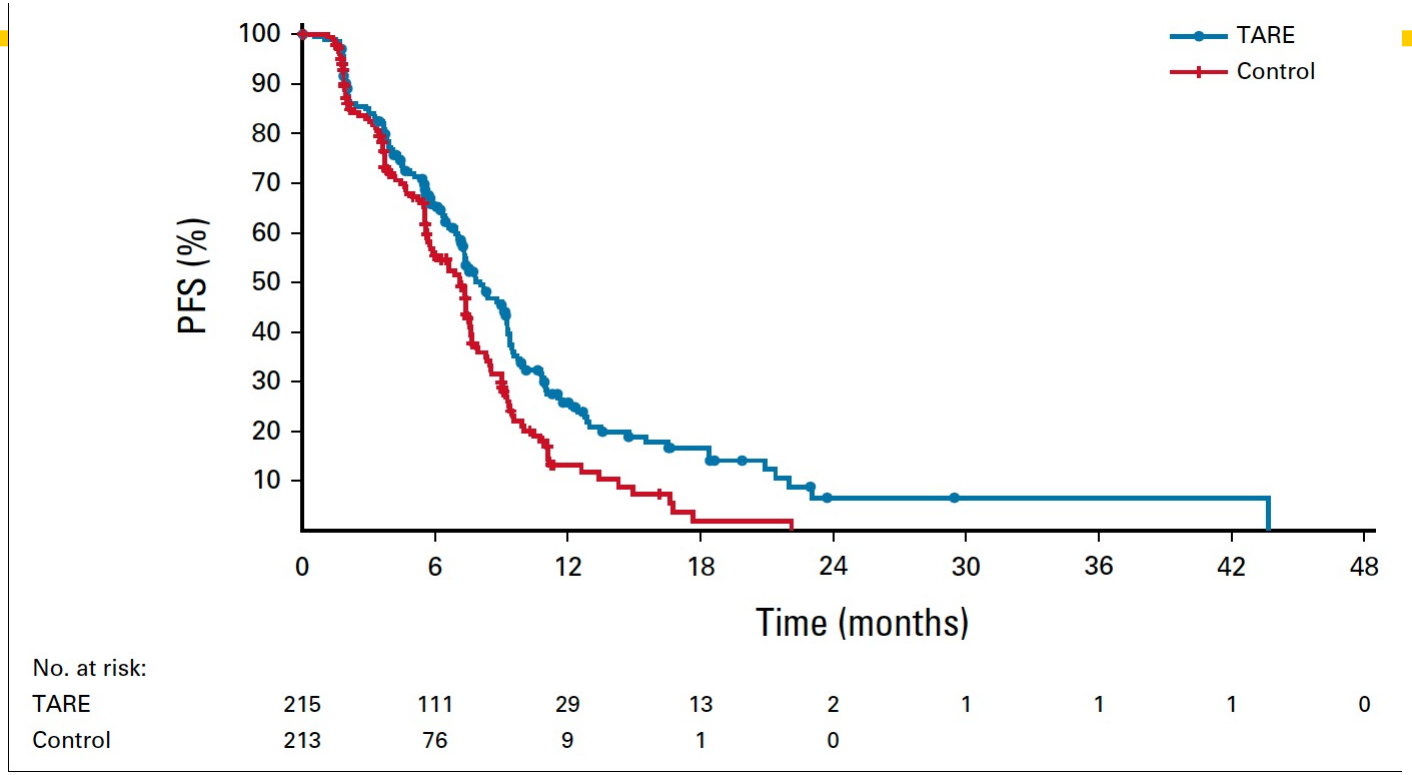
CONSORT Diagram

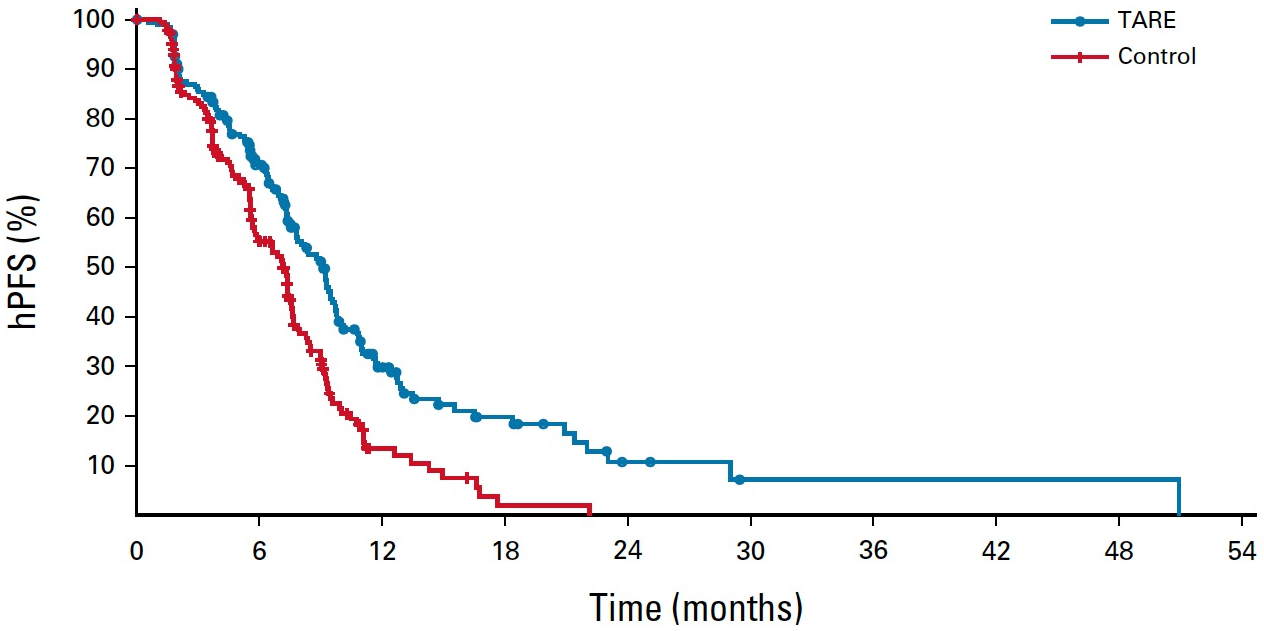


	TARE (N=215)
Patients receiving TARE	187 (87%)
Reasons for not receiving TARE	28 (13%)
Lung Shunt	4 (1.8%)
Gastrointestinal deposition	6 (2.8%)
Investigator decision	6 (2.8%)
Patient decision	1 (0.4%)
Early withdrawal	6 (2.8%)
Missing	5 (2.3%)

Inherent challenge in device trials.
Note: 22 (10.3%) of control group received no therapy



Primary Objective: Median PFS:
TARE: 8.0 (95% CI: 7.2-9.2)
Control: 7.2 (95% CI: 5.7-7.6)
HR=0.69, p=0.0013



No. at risk:										
TARE	215	118	32	14	4	1	1	1	1	0
Control	213	76	9	1	0					

Primary Objective: Median hPFS:
TARE: 9.1 (95% CI: 7.8-9.7)
Control: 7.2 (95% CI: 5.7-7.6)
HR=0.59, p<0.0001

Outcome	TARE (n = 215)	Control (n = 213)
Best overall response,[a] No. (%)		
CR	2 (0.9)	3 (1.4)
PR	71 (33.0)	42 (19.7)
SD	98 (45.6)	110 (51.6)
PD	27 (12.6)	27 (12.7)
Not evaluable or missing	0/17 (7.9)	1 (0.5)/30 (14.1)
ORR		
CR plus PR, No. (%) (95% CI)	73 (34.0) (28.0 to 40.5)	45 (21.1) (16.2 to 27.1)
Difference (95% CI)	12.8% (4.0 to 21.4)	
Superiority 1-sided *P*	.0019	
DCR		
CR plus PR plus SD, No. (%) (95% CI)	171 (79.5) (73.6 to 84.4)	155 (72.8) (66.4 to 78.3)
Difference (95% CI)	6.8% (–1.6 to 15.1)	
Superiority 1-sided *P*	.0626	

Secondary Objective ORR/DCR:
ORR: 34.0% vs 21.1% (p=0.0019)
DCR: 79.5% vs 72.8% (p=0.626)

	TheraSphere (N=215)	Control (N=213)
OS		
Total events (i.e., deaths)	182 (84.7%)	165 (77.5%)
Median OS in months (CI)	14.0 (11.8, 15.5)	14.4 (12.8, 16.4)
OS rate at 6 months (CI)	88.5% (83.3%, 92.1%)	87.8% (82.3%, 91.7%)
OS rate at 12 months (CI)	56.3% (49.2%, 62.8%)	62.4% (55.0%, 68.9%)
HR (CI)	1.07 (0.86, 1.32)	
Superiority Log-rank 1-sided p-value	0.7229	

Secondary Objective OS:
14.0 vs 14.4 months (p=0.7229)

Post-Progression Therapy

ITT population	TheraSphere (N=215)	Control (N=213)
Total Number of Patient receiving Post Progression mCRC Treatment [a]	110 (51.2%)	123 (57.7%)
Chemoembolization	3 (1.4%)	7 (3.3%)
Ablation	1 (0.5%)	6 (2.8%)
Resection	3 (1.4%)	5 (2.3%)
TARE	16 (7.4%)	28 (13.1%)
Other procedure	6 (2.8%)	7 (3.3%)
Systemic Therapy	105 (48.8%)	114 (53.5%)

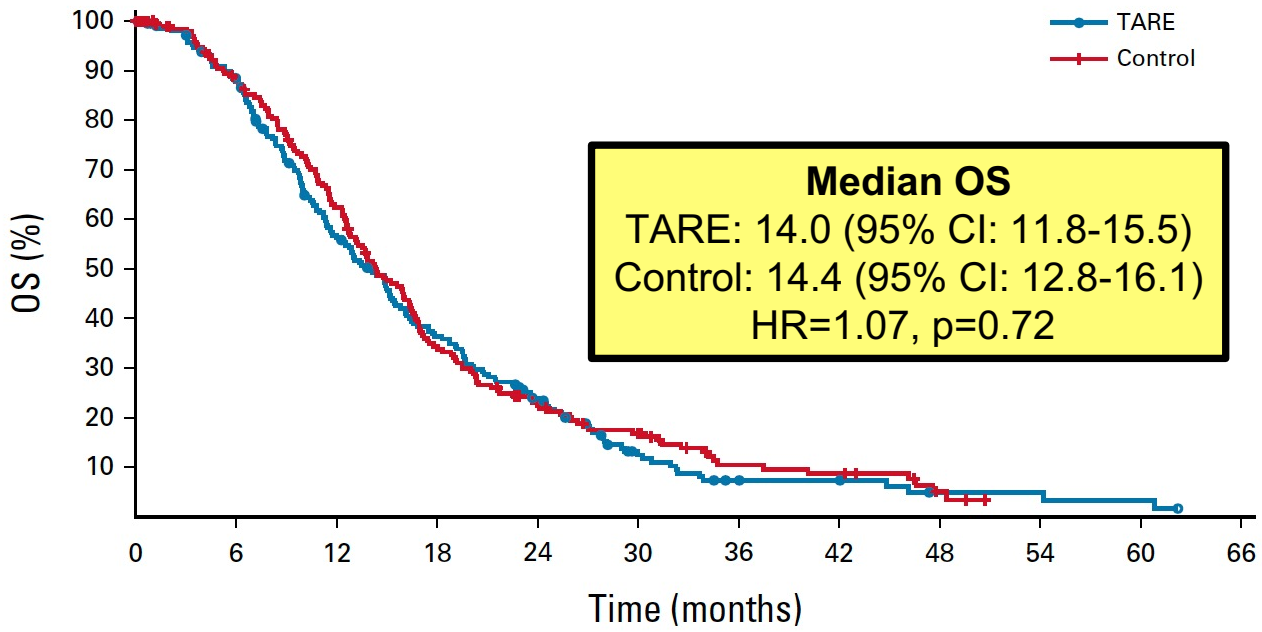
This is the challenge of OS in trials with CRC

editorials

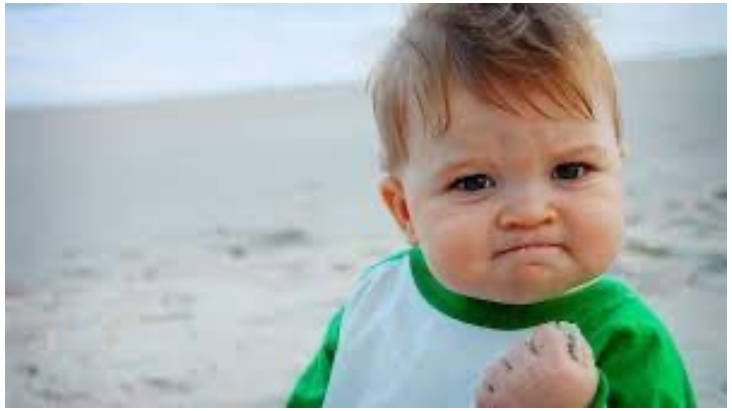
Transarterial Radioembolization in Patients With Unresectable Colorectal Cancer Liver Metastases

Robert W. Lentz, MD[1] and Wells A. Messersmith, MD[1]

In summary, the EPOCH trial provides minimal support for the addition of TARE to standard second-line systemic therapy in unresectable CLM, as did the FOXFIRE, SIR-FLOX, and FOXFIRE-Global trials in the first-line setting.

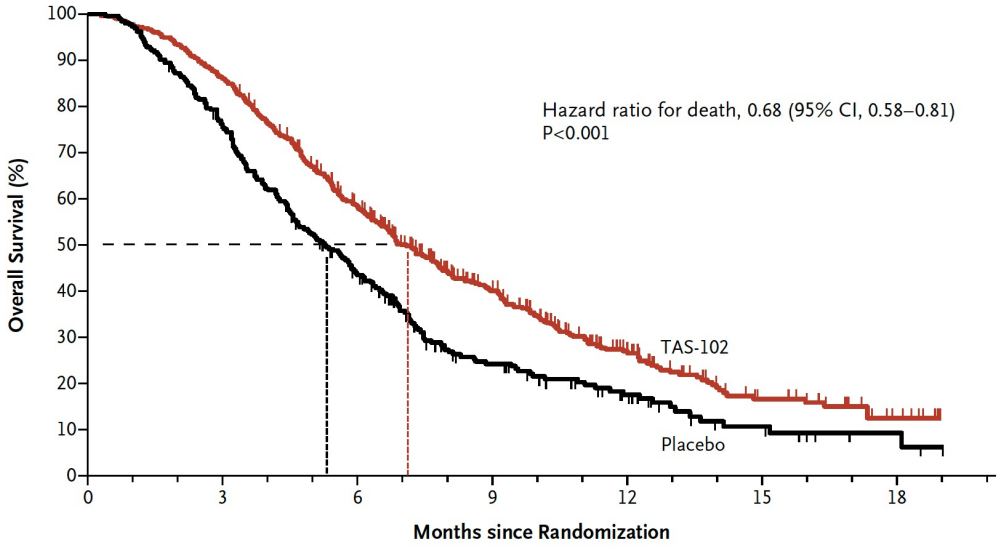


No. at risk:												
TARE	215	183	112	71	43	17	8	7	3	3	2	0
Control	213	164	115	62	38	25	12	10	3	0		



A Positive IR Trial!
Well-constructed
Well-executed

OS is the ONLY thing that matters



No. at Risk							
TAS-102	534	459	294	137	64	23	7
Placebo	266	198	107	47	24	9	3

Trifluridine and tipiracil
HR: 0.68
Increased OS: 1.8 months
Vs. Placebo
NEJM 2015

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2020
Colon Cancer

NCCN Guidelines Index
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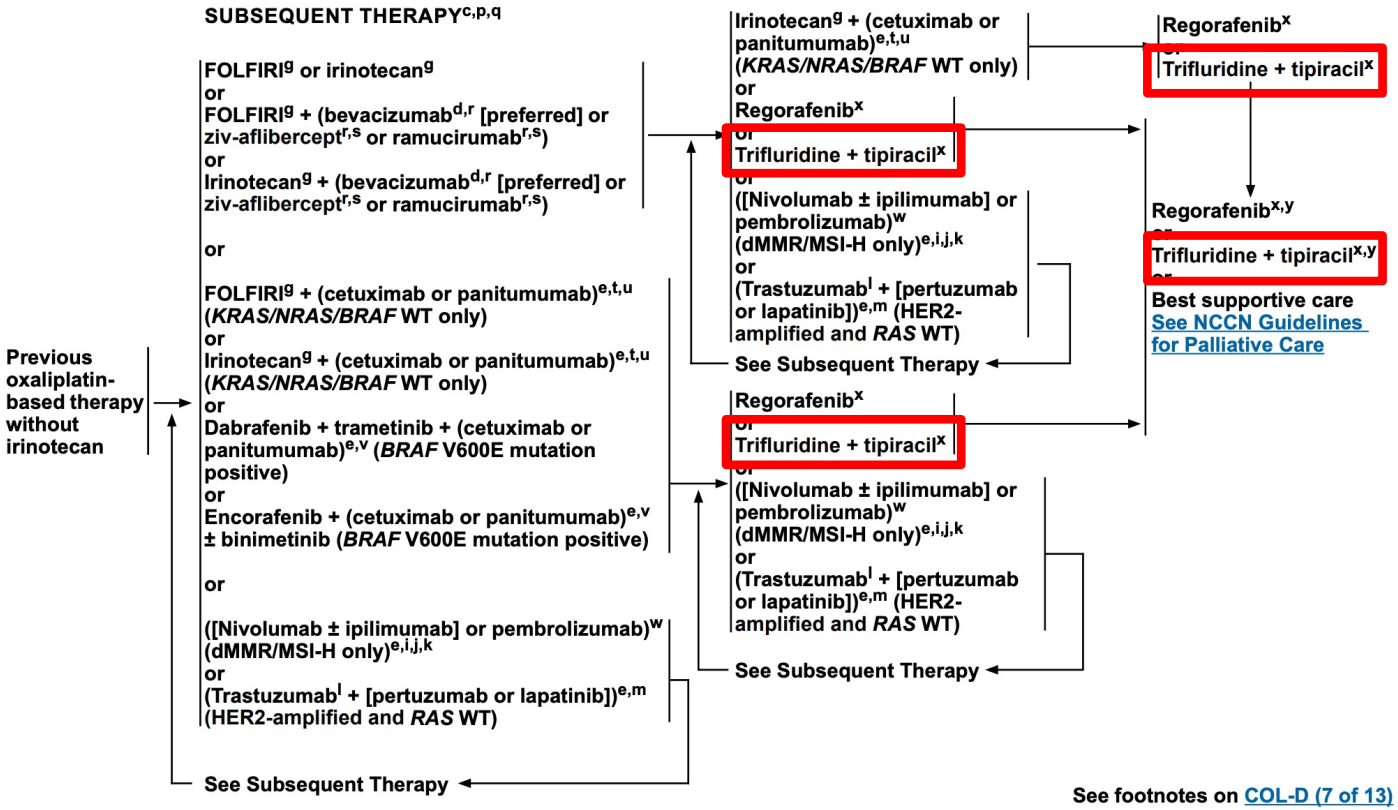
Discussion

CONTINUUM OF CARE - SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE[a,b,o]



See footnotes on COL-D (7 of 13)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

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International recommendations for personalised selective internal radiation therapy of primary and metastatic liver diseases with yttrium-90 resin microspheres

Hugo Levillain[1] · Oreste Bagni[2] · Christophe M. Deroose[3] · Arnaud Dieudonné[4] · Silvano Gnesin[5] · Oliver S. Grosser[6] · S. Cheenu Kappadath[7] · Andrew Kennedy[8] · Nima Kokabi[9] · David M. Liu[10] · David C. Madoff[11] · Armeen Mahvash[12] · Antonio Martinez de la Cuesta[13] · David C. E. Ng[14] · Philipp M. Paprottka[15] · Cinzia Pettinato[16] · Macarena Rodríguez-Fraile[13] · Riad Salem[17] · Bruno Sangro[13] · Lidia Strigari[18] · Daniel Y. Sze[19] · Berlinda J. de Wit van der veen[20] · Patrick Flamen[1]

EJNMMI 2021;48:1570-1584

76 CRC
15 NET

Table 4 Key studies on dose-response with ^{90}Y-resin microspheres

Study	Population	Activity prescription method	Lesion dosimetry assessment	Response assessment	Results
van den Hoven et al. 2016 [28]	Chemorefractory mCRC ($n = 30$)	BSA	^{90}Y-PET 3D voxel-based	Tumour-absorbed dose quantified on ^{90}Y-PET versus TLG on ^{18}F-FDG PET	50% reduction in TLG at 1 month associated with prolonged OS At least 40–60 Gy required to achieve 50% reduction in TLG
Levillain et al. 2018 [29]	Liver-only mCRC progressing after chemotherapy ($n = 24$)	Partition model	^{90}Y-PET 3D voxel-based	TLG for each target lesion measured on FDG PET/CT	Cut-offs of 39 Gy and 60 Gy predict non-metabolic response and high-metabolic response, respectively
Willowson et al. 2017 [30]	Unresectable mCRC progressing despite chemotherapy ($n = 22$)	Modified BSA	^{90}Y-PET 3D voxel-based	Peak standardised uptake value and TLG	Approximately 50 Gy derived as the critical threshold for a significant response (> 50% reduction in TLG)
Stigari et al. 2010 [31]	Unresectable HCC ($n = 73$)	BSA	^{90}Y-BECT 3D voxel-based	CR and PR according to RECIST	Median dose to achieve CR/PR was 99 Gy
Hermann et al. 2020 [32]	Locally advanced unresectable HCC ($n = 121$)	BSA	^{99m}Tc-MAA SPECT 3D voxel-based	Retrospective assessment of OS in group receiving tumour radiation-absorbed dose < 100 Gy or ≥ 100 Gy	Median OS 14.1 month in those receiving ≥ 100 Gy Median OS 6.1 months in those receiving < 100 Gy
Garin et al. 2019 [52]	HCC with PVT	Multiple	MIRD and 3D voxel-based	Review of studies using treatment response and OS	Predictor of response and OS with a threshold of 100–120 Gy
Levillain et al. 2019 [4]	Unresectable and chemorefractory ICC ($n = 58$)	BSA or partition model	^{99m}Tc-MAA SPECT 3D voxel-based	OS	Median OS was 5.5 months when BSA used (mean radiation dose to tumour of 38 Gy) Median OS was 14.9 months when partition model was used (mean radiation dose to tumour of 86 Gy)
Chansanti et al. 2017 [33]	Unresectable mNET ($n = 15$)	Partition model	^{99m}Tc-MAA SPECT MIRD	CR and PR according to mRECIST	Cut-off of ≥ 191.3 Gy for tumour-specific absorbed dose predicted tumour response with 93% specificity < 72.8 Gy predicted non-response with 100% specificity

BSA, body surface area; *CR*, complete response; *CT*, computed tomography; *FDG*, fluorodeoxyglucose; *^{99m} Tc-MAA*, technetium-99 m labelled macroaggregated albumin; *HCC*, hepatocellular carcinoma; *ICC*, intrahepatic cholangiocarcinoma; *mCRC*, metastatic colorectal cancer; *mNET*, metastatic neuroendocrine tumour; *OS*, overall survival; *PET*, positron emission tomography; *BECT*, ^{90} Y bremsstrahlung emission computed tomography; *PR*, partial response; *TLG*, total lesion glycolysis

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Systemic Therapy Improvements Will Render Locoregional Treatments Obsolete for Patients with Cancer with Liver Metastases

Satya Das, MD, MSCI*, Jordan Berlin, MD

Surg Oncol Clin N Am 2021