Locoregional Strategies for Downstaging HCC to Transplantation

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Disclosures

Personal financial interests:

Advisory role: Sirtex Medical, Ipsen, BMS, Oncosil, Bayer, New B Innovation, MSD, BTG Plc, Guerbet, Roche, AUM Bioscience, L.E.K. Consulting, AstraZeneca, Eisai, Genentech, IQVIA, Abbott

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Leadership roles:

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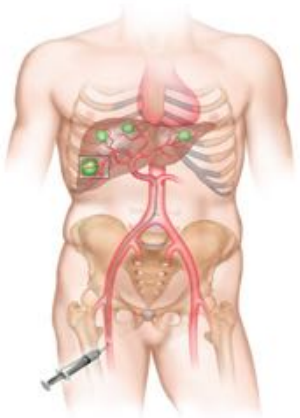
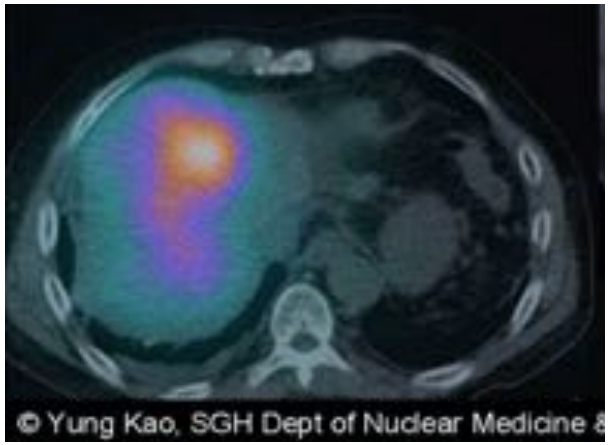
As in Resection:

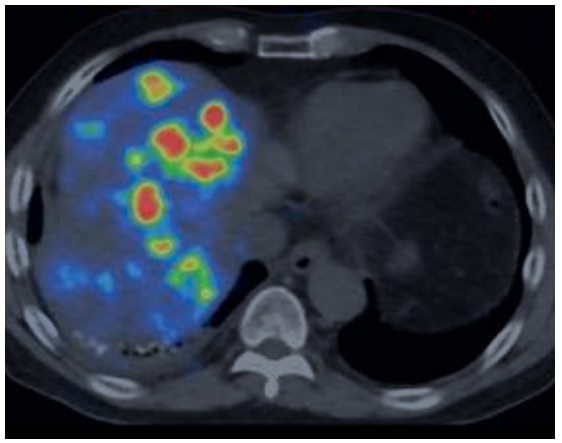
What is Rationale behind Downstaging of HCC to Transplantation

1. Convert HCC with high tumor burden beyond transplant criteria to HCC with lower tumor burden within transplant criteria – *selecting for good biology*

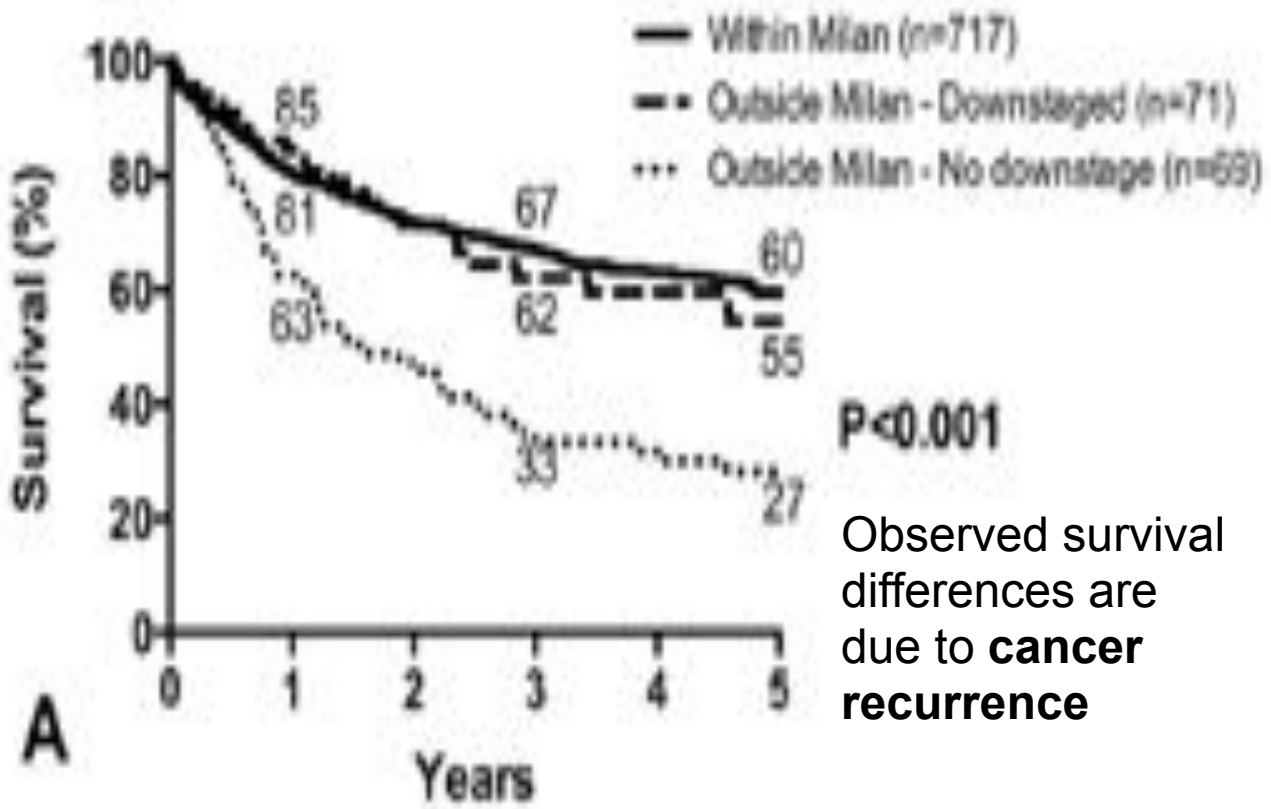
2. To improve tumor biology prior to liver transplantation and thus improve survival – *beyond selecting for good biology*







Is successful down-staging a surrogate for good Biology



Observed survival differences are due to **cancer recurrence**

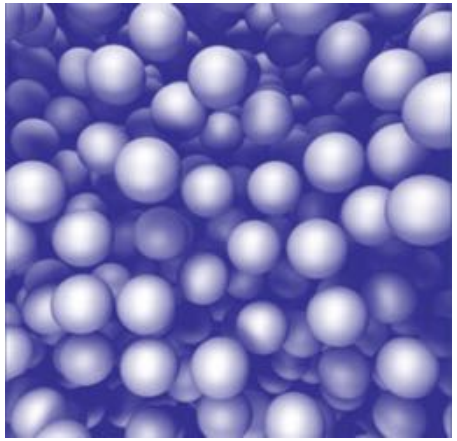
Kaplan-Meier recurrence-free survival curves with 1-, 3-, and 5-year estimates comparing (A) recipients within MC, outside MC and downstaged to MC, and outside MC not downstaged to MC

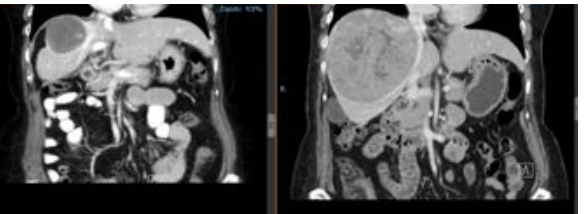
- **71** patients originally beyond MC and successfully **down-staged** to MC had **equivalent recurrence-free survival** at 1, 3, and 5-years compared with **717** patients originally within MC
- Showed **significantly superior survival** compared with **69** patients beyond MC who were not down-staged
- **Higher incidence of *microvascular invasion*** in recipients beyond MC who could not be down-staged, compared with recipients down-staged to MC (49% vs 22%, p = 0.012)

Agopian et al., 2014

Currently 2 ways to Downstage HCC using loco-regional therapy

- **Trans-arterial chemo-embolisation (TACE):**
  - widely used
  - used mainly in *HCC, NETs* (includes DC Beads)
- **Selective Internal Radiation Therapy (SIRT):**
  - also known as Radio-embolization **(TARE)**
  - higher disease control
  - Suitable for portal vein invasion
  - SIR-Sphere®, Thera-Sphere®

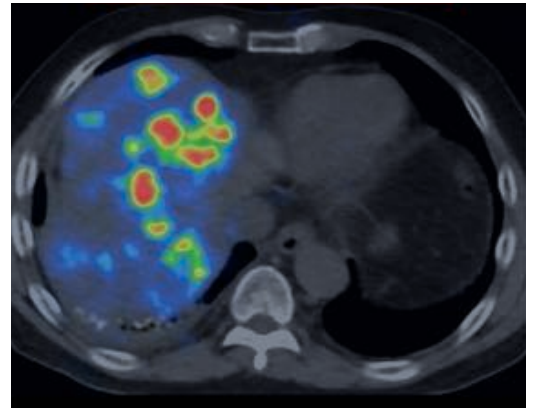




SIR-Spheres®

TheraSphere®

Efficacy of SIRT Y90 versus TACE in down-staging HCC



PREVIOUS NEXT

Original Research
Vascular and Interventional Radiology

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^{90}Y Radioembolization versus Drug-eluting Bead Chemoembolization for Unresectable Hepatocellular Carcinoma: Results from the TRACE Phase II Randomized Controlled Trial

Elisabeth Dhondt, Bieke Lambert[1], Laurens Hermie, Lynn Huyck, Peter Vanlangenhove, Anja Geerts, Xavier Verhelst, Maridi Aerts[2], Aude Vanlander, Frederik Berrevoet, Roberto Ivan Troisi[3], Hans Van Vlierberghe, Luc Defreyne

Author Affiliations

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Null Hypothesis: There would be no difference in time to progression between Y90 and TACE

- **Background**: BCLC only recommends **TACE** for intermediate or unresectable HCC without metastasis but retrospective studies have shown that selective internal radiation therapy (**SIRT**) with yttrium-90 microspheres aka transarterial radioembolization (RE) can offer superior outcomes.
- **DEB-TACE** was chosen as comparator as it offered consistent methodology compared to conventional TACE, and but equal clinical outcomes and less AE than conventional TACE
- **Therasphere** was choses are the Y90 carrier, aiming for an absorbed dose of **120 Gy**
- **Design**: open-label, single center, superiority, randomized controlled trial (NCT01381211)
- **Primary outcome**: Time to overall tumor progression **(TTP)** according to mRECIST
- **Secondary endpoints**:
  - Overall survival (OS)
  - Progression free survival (PFS)

Statistical Analysis

- **Assumed effect size:** 20% improvement in TTP with Y90
- Type I error: 5% (two-sided) statistical power: 90%
- **Sample size** required: 136 patients randomized in a 1:1 ratio

- **Interim analysis**: at 45 events (progression)
  - Null hypothesis will be rejected when HR > 2.60 or < 0.39 or when p < 0.0024
- **Final analysis**:
  - Null hypothesis will be rejected when HR >1.49 or < 0.67 or when p < 0.049
- **TTP** to be estimated with **Kaplan-Meier** method and compared using log-rank test
- **HR** to be compared using **Cox-proportional hazard model**

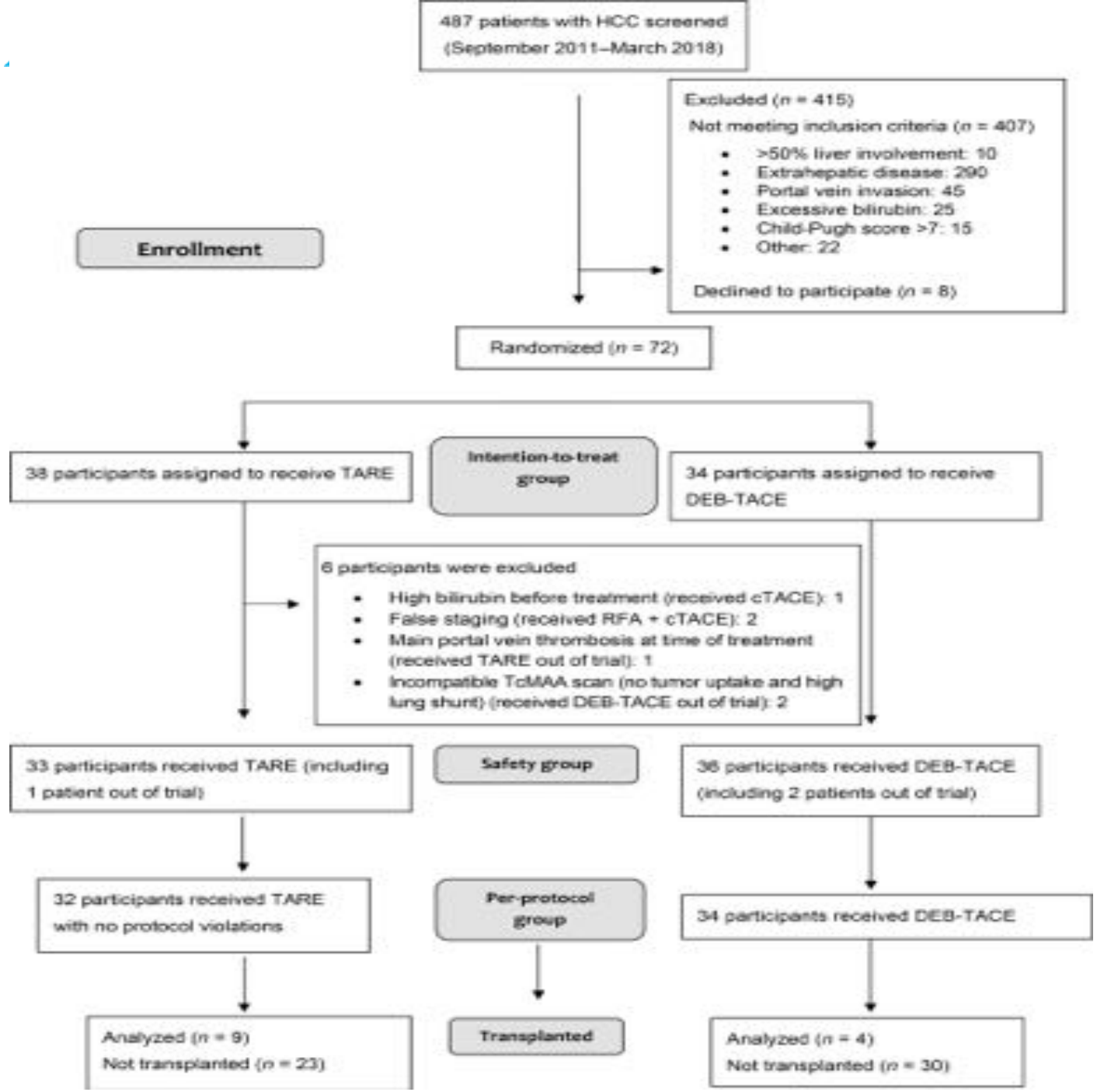
Participants

INCLUSION CRITERIA

- HCC diagnosed using **EASL guidelines**
- **BCLA A or B** not amendable to resection, transplantation or ablation
- **ECOG 0 -1**
- **Child-Pugh score** up to 7

EXCLUSION CRITERIA

- > 50% of liver involved with HCC
- Extra-hepatic disease
- Invasion of main, right or left portal vein
- Serum bilirubin > 34 micromol/L (or over 44 micromole/L if only single segment involved.
- Child-Pugh score > 7



Trial flow diagram. cTACE = conventional transarterial chemoembolization, DEB = drug-eluting bead, HCC = hepatocellular carcinoma, RFA = radiofrequency ablation, TACE = transarterial chemoembolization, TARE = transarterial radioembolization, TcMAA = technetium 99m macroaggregated albumin.

Median FU **TARE**: 28 months
Median FU **TACE**: 15.6 months

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Table 1: Baseline Characteristics in the ITT and PP Groups

Characteristic	ITT Group			PP Group		
	TARE (n = 38)	DEB-TACE (n = 34)	*P* Value	TARE (n = 32)	DEB-TACE (n = 34)	*P* Value
Age (y)*	67 (63–72) [51, 85]	68 (61–71) [38, 84]	.81	68 (64–74) [54, 85]	68 (61–71) [38, 84]	.53
Sex			>.99			>.99
M	33 (87)	30 (88)		28 (88)	30 (88)	
F	5 (13)	4 (12)		4 (12)	4 (12)	
Race			.60			>.99
White	37	32		31	32	
Black	1	2		1	2	
Cause of HCC			.56			.79
Alcohol use disorder	27 (71)	24 (70)		21 (66)	24 (70)	
Nonalcoholic steatohepatitis	1 (2.6)	2 (5.9)		1 (3.1)	2 (5.9)	
Hemochromatosis	1 (2.6)	2 (5.9)		1 (3.1)	2 (5.9)	
Viral	5 (13)	5 (15)		5 (16)	5 (15)	
Unknown	4 (10)	1 (2.9)		4 (12)	1 (2.9)	
Child-Pugh score			.24			.43
A	36 (95)	29 (85)		30 (94)	29 (85)	
B	2 (5.3)	5 (15)		2 (6.3)	5 (15)	
ECOG performance status			.73			>.99
0	34 (90)	29 (85)		28 (88)	29 (85)	
1†	4 (11)	5 (15)		4 (13)	5 (15)	
α-fetoprotein (ng/dL)			.73			.71
<400	33 (87)	28 (82)		28 (88)	28 (82)	
≥400	4 (10)	5 (15)		3 (9.4)	5 (15)	
Data missing	1 (2.6)	1 (2.9)		1 (3.1)	1 (2.9)	
Total bilirubin (μmol/L)*	11.1 (8.6–20.5) [3.4, 27.4]	13.7 (10.3–18.1) [1.9, 27.4]	.46	11.1 (8.6–20.5) [3.4, 27.4]	13.7 (10.3–18.1) [1.9, 27.4]	.46
BCLC tumor staging			.52			.73
A	7 (18)	4 (12)		5 (16)	4 (12)	
B	31 (82)	30 (88)		27 (84)	30 (88)	
Prior resection	3 (7.9)	5 (15)	.50	2 (6.3)	5 (15)	.26
Prior ablation	1 (2.6)	1 (2.9)		0 (0)	1 (2.9)	
Tumor burden			>.99			.81
Unilobar	19 (50)	16 (47)		15 (47)	16 (47)	
Bilobar	19 (50)	18 (53)		17 (53)	18 (53)	
Tumor load			.10			.14
≤5 nodules	18 (47)	23 (68)		15 (47)	23 (68)	
>5 nodules	20 (53)	11 (32)		17 (53)	11 (32)	
Lesions			.08			.07
Solitary	8 (21)	4 (12)		7 (22)	4 (12)	
Multifocal	30 (79)	30 (88)		25 (78)	30 (88)	
2–3 foci	10	19		8	19	
4–10 foci	17	10		14	10	
>10 foci	3	1		3	1	
Largest tumor size (cm)			.27			.17
Median with IQR	4.2 (3.1–5.6)	4.7 (3.7–6.7)		4.2 (3.2–5.6)	4.7 (3.7–6.7)	
Mean with 95% CI	4.6 (3.9, 5.3)	5.3 (4.5, 6.2)		4.5 (3.9, 5.1)	5.3 (4.5, 6.2)	
Minimum and maximum	1.5, 12.8	1.3, 15.0		2.0, 9.4	1.3, 15.0	

- Majority were **multifocal**
  - 79% vs 88%
- **Median diameter** of larger tumour
  - 4.3 cm vs 4.7 cm

Table 2: Treatment Data in the Safety Group

Treatment Parameter of Interest	TARE (n = 33)*	DEB-TACE (n = 36)†	*P* Value
Time from randomization to first treatment (d)‡	24 (20–29) [7, 118]	7.5 (4.0–15) [1, 69]	<.001§
Treatment sessions per participant			<.001‖
1	16	2	
2	17	11	
3	0	12	
4	0	9	
5	0	2	
Median	2	3	
No. of participants with a lesion treated more than once			
Target lesion 1	NA	19/36 (53)	
Target lesion 2	NA	11/32 (34)	
Nontarget lesions	NA	14/28 (50)	
Time interval between treatment sessions (d)‡	46 (41–54) [32, 84]	39 (29–49) [6, 87]	.03§
Total treatment period (d)‡	32 (0–46) [0, 84]	82 (56–122) [0, 266]	<.001§
Approach			>.99‖
Unilobar	16	17	
Bilobar	17	19	
Treatment approach			<.001‖
Selective	7	29	
Lobar	10	3	
Near whole liver	7	4	
Whole liver	9	0	

Note.—Unless otherwise specified, data are numbers of participants, and data in parentheses are percentages. DEB = drug-eluting bead, NA = not applicable, TACE = transarterial chemoembolization, TARE = transarterial radioembolization.

* Thirty-two participants as per protocol plus one participant originally randomized to the TARE arm but who received TARE out of trial (main portal vein thrombosis).

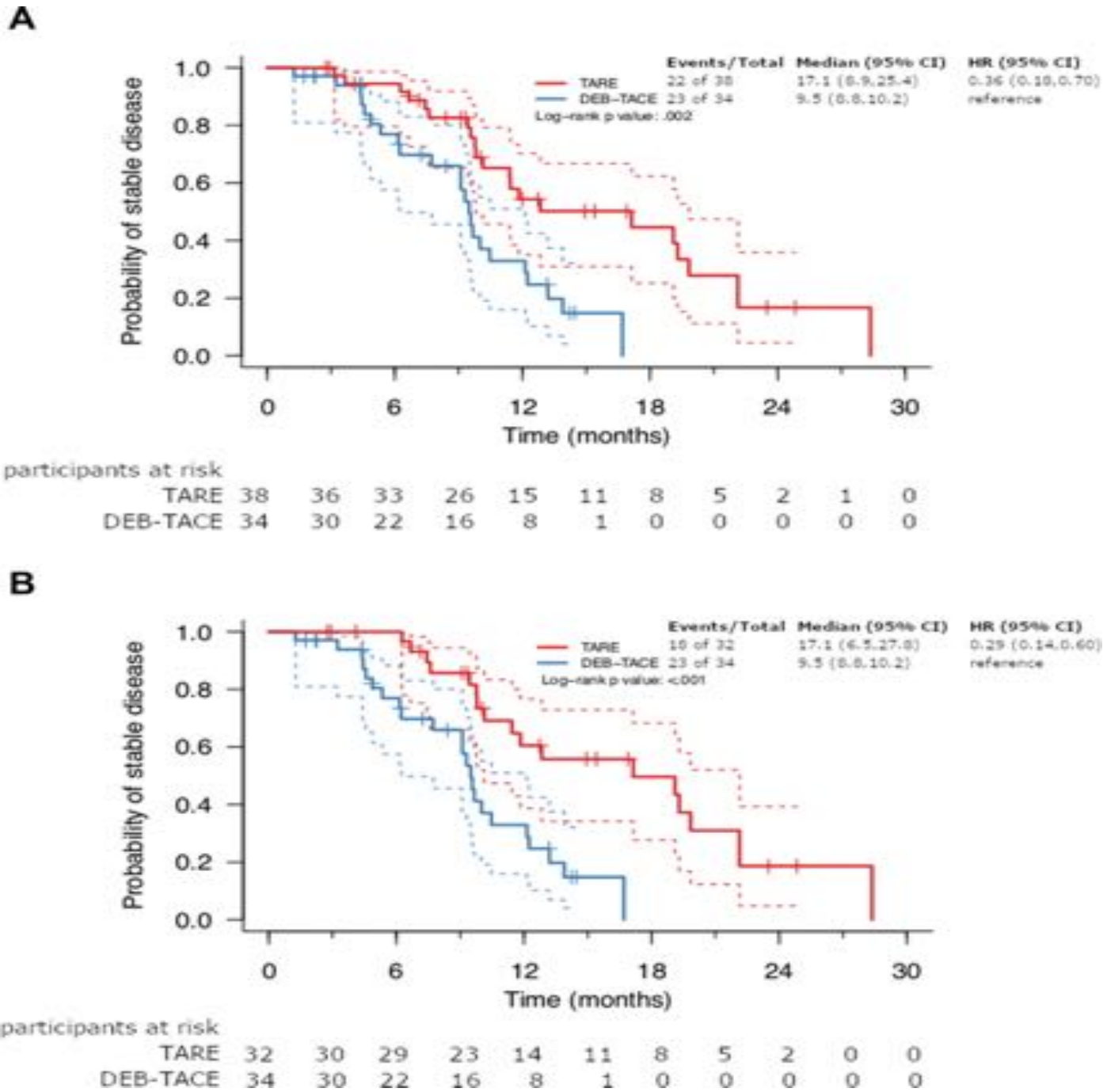
† Thirty-four participants as per protocol plus two participants originally randomized to the TARE arm but who received DEB-TACE out of trial (incompatible technetium 99m–labeled macroaggregated albumin scintigraphy).

‡ Data are medians, with IQRs in parentheses and minimum and maximum values in brackets.

§ *P* values were calculated by using the Mann-Whitney *U* test.

‖ *P* values were calculated by using the Fisher exact test.

Interim analysis: at 45 events (progression) – primary outcome



Efficacy outcomes in participants in the Transarterial Radioembolization versus Chemoembolization for the Treatment of Hepatocellular Carcinoma (i.e TRACE) trial randomized to transarterial radioembolization (**TARE**) or drug-eluting bead (DEB) transarterial chemoembolization (**TACE**). Kaplan-Meier plots show **time to overall tumor progression** in:

(A) the **intention-to-treat group** **17.1 vs 9.5 months** p = 0.002 **HR= 0.35** (0.15 – 0.70)
(B) the **per-protocol group** **17.1 vs 9.5 months** p < 0.001 **HR = 0.29** (0.14 – 0.60)

P values were calculated by using the log-rank test. Dashed lines indicate 95% CIs. HR = hazard ratio.

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https://doi.org/10.1148/radiol.211806

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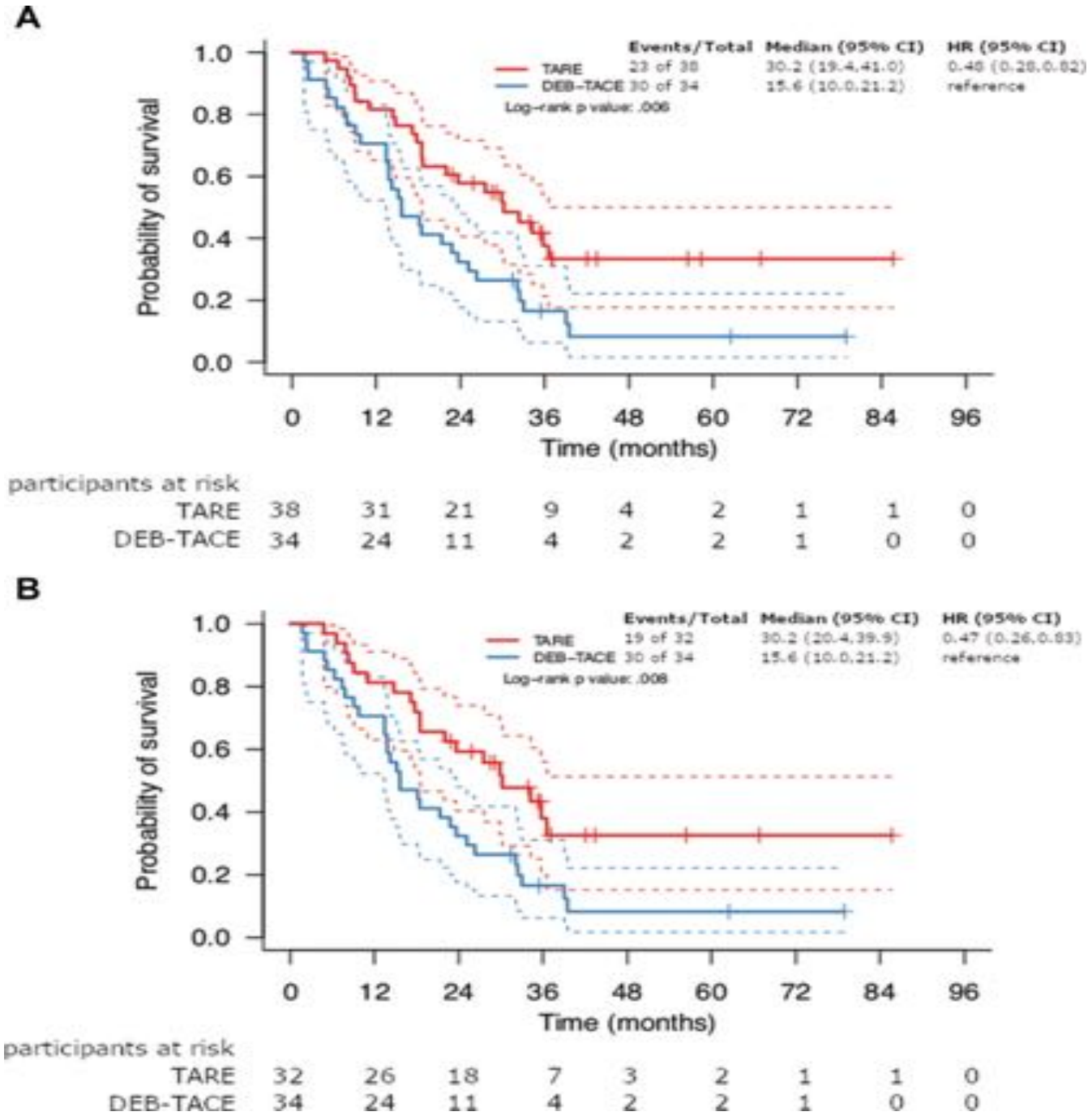
Statistical Analysis

- **Assumed effect size:** 20% improvement in TTP with TARE
- Type I error: 5% (two-sided) statistical power: 90%
- **Sample size** required: 136 patients randomized in a 1:1 ratio

- **Interim analysis**: at 45 events (progression)
  - Null hypothesis will be rejected when HR > 2.60 or < 0.39 or when p < 0.0024
- **Final analysis**:
  - Null hypothesis will be rejected when HR >1.49 or < 0.67 or when p < 0.049
- **TTP** to be estimated with **Kaplan-Meier** method and compared using log-rank test
- **HR** to be compared using **Cox-proportional hazard model**

Interim analysis: at 45 events (progression) – secondary outcome



Survival outcomes in participants in the Transarterial Radioembolization versus Chemoembolization for the Treatment of Hepatocellular Carcinoma (i.e TRACE) trial randomized to transarterial radioembolization (**TARE**) or drug-eluting bead (DEB) transarterial chemoembolization (**TACE**). Kaplan-Meier plots show overall survival in:

(A) the **intention-to-treat group** **30.2 vs 15.6 months** p=0.006 HR=0.48 (0.28 – 0.82)
(B) the **per-protocol group**. **30.2 vs 15.6 months** p=0.008 HR 0.47 (0.26 – 0.83)

P values were calculated by using the log-rank test. Dashed lines indicate 95% CIs. HR = hazard ratio.

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Table 3: SAEs until 6 Months after Treatment and 30-day Mortality in the Safety Group

No. and Type of SAEs	TARE (n = 33)	DEB-TACE (n = 36)	P Value*
No. of participants with at least one SAE†	13 (39)	19 (53)	.47
Total no. of SAEs	20	34	
No. of grade 3 toxicities	19	29	
Blood and lymphatic system disorders	0	1	
Musculoskeletal and connective tissue disorders	0	2	
Nervous system disorders	0	1	
Cardiac disorders	0	2	
Renal and urinary disorders	5	5	
Hepatobiliary disorders	14	12	
Respiratory, thoracic, and mediastinal disorders	0	6	
No. of participants with grade 5 toxicities	1 (3.0)	5 (14)	.21
Thirty-day mortality	0 (0)	3 (8.3)	.24

Note.—Data in parentheses are percentages. DEB = drug-eluting bead, SAE = serious adverse event, TACE = transarterial chemoembolization, TARE = transarterial radioembolization.

* P values were calculated by using the Fisher exact test.

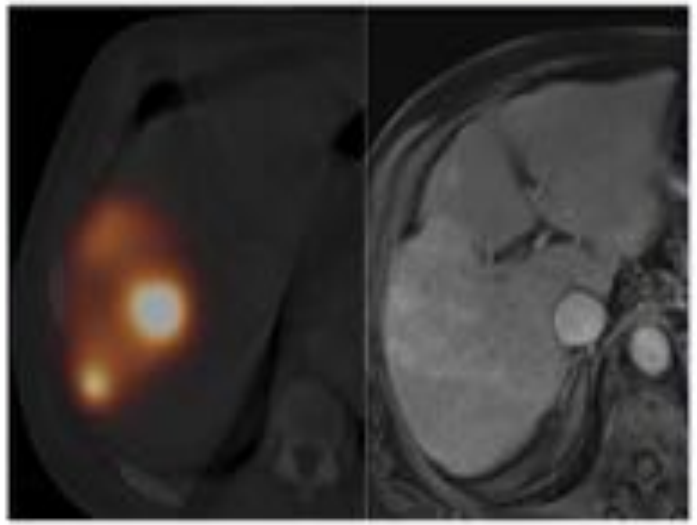
† Adverse event grade 3–5 according to the Common Terminology Criteria for Adverse Events version 4.03.

Table 4: Grade 5 Serious Adverse Events

Participant No.	Treatment Arm	Treatment Session Closest to Event	Days Since Last Treatment	Days Since First Treatment	CTCAE Category	Detailed Information	Relation with Treatment
1	TARE	Second	87	122	Hepatobiliary	Radiation-induced liver disease	Definite
2	DEB-TACE	Third	86	142	Unknown cause	Sudden death while listed for transplant	Unlikely
3	DEB-TACE	Second	6	59	Infections and infestations	Septic shock	Definite
4	DEB-TACE	Second	78	112	Infections and infestations	Liver abscess with septic shock	Definite
5	DEB-TACE	Third	16	180	Infections and infestations	Metabolic lactate acidosis and acute kidney injury	Definite
6	DEB-TACE	First	24	24	Cardiac	Non–ST segment elevation myocardial infarction	Unlikely

Note.—CTCAE = Common Terminology Criteria for Adverse Events version 4.03, DEB = drug-eluting bead, TACE = transarterial chemoembolization, TARE = transarterial radioembolization.

^{90}Y Radioembolization versus Drug-eluting Bead Chemoembolization for Unresectable Hepatocellular Carcinoma: Results from the TRACE Phase II Randomized Controlled Trial



Left: SPECT image after technetium 99m–labeled macroaggregated albumin administration confirms tracer uptake by hepatocellular carcinomas (HCCs). Right: No HCCs could be identified on T1-weighted VIBE at 15 months.

- This prospective phase II randomized controlled trial (TRACE) showed the median time to progression was 17.1 months in the yttrium 90 radioembolization (TARE) arm (*n* = 38) versus 9.5 months in the drug-eluting bead (DEB) transarterial chemoembolization (TACE) arm (*n* = 34) (hazard ratio [HR], 0.36; *P* = .002), justifying early termination of the study.

- Median overall survival was 30.2 months after TARE versus 15.6 months after DEB-TACE (HR, 0.48; *P* = .006).

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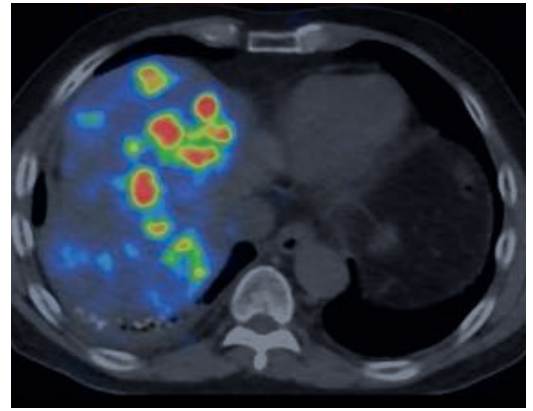
Radiology

Real World data in Efficacy of SIRT Y90 versus TACE in down-staging HCC to transplant criteria



Multicenter Study > Gastroenterology. 2021 Nov;161(5):1502-1512.
doi: 10.1053/j.gastro.2021.07.033. Epub 2021 Jul 28.

Downstaging Outcomes for Hepatocellular Carcinoma: Results From the Multicenter Evaluation of Reduction in Tumor Size before Liver Transplantation (MERITS-LT) Consortium

Neil Mehta [1], Catherine Frenette [2], Parissa Tabrizian [3], Maarouf Hoteit [4], Jennifer Guy [5], Neehar Parikh [6], T Tara Ghaziani [7], Renu Dhanasekaran [7], Jennifer L Dodge [8], Brahma Natarajan [9], Matthew L Holzner [3], Leana Frankul [2], Wesley Chan [9], Austin Fobar [6], Sander Florman [3], Francis Y Yao [10]

Affiliations + expand

PMID: 34331914 PMCID: PMC8545832 DOI: 10.1053/j.gastro.2021.07.033
Free PMC article

Abstract

Background & aims: United Network of Organ Sharing (UNOS) has adopted uniform criteria for downstaging (UNOS-DS) of hepatocellular carcinoma (HCC) before liver transplantation (LT), but the downstaging success rate and intention-to-treat outcomes across broad geographic regions are unknown.

Table 1.

United Network for Organ Sharing (UNOS) Down-staging Protocol

Inclusion Criteria
HCC exceeding Milan criteria but meeting one of the following: 1. Single lesion 5.1–8 cm 2. 2–3 lesions each ≤ 3 cm with the sum of the maximal tumor diameters ≤ 8 cm 3. 4–5 lesions each ≤ 3 cm with the sum of the maximal tumor diameters ≤ 8 cm Plus absence of vascular invasion or extra-hepatic disease based on cross-sectional imaging
Criteria for Successful Down-staging
Residual tumor size and diameter within Milan criteria (1 lesion ≤5 cm, 2–3 lesions ≤3 cm) a) Only viable tumor(s) are considered; tumor diameter measurements should not include the area of necrosis from tumor directed therapy b) If there is more than one area of residual tumor enhancement, then the diameter of the entire lesion should be counted towards the overall tumor burden
Criteria for Down-staging Failure and Exclusion from Liver Transplant
1. Progression of tumor(s) to beyond inclusion/eligibility criteria for down-staging (as defined above) 2. Tumor invasion of a major hepatic vessel based on cross-sectional imaging 3. Lymph node involvement by tumor or extra-hepatic spread of tumor 4. Infiltrative tumor growth pattern 5. Per current UNOS policy, if AFP ≥ 1000 ng/mL then transplant cannot be undertaken unless AFP level decreases to < 500 ng/mL with local-regional therapy
Timing of Liver Transplant in Relation to Down-staging
1. There should be a minimum observation period of 3 months of disease stability from successful down-staging to LT 2. Per current UNOS policy, patient must remain within Milan criteria for 6 months after successful down-staging before receiving MELD exception points

- The Milan criteria remained the gold standard for liver transplant candidate selection in the US
- In 2017 UNOS/OPTN standardized criteria for downstaging
- This offered the opportunity for large multi-center downstaging studies
- This is the *first prospective multi-center downstaging study* from the MERITS-LT consortium of 7 centers from 4 UNoS regions

Table 2.

Baseline and Tumor Treatment Characteristics of the Down-staging Group

Study Variable	Overall (n=209)
Median Age (IQR)	63 (58–67)
Male (%)	178 (85.2)
Race/Ethnicity (%) Caucasian Hispanic Asian African American	 125 (60.0) 46 (22.0) 23 (11.2) 10 (4.9)
Liver Disease Etiology (%) Hepatitis C Alcohol NAFLD Hepatitis B Other	 125 (59.8) 33 (15.8) 23 (11.0) 16 (7.7) 12 (5.7)
Median CTP Score (IQR)* Child's A (CTP 5–6, %) Child's B (CTP 7–9, %) Child's C (CTP 10–15, %)	6 (5–6) 151 (75.5) 43 (21.5) 6 (3.0)
Median MELD (IQR)	9 (7–11)
Median AFP ng/mL (IQR) >100 (%) ≥1000 (%)	13 (5–74) 48 (25.0) 24 (11.5)
Median AFP-L3% (IQR)**	10.3 (4.6–16.9)
Median DCP (IQR)**	2.5 (0.5–19.9)
Median NLR (IQR)	2.5 (1.7–3.8)
Median PLR (IQR)	86.3 (66.0–117.4)
Number of HCC Lesions 1 lesion 2–3 lesions 4–5 lesions	 67 (32.1) 113 (54.1) 29 (13.9)
Initial Total Tumor Diameter (cm) (IQR)	6.2 (5.6–7.3)
Number LRT Received (%) 1 2 3 4 ≥5	 44 (21.1) 53 (25.4) 41 (19.6) 25 (12.0) 46 (22.0)
Type of LRT Received (%) Received 1+ TACE Received 1+ Y-90 Received 1+ Ablation	 169 (80.9) 84 (40.2) 59 (28.2)
Type of 1st LRT Received (%) TACE Y-90 Other	 132 (63.1) 62 (29.7) 15 (7.2)

*n=200

**n=83

- 7 high-volume LT centers in 4 UNOS regions with HCC meeting UNOS-DS eligibility criteria were enrolled from 2016–2019 and prospectively followed.
- The specific type of LRT used was at the discretion of each of the center's multidisciplinary tumor boards – TACE= 132 Y90 = 62
- Primary outcome was probability of and factors associated with successful down-staging and protocol dropout due to tumor progression or liver-related death.
- Secondary outcomes included probability of LT, post-LT survival, and HCC recurrence.
- This is not an RCT.
- There is no defined sample-size

Table 3.

Clinical Characteristics and Outcomes by Type of 1st Down-staging Treatment

Variable	TACE (n=132)	Y-90 (n=62)	p-value
Median Age (IQR)	63 (58–67)	63 (60–66)	0.65
Male (%)	122 (92.4)	45 (72.6)	<0.001
CTP Class (%)* Child's A Child's B Child's C	 91 (72.2) 29 (23.0) 6 (4.8)	 50 (80.6) 12 (19.4) 0	0.16
Median MELD (IQR)	9 (7–12)	8.5 (7–10)	0.04
Median AFP ng/mL (IQR)	11.7 (4.9–58.0)	17.9 (5.7–238.4)	0.11
Number of HCC Lesions 1 lesion 2–3 lesions 4–5 lesions	 32 (24.2) 80 (60.6) 20 (15.2)	 30 (48.4) 25 (40.3) 7 (11.3)	0.003
Initial Total Tumor Diameter (cm) (IQR)	6.3 (5.6–7.3)	6.3 (5.8–7.3)	0.67
# Lesions Treated with 1st LRT (IQR)	1 (1–2)	1 (1–2)	0.07
mRECIST Response to 1st LRT Complete Response Partial Response Stable Disease Progressive Disease	 37 (28.0) 69 (52.3) 14 (10.6) 12 (9.1)	 17 (27.4) 30 (48.4) 7 (11.3) 8 (12.9)	0.67
Median #LRT Received (IQR)	3 (2–3)	2 (1–3)	0.006
Ever Down-Staged (%) Time to Down-Staged (mo) (IQR)	113 (85.6) 2.9 (1.3–5.6)	50 (80.6) 2.4 (1.7–4.6)	0.38 0.73
Down-Staging Protocol Dropout (%) Time to Dropout (mo) (IQR)	48 (36.4) 8.4 (5.8–13.0)	20 (32.3) 10.2 (6.6–14.7)	0.58 0.33
LT (%) Time to LT (mo) (IQR) AFP prior to LT (IQR)	44 (33.3) 18.3 (10.8–25.2) 4.3 (3.0–21.7)	14 (22.6) 13.9 (11.2–19.2) 9.2 (6.0–16.0)	0.18 0.19 0.18
Explant Pathology (%) Completely Necrotic Tumor(s) Beyond Milan Explant Microvascular Invasion	9 (20.5) 19 (43.2) 9 (20.5)	4 (30.8) 3 (23.1) 1 (7.7)	0.76 0.44 0.29

*n=188

Intention-to-Treat Outcomes

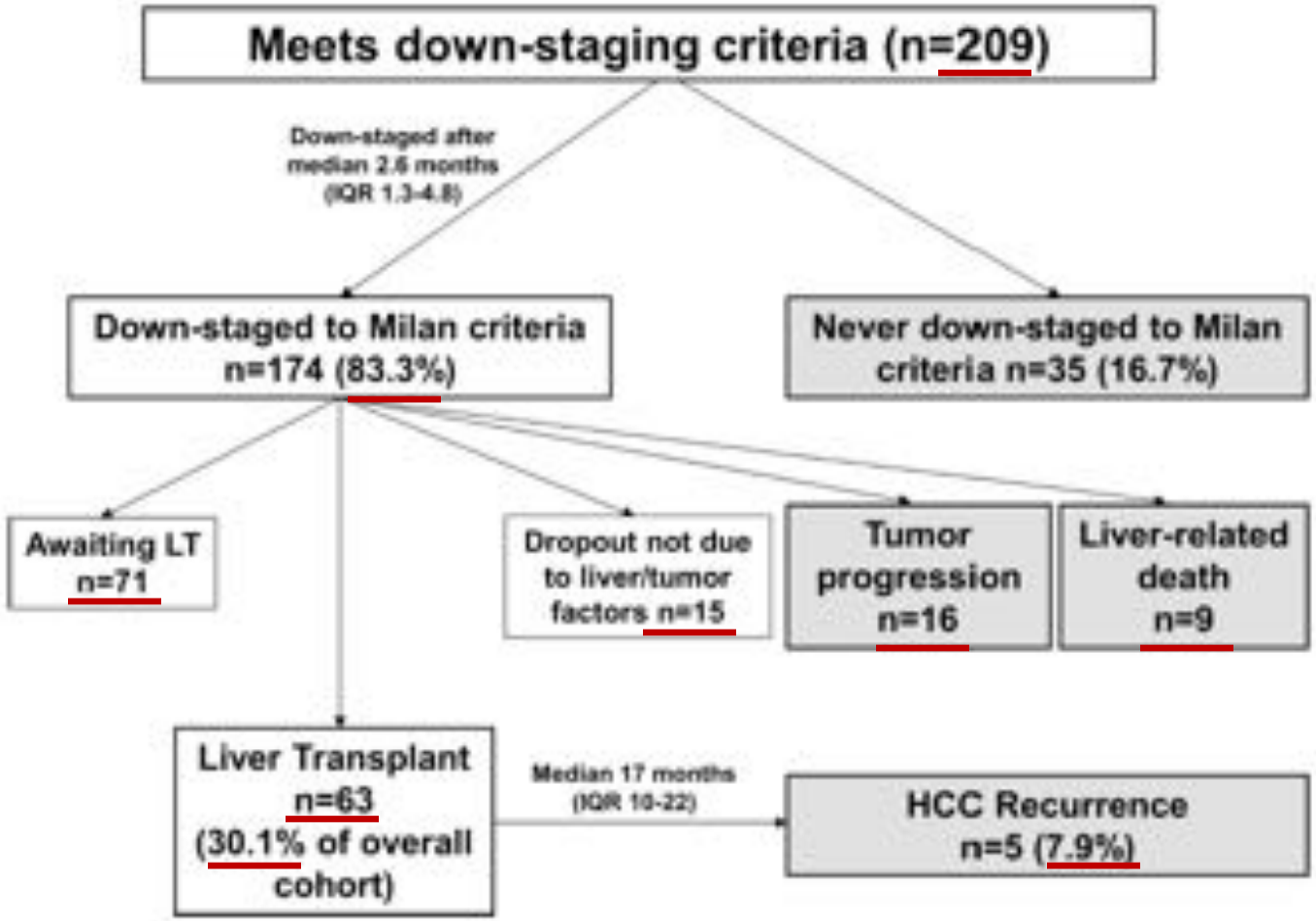


Figure 1.
Summary of the intention-to-treat outcome of the 209 patients enrolled in the prospective down-staging protocol

Intention-to-treat Outcomes

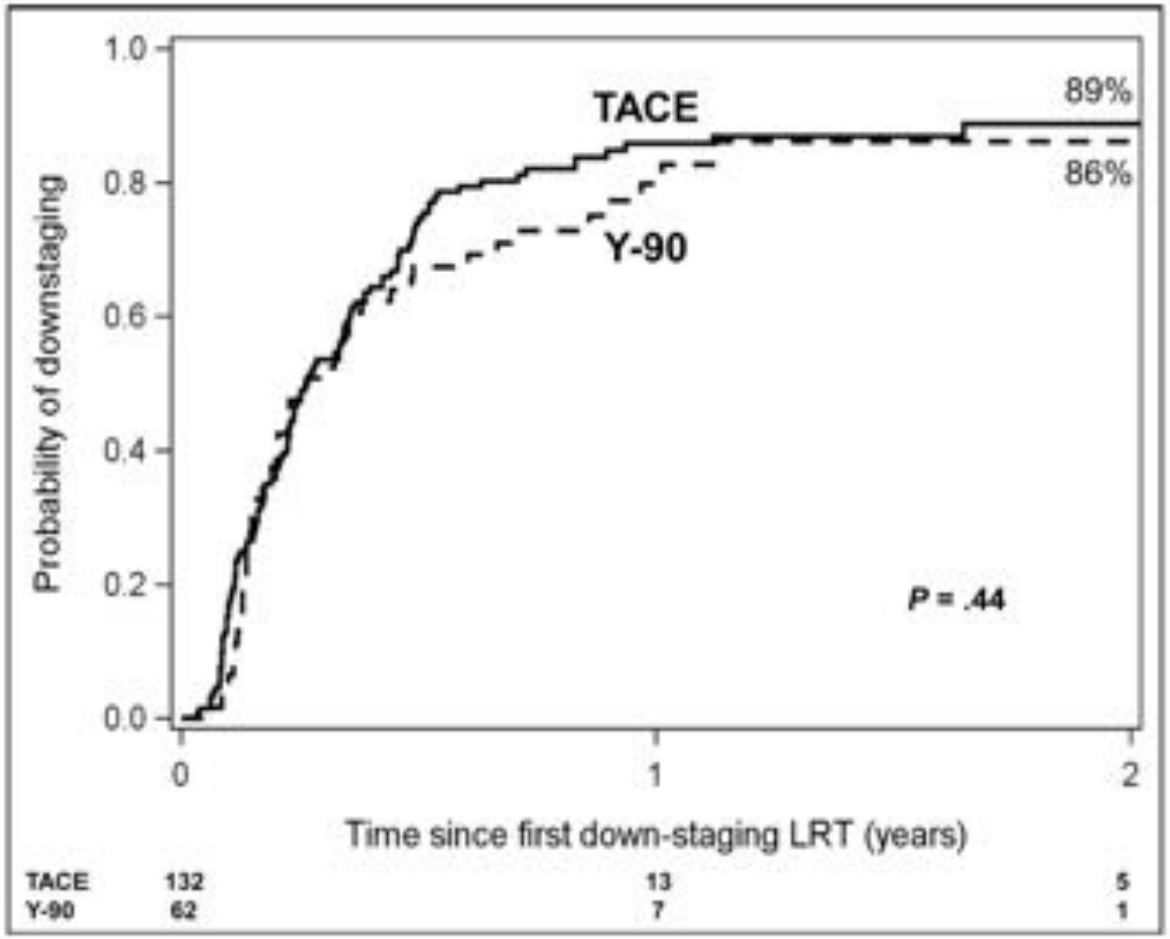


Figure 2.
Kaplan-Meier probability of successful down-staging by type of first local-regional therapy (TACE versus Y-90)

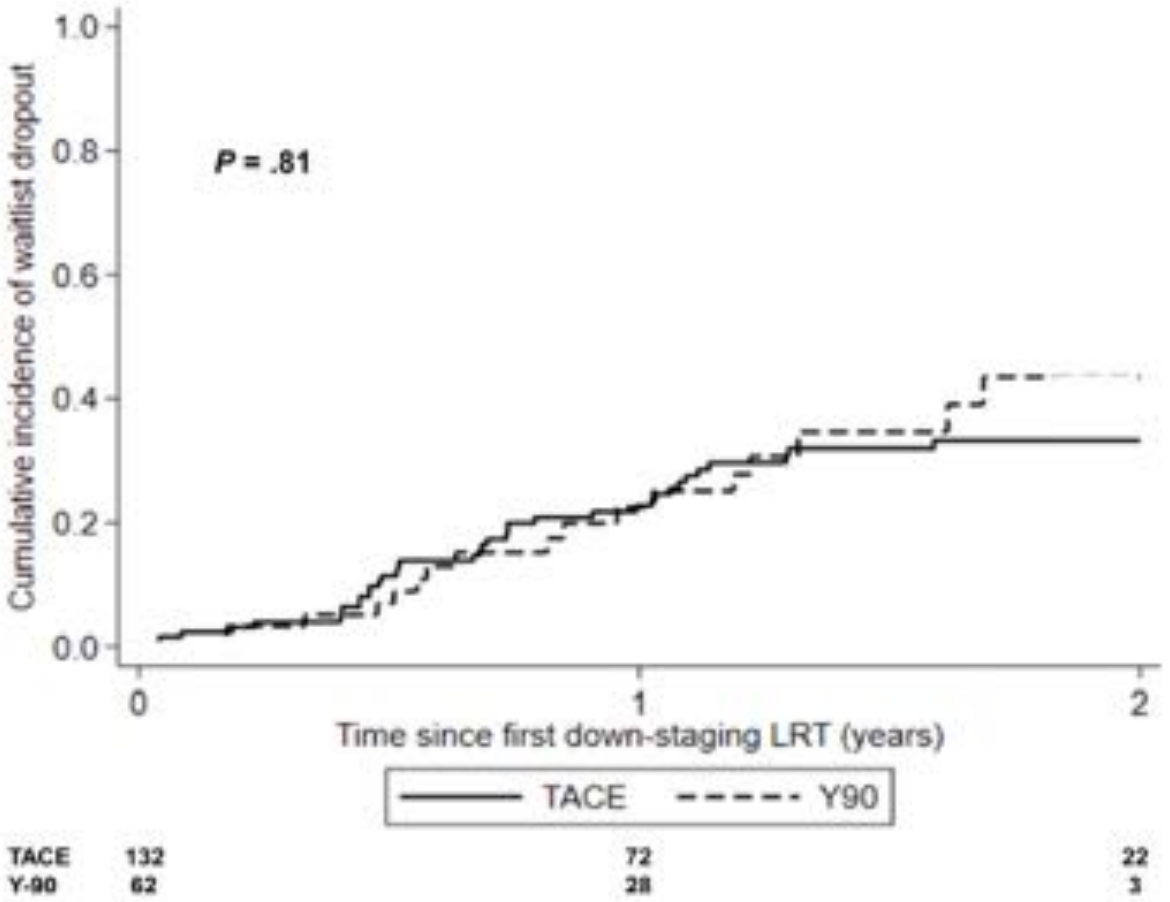


Figure 3.
Kaplan-Meier probability of protocol dropout from date of first down-staging treatment

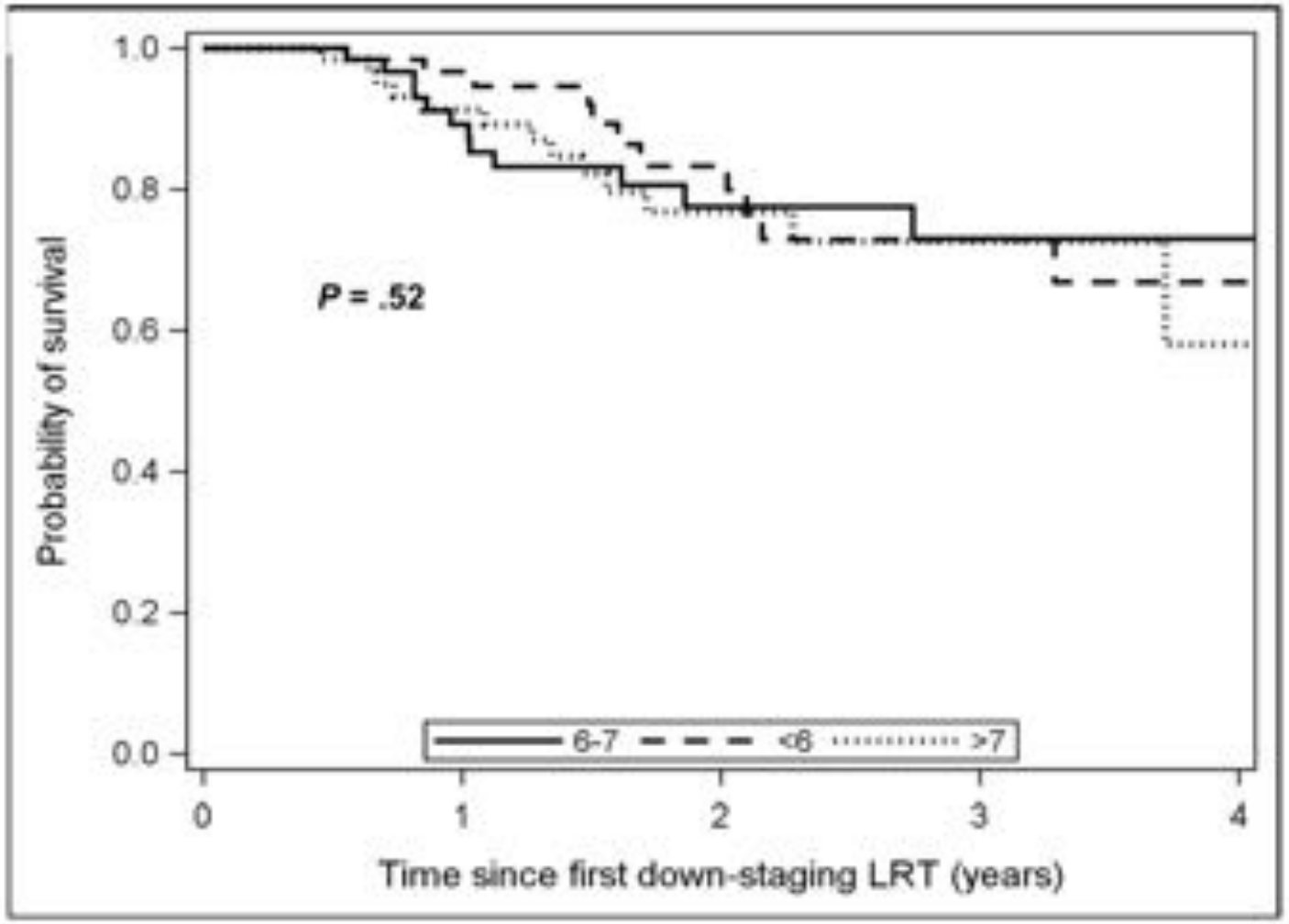
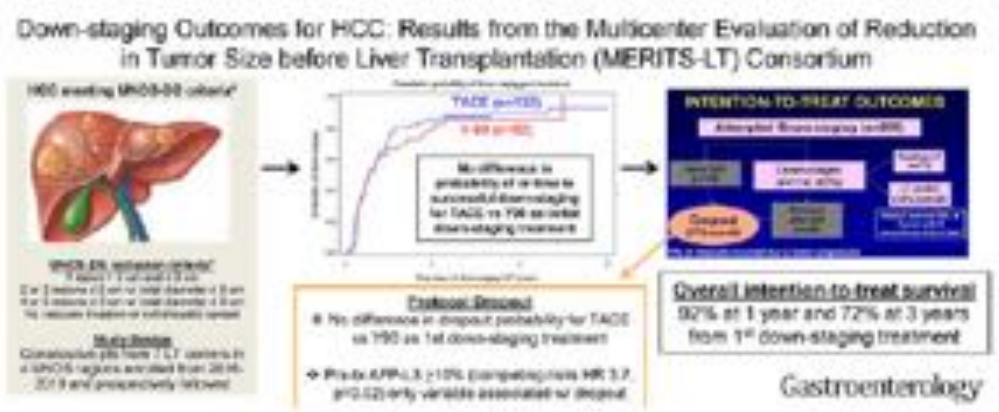


Figure 4.
Kaplan-Meier probability of intention-to-treat survival from first down-staging treatment stratified by initial total tumor burden



Conclusion: between TACE and Y90

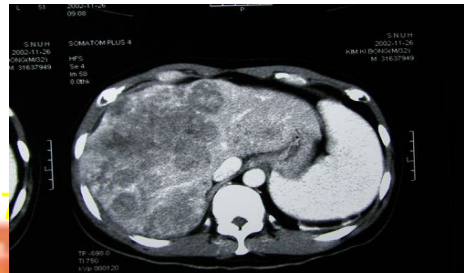
- No difference in protocol dropout
- No difference in downstaging
- No difference in recurrence after transplant

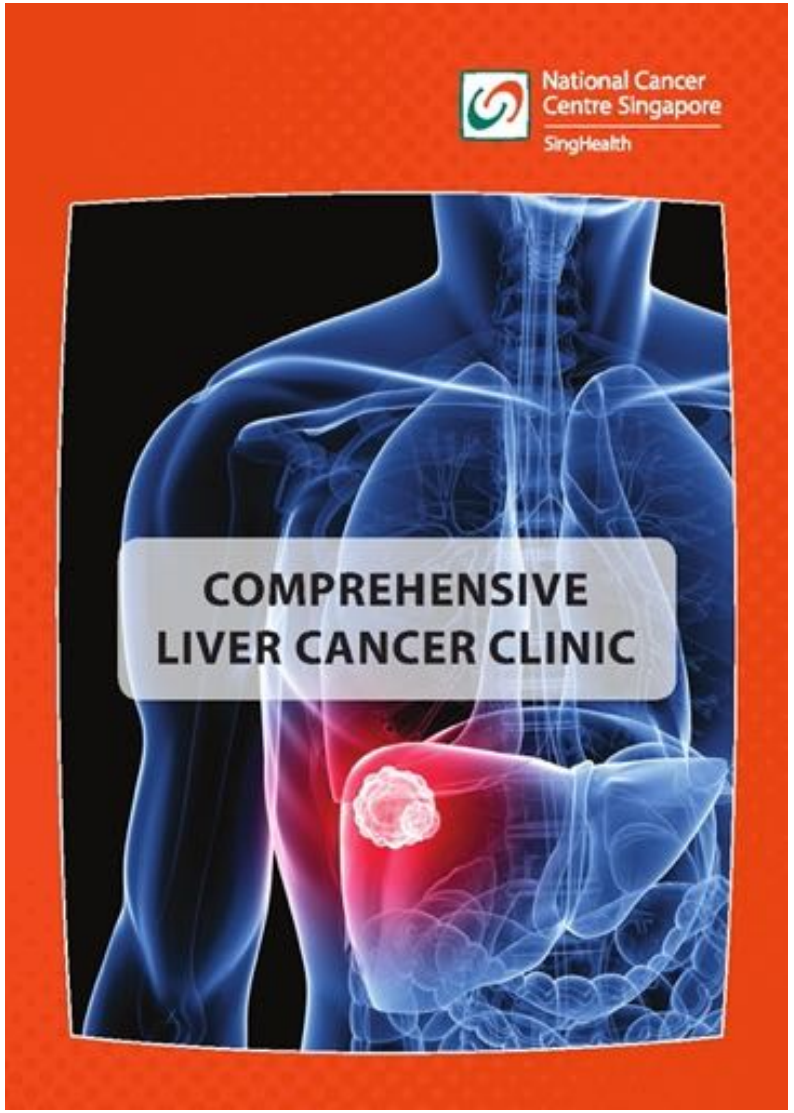
Conclusions

- RCT shows Y90 superior to TACE in terms of
  - **Recurrence-free survival** : **17.1 vs 9.5 months** p = 0.002 **HR= 0.35** (0.15 – 0.70)
  - **Overall survival** : **30.2 vs 15.6 months** p=0.006 HR=0.48 (0.28 – 0.82)

- The MERITS-LT study (not an RCT) shows that between TACE and Y90
  - No difference in protocol dropout
  - No difference in downstaging
  - No difference in recurrence after transplant

- Efficacy of downstaging is not necessarily the same as efficacy in downstaging to transplantation

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Thank You!