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
Vanderbilt University Medical Center

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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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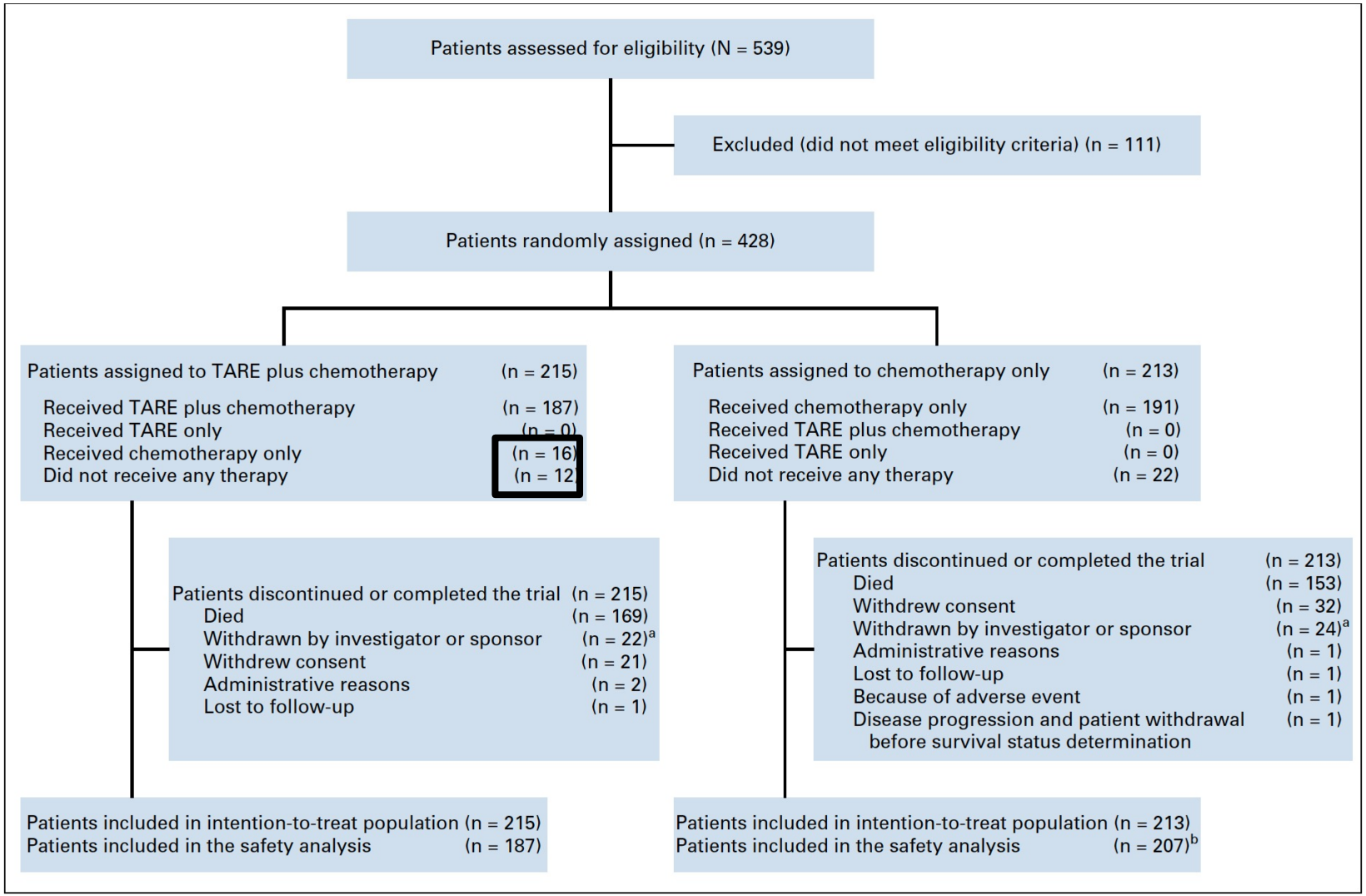
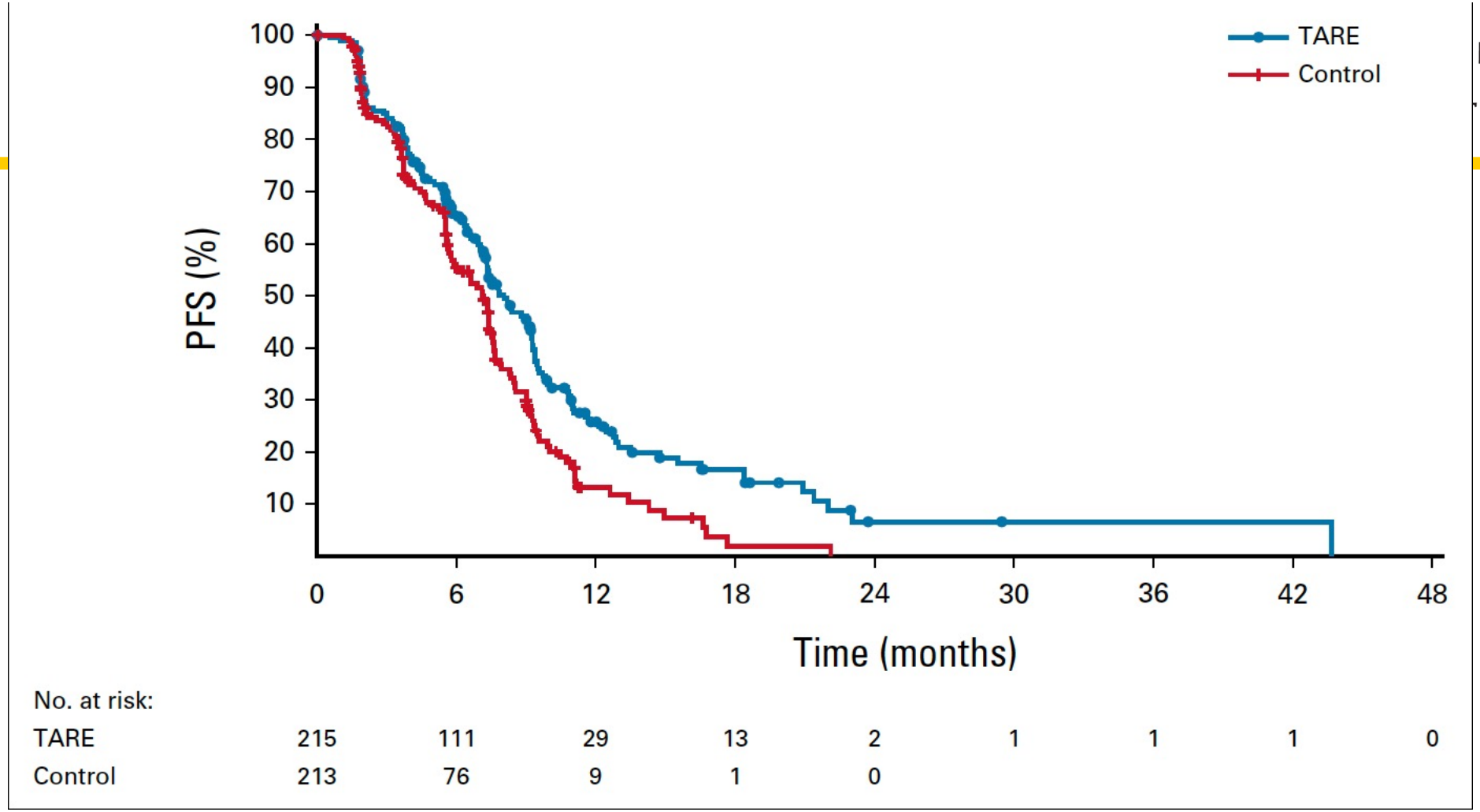
CONSORT Diagram

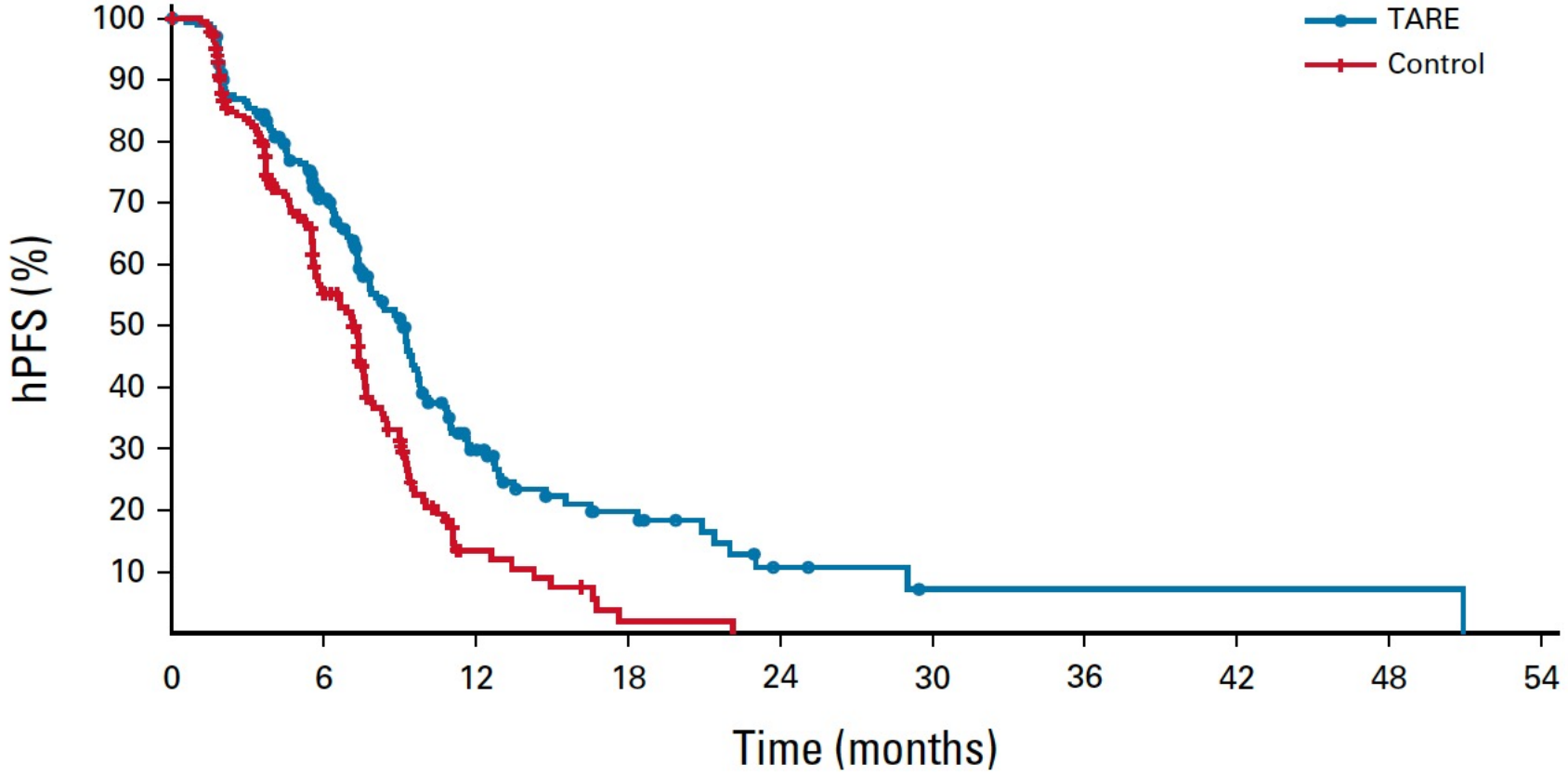


	TARE (N=215)
Patients receiving TARE	187 (87%)
Reasons for not receiving TARE	28 (13%)
Lung Shunt	4 (1.8%)
Gastrointestinal deposition	6 (2.8%)
Investigator decision	6 (2.8%)
Patient decision	1 (0.4%)
Early withdrawal	6 (2.8%)
Missing	5 (2.3%)

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

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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

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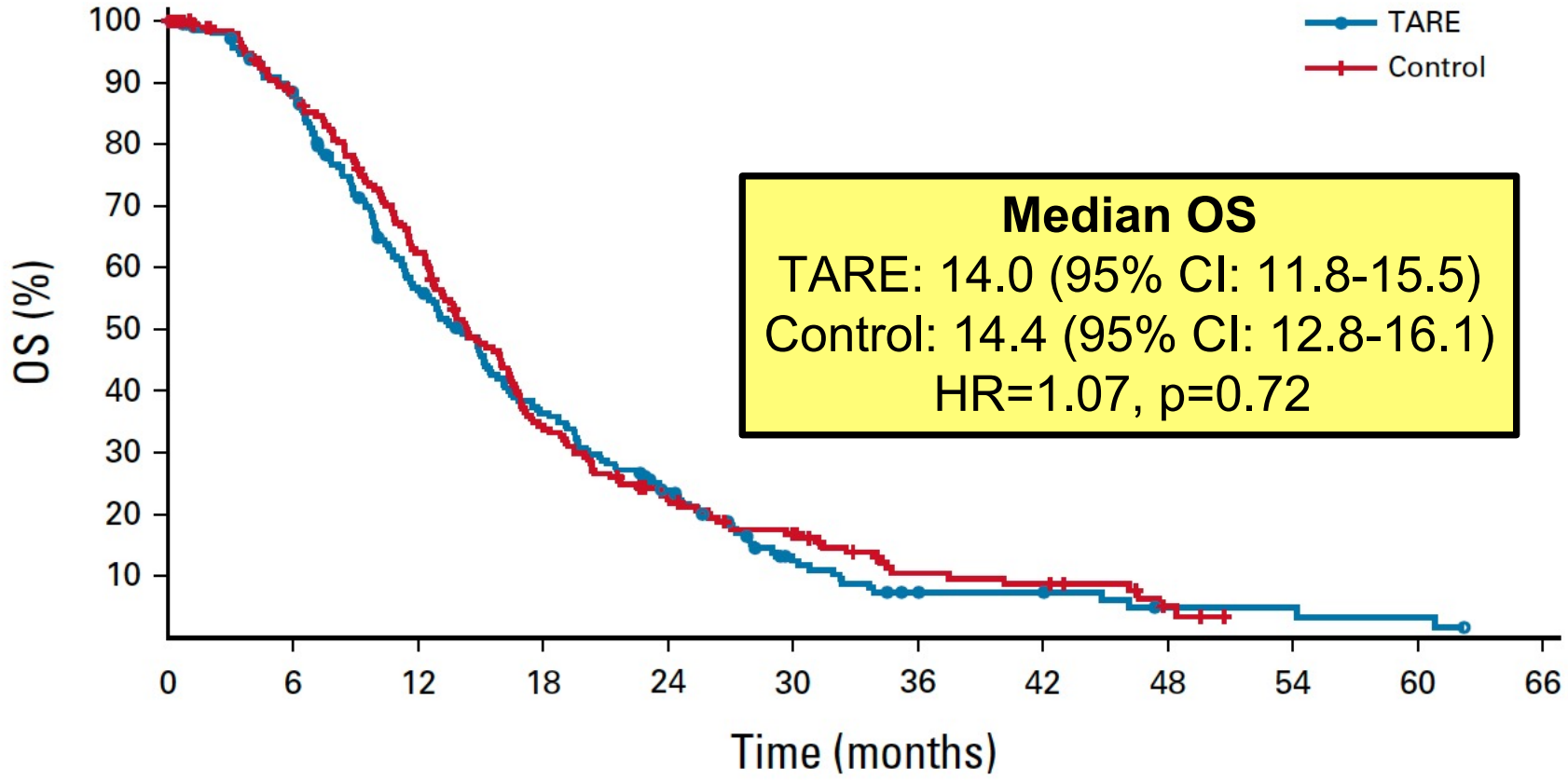
editorials

Transarterial Radioembolization in Patients With Unresectable Colorectal Cancer Liver Metastases

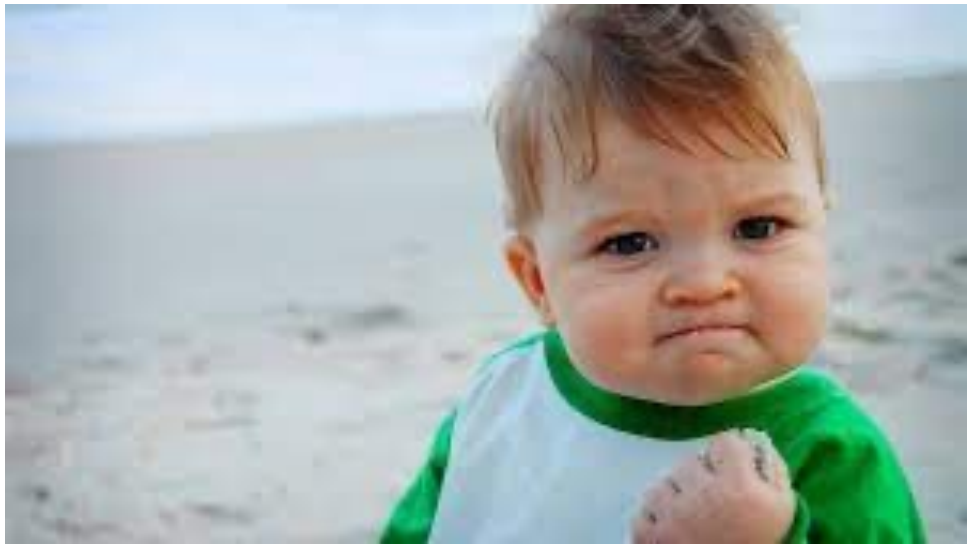
Robert W. Lentz, MD[1] and Wells A. Messersmith, MD[1]

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.



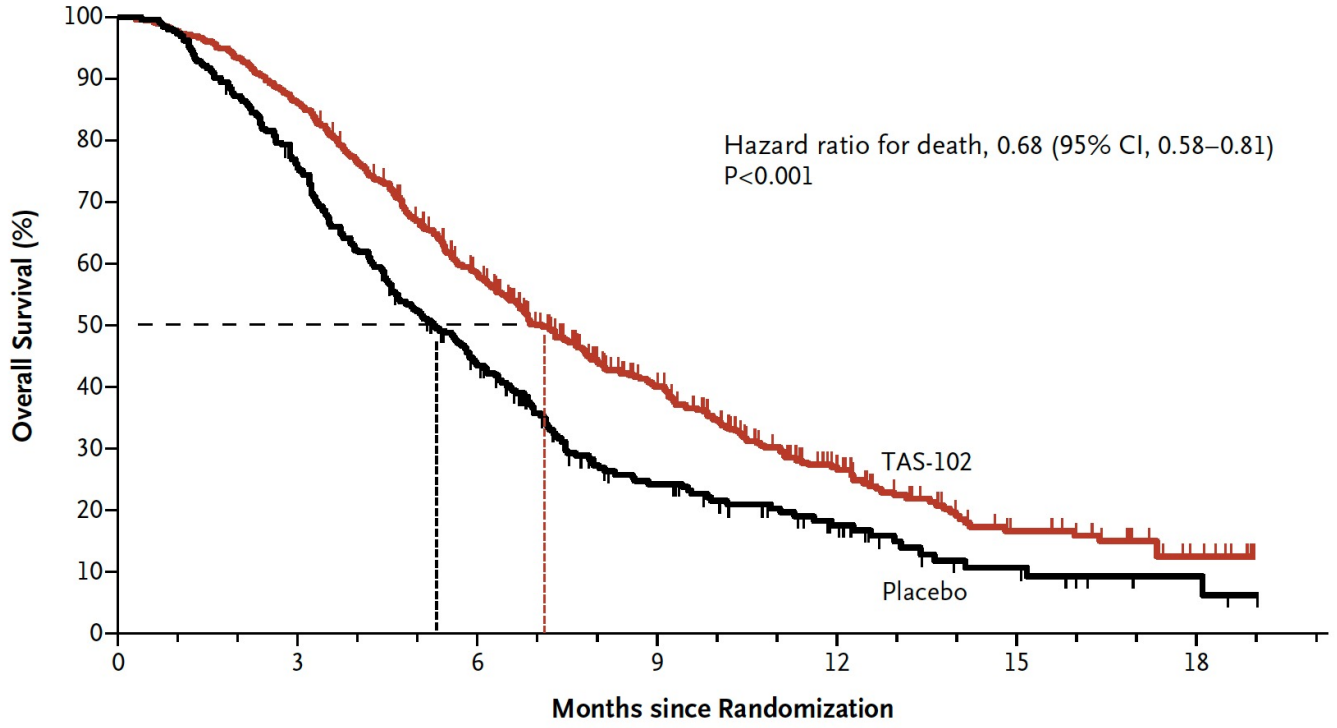
Median OS
TARE: 14.0 (95% CI: 11.8-15.5)
Control: 14.4 (95% CI: 12.8-16.1)
HR=1.07, p=0.72

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

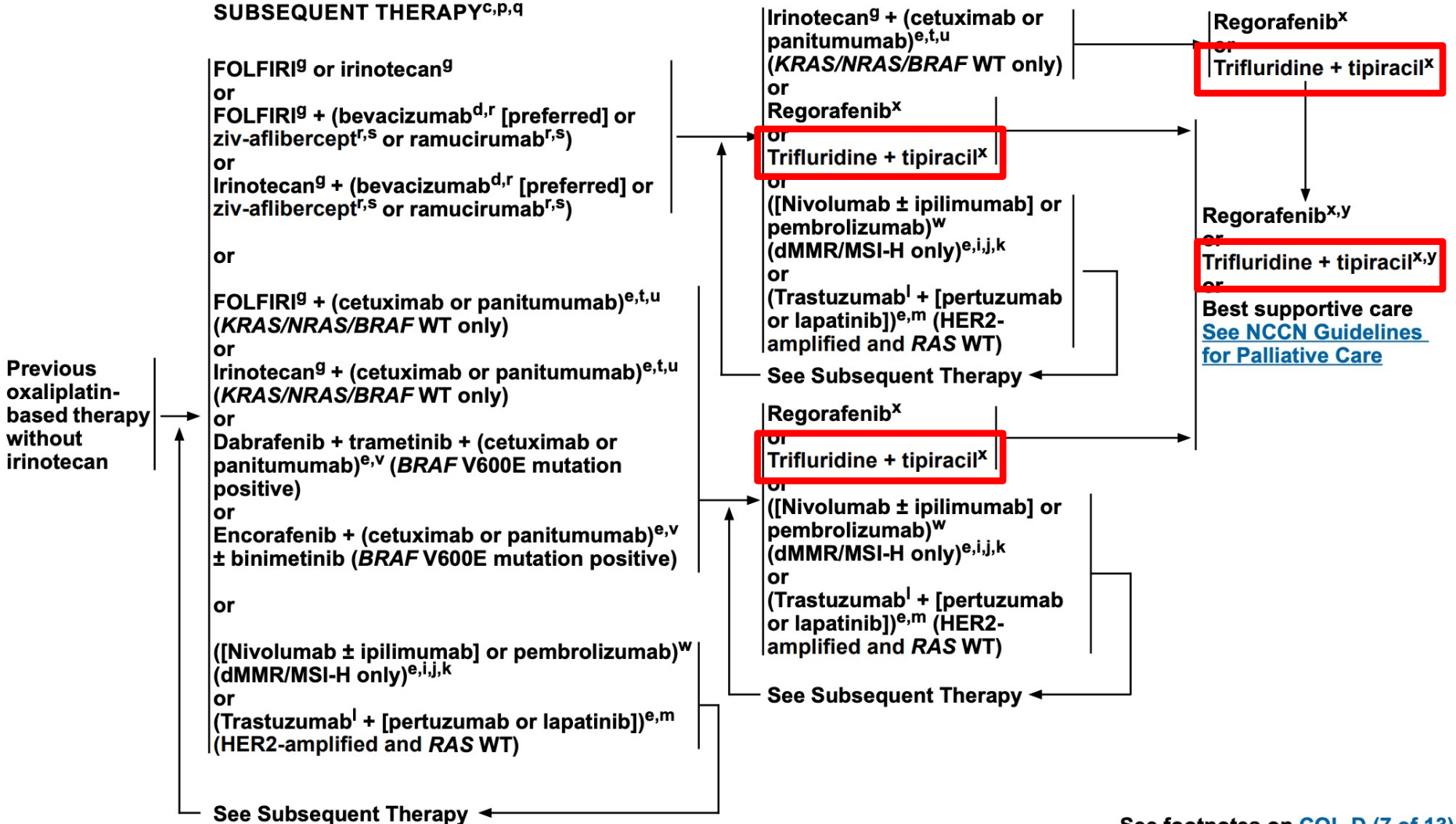
OS is the ONLY thing that matters



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

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]

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76 CRC
15 NET

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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