Y90 RADIOEMBOLIZATION FOR HCC : CURRENT STATUS

CIO 2020

William S Rilling MD, FSIR
Professor of Radiology and Surgery
Director, Vascular and Interventional Radiology
Medical College of Wisconsin

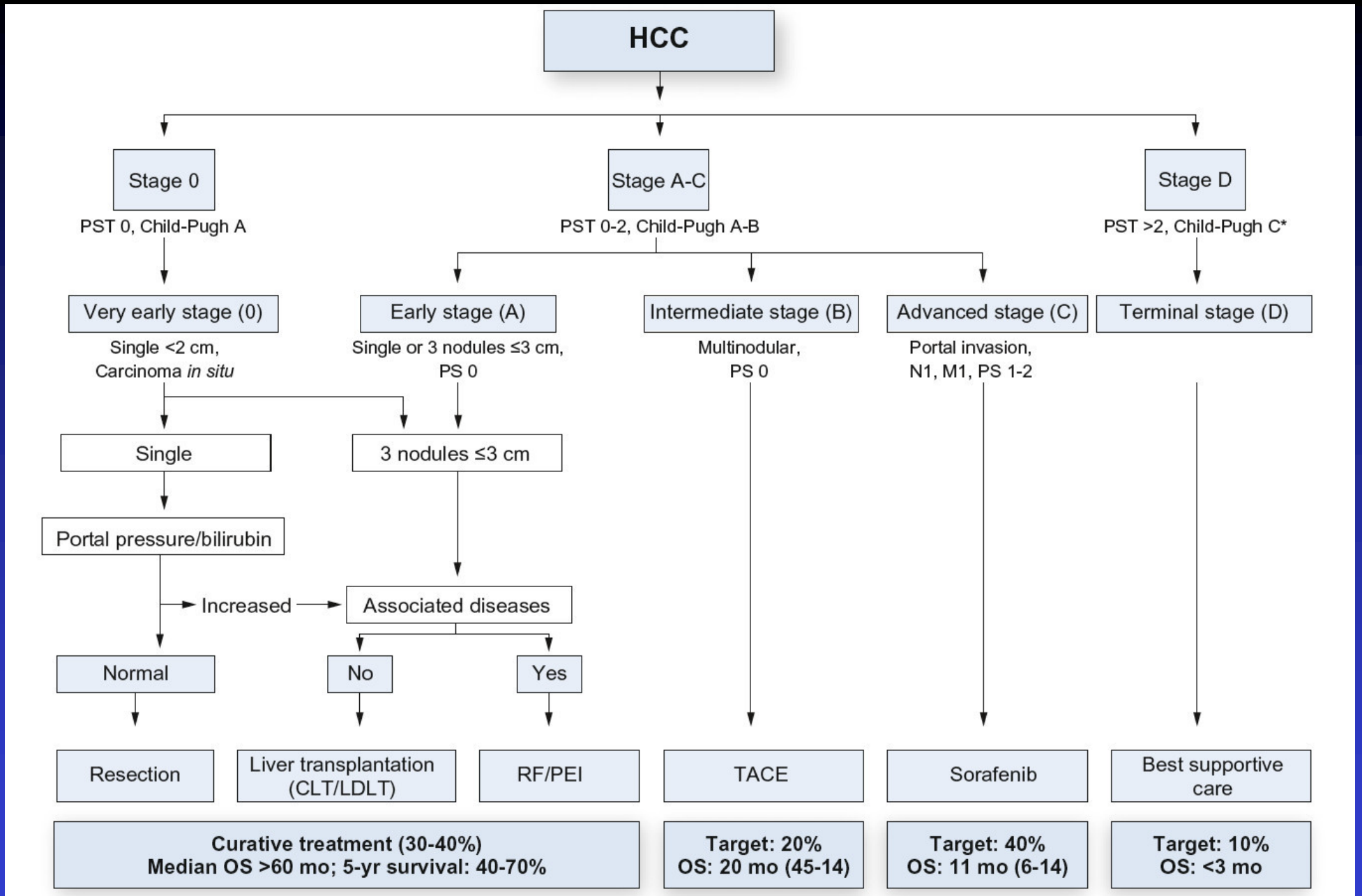
MEDICAL COLLEGE OF WISCONSIN

DISCLOSURES

- Research support : Siemens Healthcare
- Consultant : B Braun, Boston Scientific, Varian, Terumo, BD Bard
- Will be discussing off label use of devices

Y90 IN HCC 2020 : REFINEMENTS IN DOSIMETRY AND PATIENT SELECTION

- Curative intent therapy
- Comparisons to cTACE
- Refinements in dosimetry
- Bridge to transplant

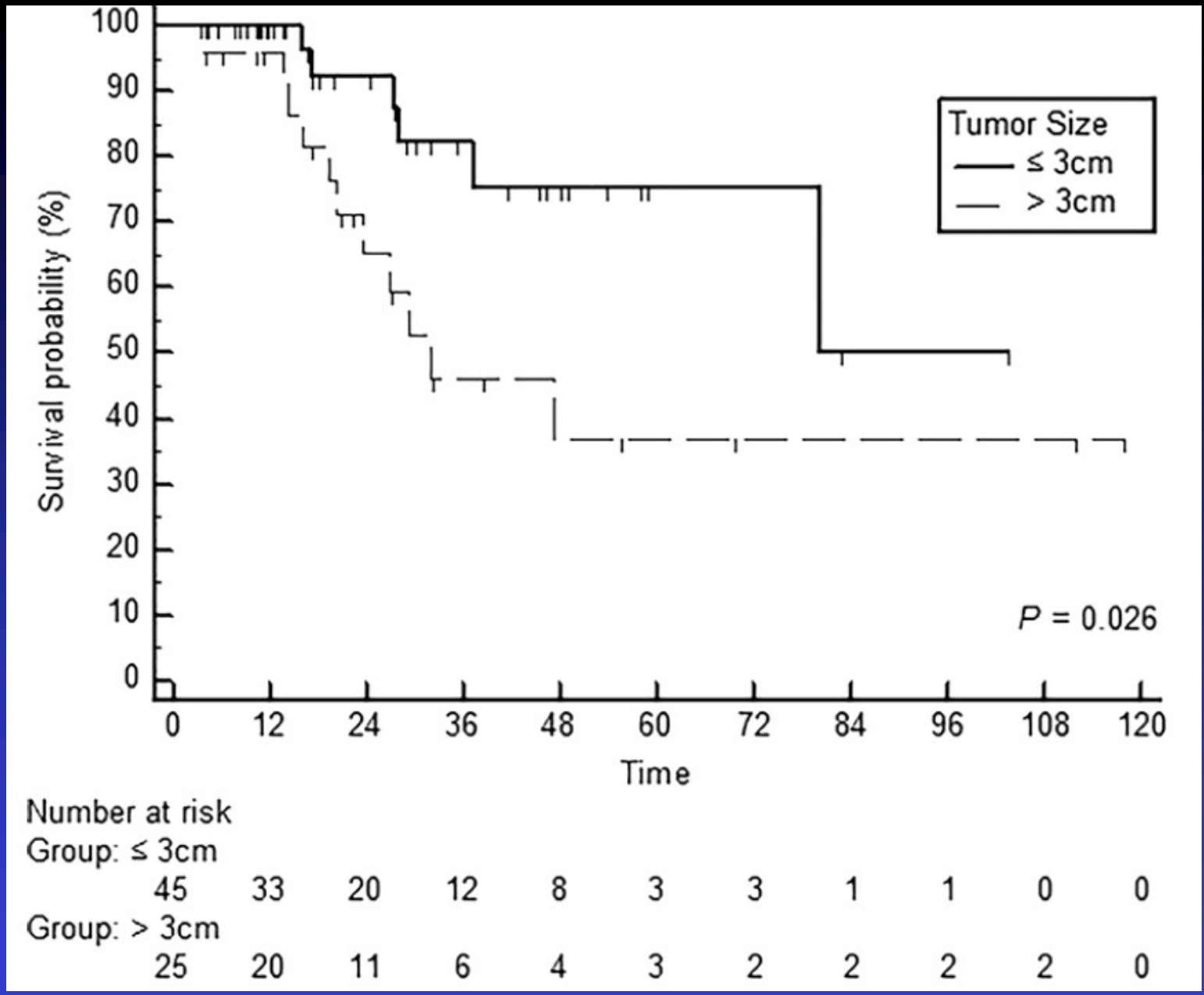

HCC
Stage 0
PST 0, Child-Pugh A
Stage A-C
PST 0-2, Child-Pugh A-B
Stage D
PST >2, Child-Pugh C*
Very early stage (0)
Single <2 cm,
Carcinoma in situ
Early stage (A)
Single or 3 nodules ≤3 cm,
PS 0
Intermediate stage (B)
Multinodular,
PS 0
Advanced stage (C)
Portal invasion,
N1, M1, PS 1-2
Terminal stage (D)
Single
3 nodules ≤3 cm
Portal pressure/bilirubin
Increased
Associated diseases
Normal
No
Yes
Resection
Liver transplantation
(CLT/LDLT)
RF/PEI
TACE
Sorafenib
Best supportive
care
Curative treatment (30-40%)
Median OS >60 mo; 5-yr survival: 40-70%
Target: 20%
OS: 20 mo (45-14)
Target: 40%
OS: 11 mo (6-14)
Target: 10%
OS: <3 mo

Radiation Segmentectomy:
Potential Curative Therapy for Early Hepatocellular Carcinoma[1]

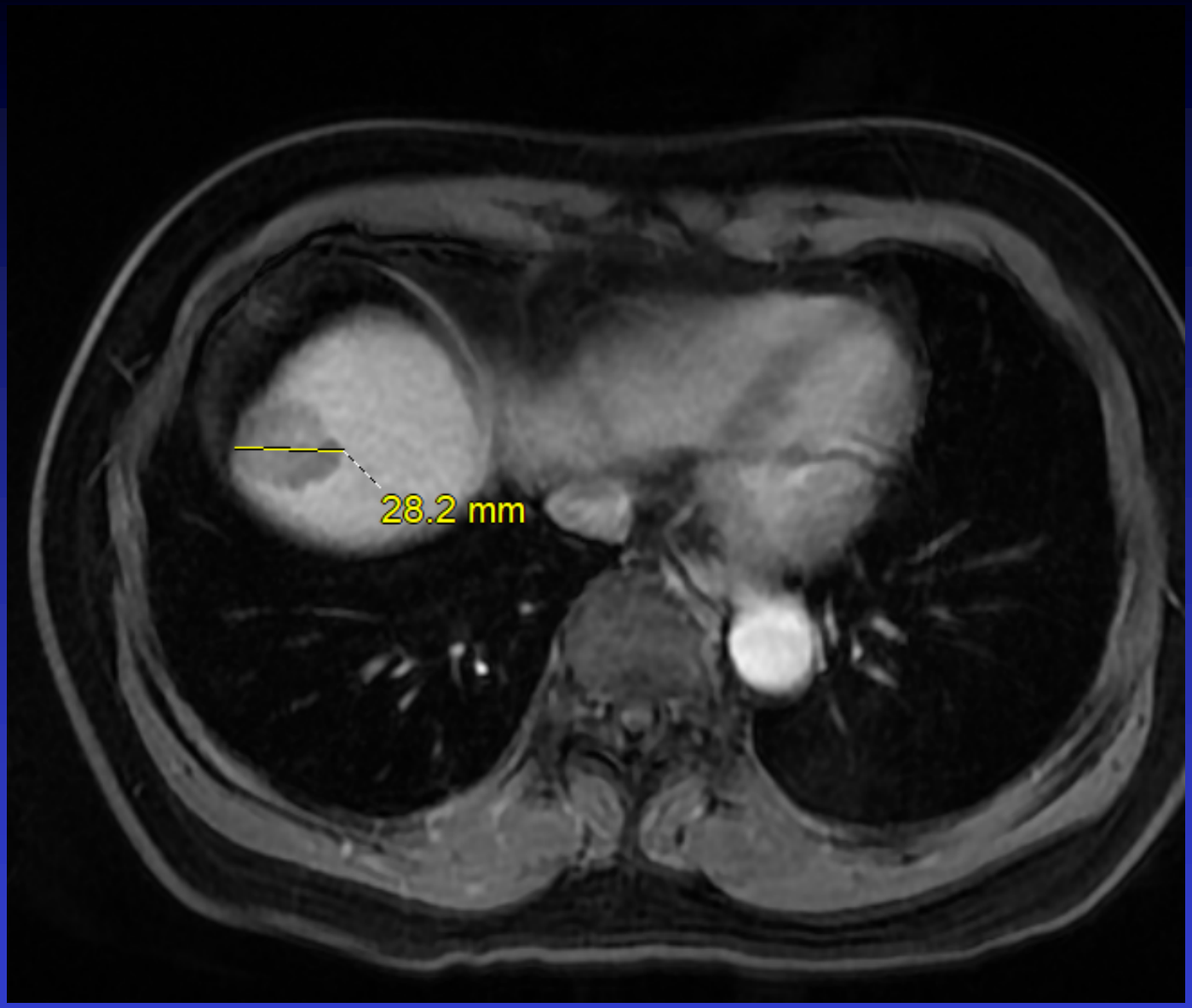
Robert J. Lewandowski, MD
Ahmed Gabr, MD
Nadine Abouchaleh, BS
Rehan Ali, MD
Ali Al Asadi, BS

Purpose: To report long-term outcomes of radiation segmentectomy (RS) for early hepatocellular carcinoma (HCC). The authors hypothesized that outcomes are comparable to curative treatments for patients with solitary HCC less than or equal to 5 cm and preserved liver function.

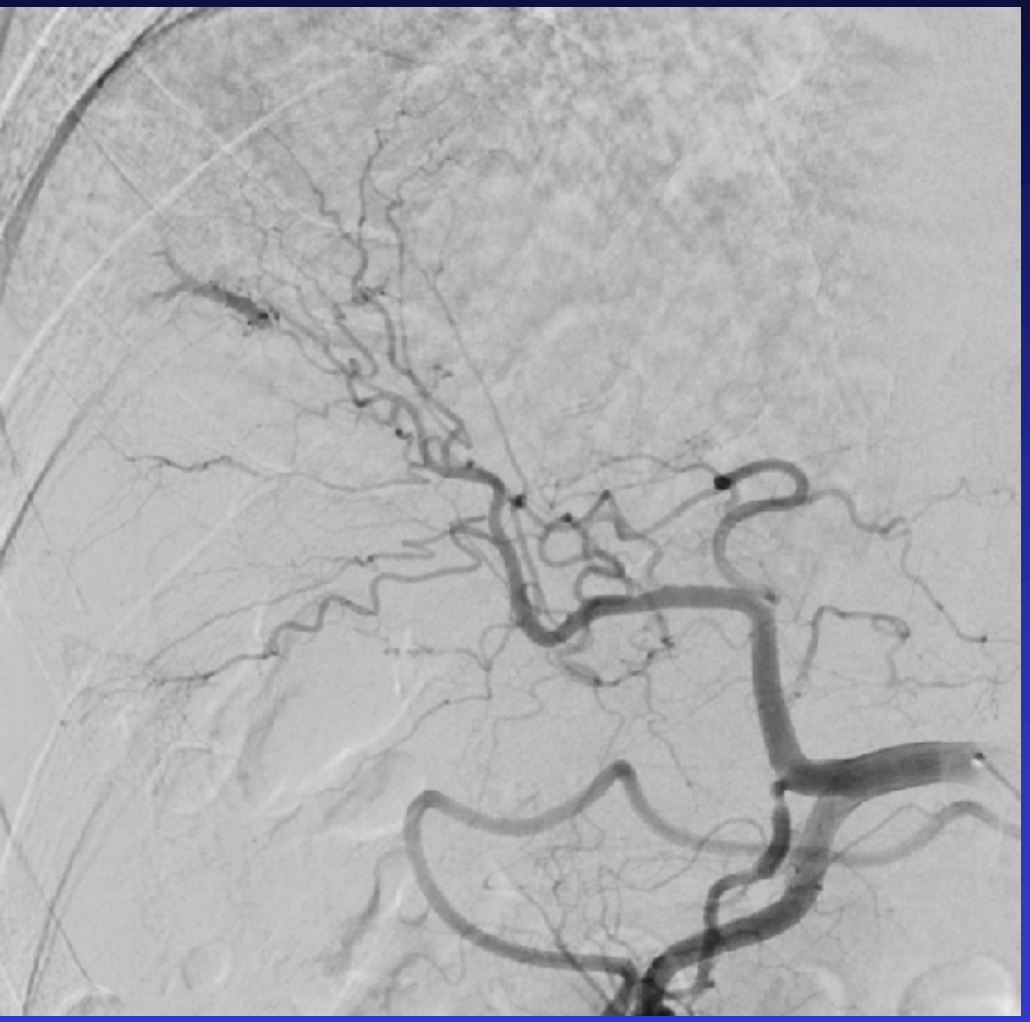
70 patients - Median time to progression was 2.4 years
72% of patients having no target lesion progression at 5 years
Median overall survival was 6.7 years
survival probability at 1, 3, and 5 years was 98%, 66%, and 57%,

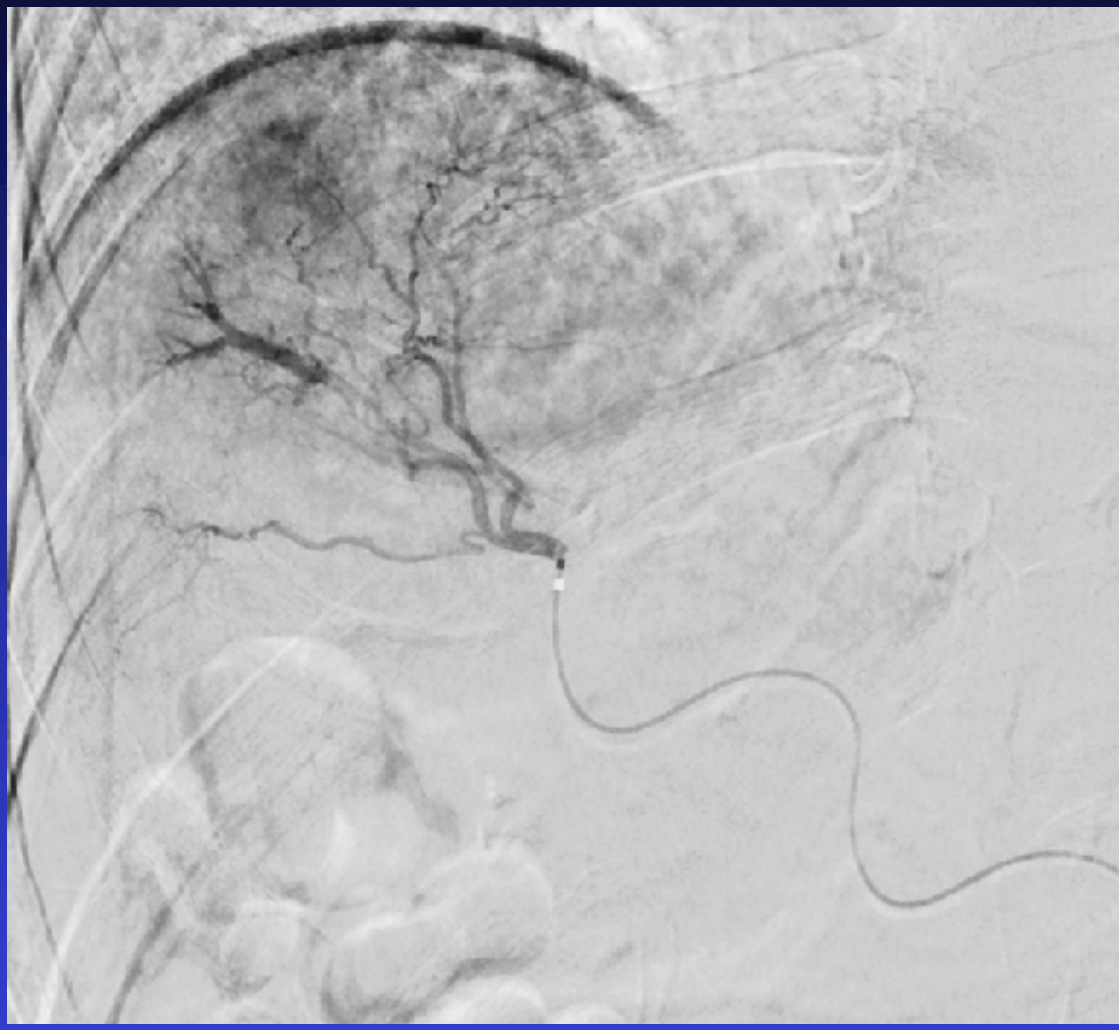


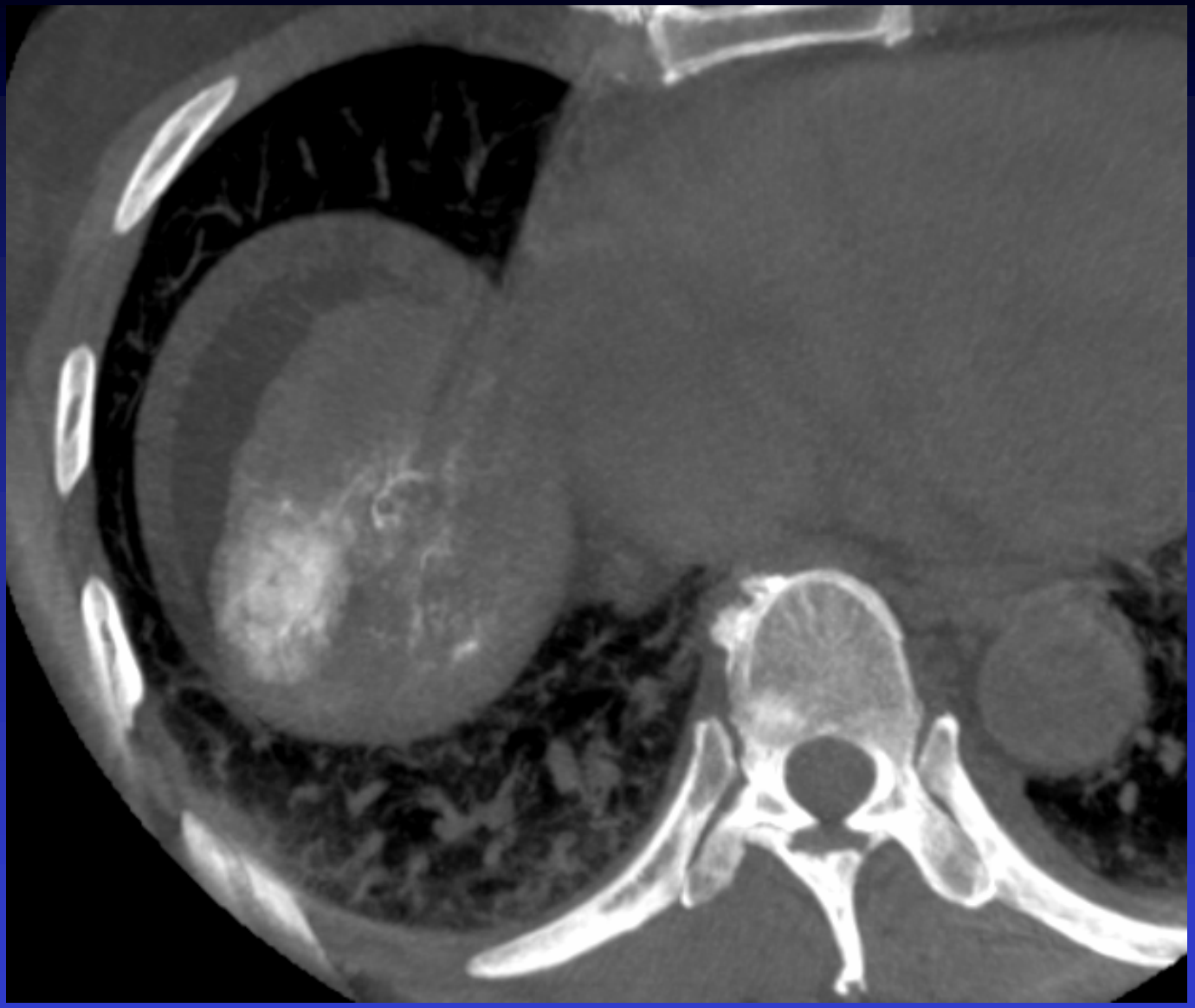
Lewandowski et al. Radiology 2018

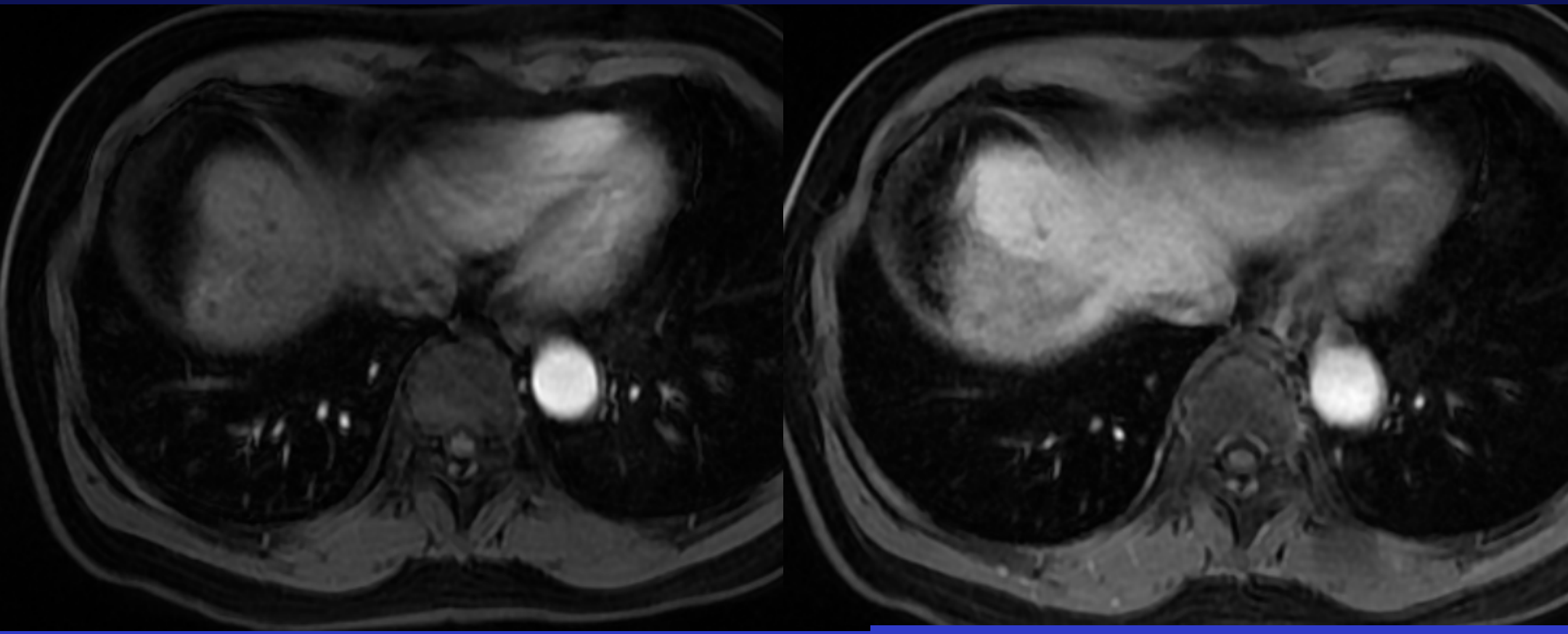


73 y.o. with HBV, CPA, ECOG 0, refused surgery

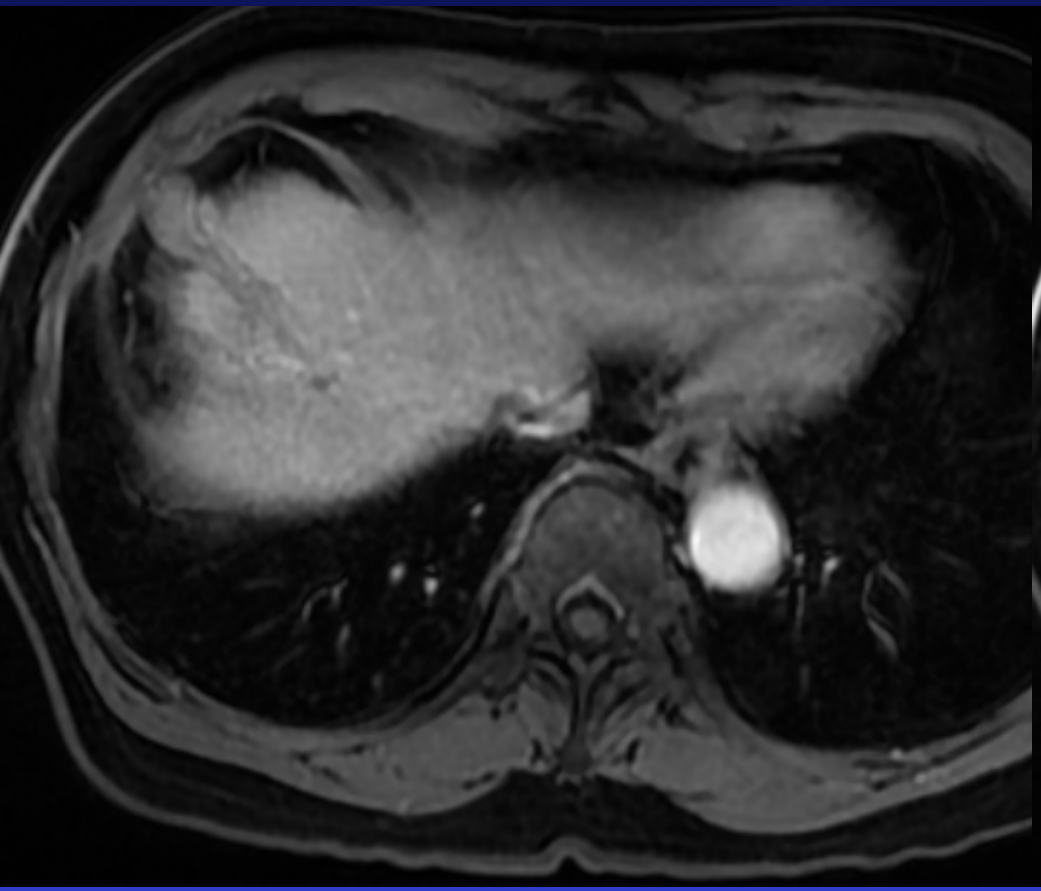


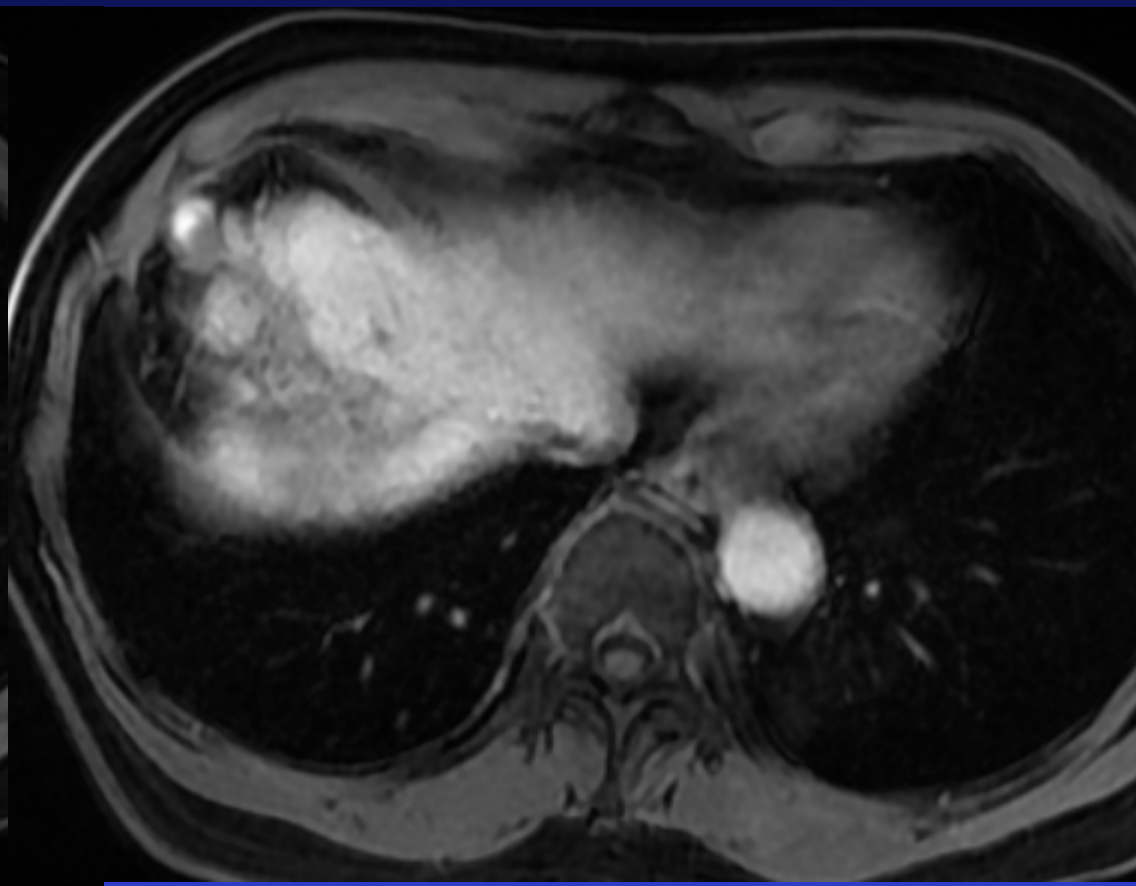






3 mo post Y90



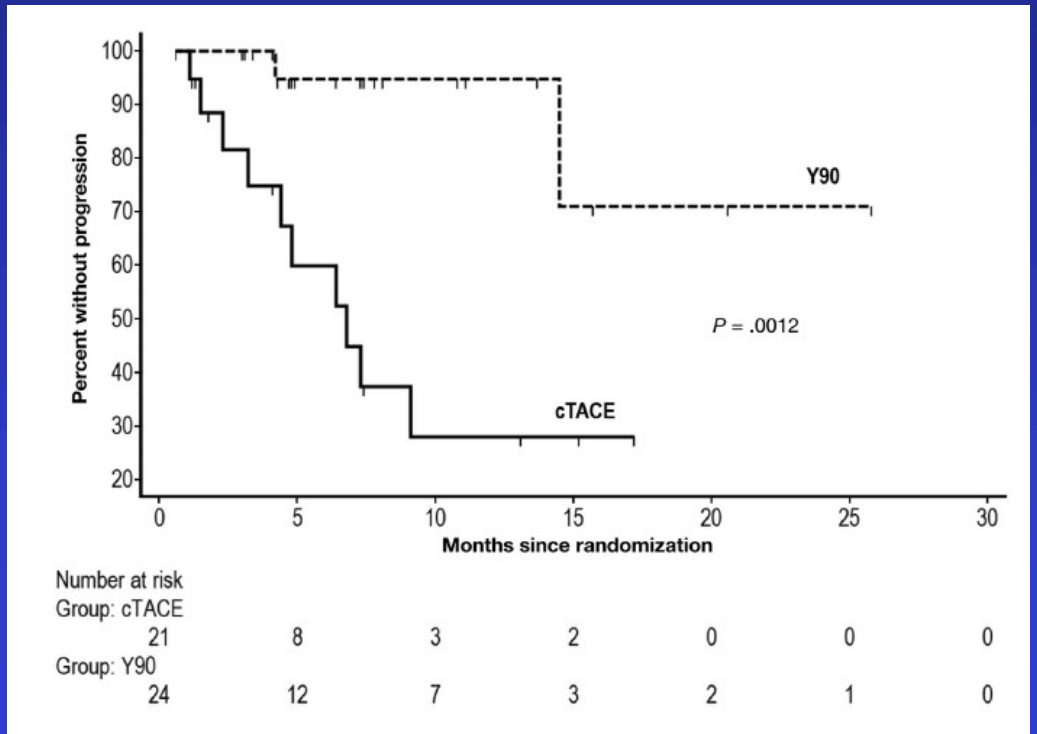


18 mo post Y90

Gastroenterology 2016;151:1155–1163

Y90 Radioembolization Significantly Prolongs Time to Progression Compared With Chemoembolization in Patients With Hepatocellular Carcinoma

Riad Salem,[1,2,3,*] **Andrew C. Gordon**,[1,*] Samdeep Mouli,[1] Ryan Hickey,[1] Joseph Kallini,[1] Ahmed Gabr,[1] Mary F. Mulcahy,[2] Talia Baker,[3] Michael Abecassis,[3] Frank H. Miller,[4] Vahid Yaghmai,[4] Kent Sato,[1] Kush Desai,[1] Bartley Thornburg,[1] Al B. Benson,[2] Alfred Rademaker,[5] Daniel Ganger,[6] Laura Kulik,[6] and Robert J. Lewandowski[1,2]



PREMIERE TRIAL

TTP 26 mo vs 6.8 mo

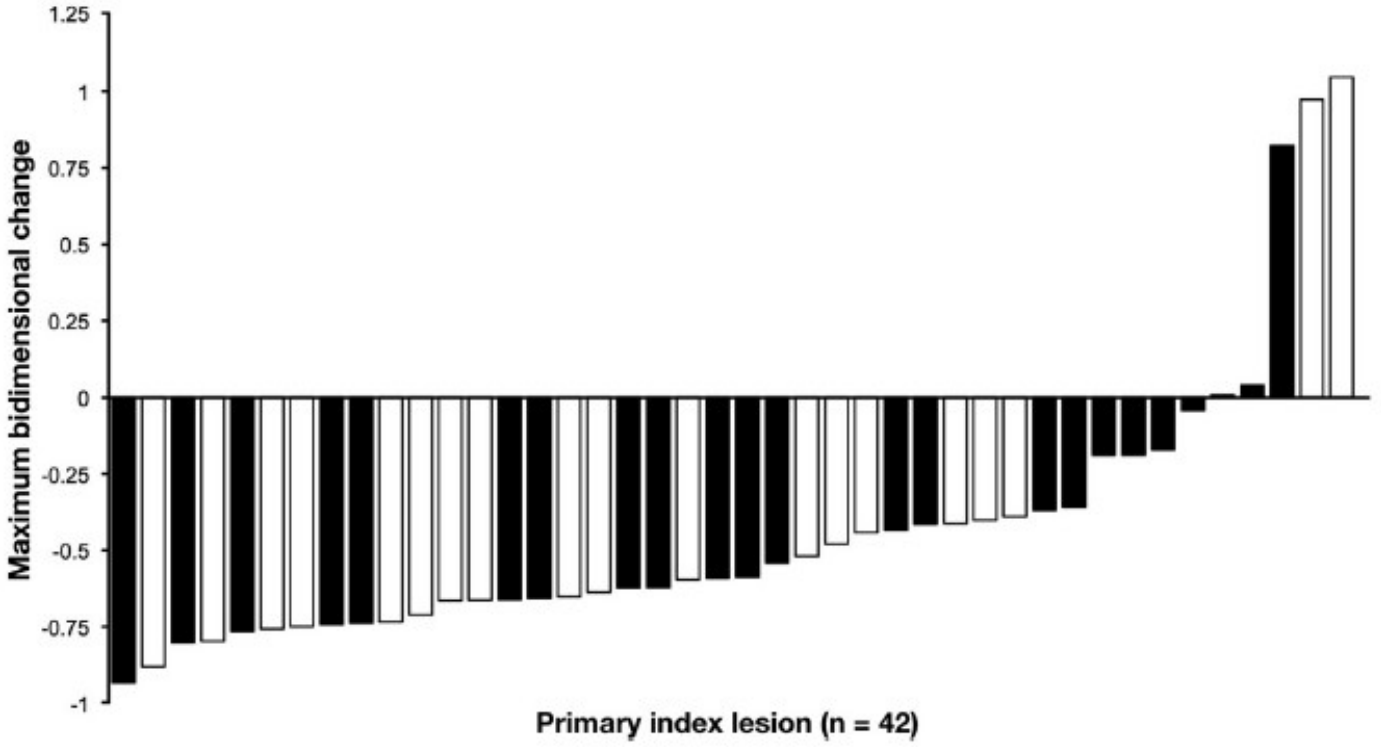


Figure 2. Waterfall plot of maximum size change for WHO measurements in (n = 42) primary index lesions after Y90 (*black bars*) vs cTACE (*white bars*). Negative values represent reductions in tumor size with a 50% or greater reduction (-) defined as a partial response and a more than 25% increase (+) in size defined as progressive disease.

CLINICAL STUDY

Radiation Segmentectomy versus Selective Chemoembolization in the Treatment of Early-Stage Hepatocellular Carcinoma

Derek M. Biederman, MD, Joseph J. Titano, MD, Ricki A. Korff, BS, Aaron M. Fischman, MD, Rahul S. Patel, MD, Francis S. Nowakowski, MD, Robert A. Lookstein, MD, and Edward Kim, MD

JVIR 2018

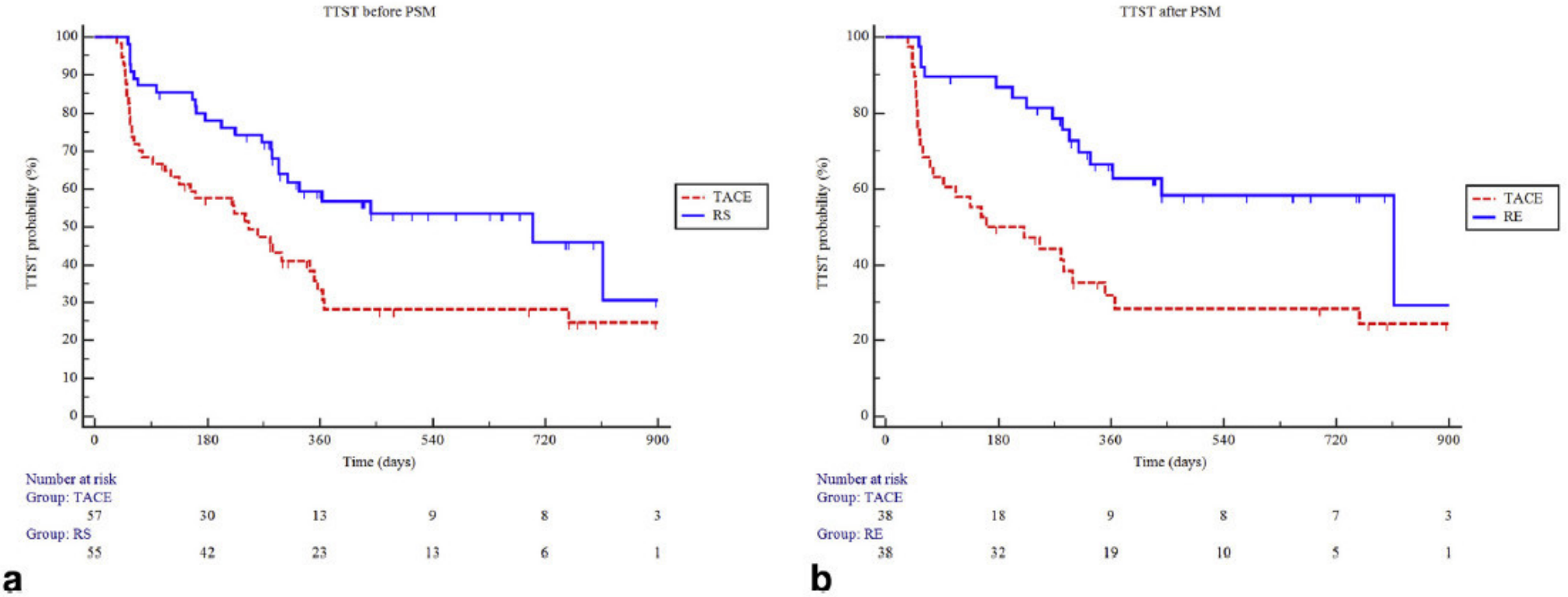


Figure 1. TTST outcomes. **(a)** Before PSM, the median (95% CI) TTST was 246 days (135–350 d) in the transarterial chemoembolization group and 700 days (300–812 d) in the RS group (HR 0.71; 95% CI, 0.55–0.92; $P = .009$, log-rank test). **(b)** After matching, the median TTST was 161 days (76–350 d) in the transarterial chemoembolization group and 812 days (363–812 d) in the RS group with a propensity score–adjusted HR of 0.21 (95% CI, 0.08–0.55; $P = .001$, stratified log-rank test).

Efficacy and safety of selective internal radiotherapy with yttrium-90 resin microspheres compared with sorafenib in locally advanced and inoperable hepatocellular carcinoma (SARAH): an open-label randomised controlled phase 3 trial

*Valérie Vilgrain, Helena Pereira, Eric Assenat, Boris Guiu, Alina Diana Ilonca, Georges-Philippe Pageaux, Annie Sibert, Mohamed Bouattour, Rachida Lebtahi, Wassim Allaham, Hélène Barraud, Valérie Laurent, Elodie Mathias, Jean-Pierre Bronowicki, Jean-Pierre Tasu, Rémy Perdrisot, Christine Silvain, René Gerolami, Olivier Mundler, Jean-Francois Seitz, Vincent Vidal, Christophe Aubé, Frédéric Oberti, Olivier Couturier, Isabelle Brenot-Rossi, Jean-Luc Raoul, Anthony Sarran, Charlotte Costentin, Emmanuel Itti, Alain Luciani, René Adam, Maïté Lewin, Didier Samuel, Maxime Ronot, Aurelia Dinut, Laurent Castera, Gilles Chatellier, on behalf of the SARAH Trial Group**

Lancet Oncol 2017; 18: 1624–36

Published Online
October 26, 2017

Summary

Background Sorafenib is the recommended treatment for patients with advanced hepatocellular carcinoma. We aimed to compare the efficacy and safety of sorafenib to that of selective internal radiotherapy (SIRT) with yttrium-90 (^{90}Y) resin microspheres in patients with hepatocellular carcinoma.

SARAH

- 467 patients in France with advanced HCC randomized to resin Y90 vs sorafenib
  - Primary endpoint : OS (8.0 Y90 vs 9.9 mo sorafenib)
  - Secondary : PFS (no difference), PFS liver (favor Y90), best response (favor Y90), QOL (favor Y90 $p < 0.0001$)

Vilgrain et al. Lancet Oncology 2017

SARAH COMMENTS

- 22 % group randomized to Y90 did not receive it but all included in analysis
- 45 % prior TACE
- ? Experience of 25 sites in France where Y90 is not approved
- 29 d vs 7d from randomization to treatment
- Very short PFS 4.1 mo (vs 26 mo for PREMIERE)
- 63% macrovascular invasion
- Do not discount the importance of QOL result

Vilgrain et al. Lancet Oncology 2017

SARAH CONCLUSIONS

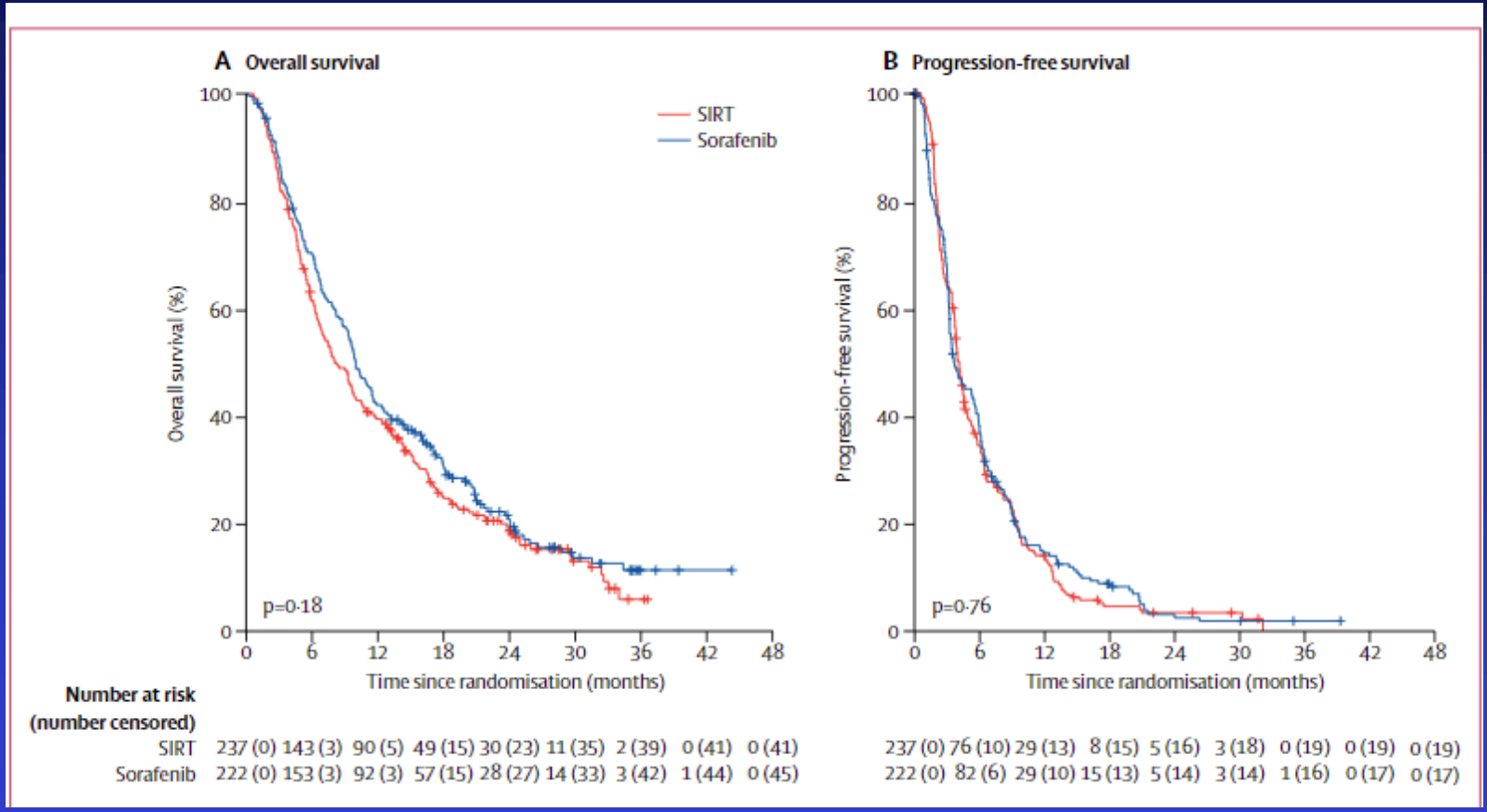
Added value of this study

In patients with locally advanced or intermediate-stage hepatocellular carcinoma after unsuccessful transarterial chemoembolisation, when compared with sorafenib, SIRT did not improve overall or progression-free survival but it significantly increased tumour response, reduced the incidence of adverse events, and improved QOL.

Implications of all the available evidence

These results suggest that SIRT might be better tolerated than sorafenib in patients with locally advanced or intermediate-stage hepatocellular carcinoma, and these results might lead to changes in the recommended treatment algorithm for these patients.

SARAH


A Overall survival
SIRT
Sorafenib
Overall survival (%)
p=0·18
Time since randomisation (months)
B Progression-free survival
Progression-free survival (%)
p=0·76
Time since randomisation (months)
Number at risk
(number censored)
SIRT 237 (0) 143 (3) 90 (5) 49 (15) 30 (23) 11 (35) 2 (39) 0 (41) 0 (41)
Sorafenib 222 (0) 153 (3) 92 (3) 57 (15) 28 (27) 14 (33) 3 (42) 1 (44) 0 (45)
237 (0) 76 (10) 29 (13) 8 (15) 5 (16) 3 (18) 0 (19) 0 (19) 0 (19)
222 (0) 82 (6) 29 (10) 15 (13) 5 (14) 3 (14) 1 (16) 0 (17) 0 (17)

Radiology

ORIGINAL RESEARCH • VASCULAR AND INTERVENTIONAL RADIOLOGY

Relationship of Tumor Radiation–absorbed Dose to Survival and Response in Hepatocellular Carcinoma Treated with Transarterial Radioembolization with ^{90}Y in the SARAH Study

*Anne-Laure Hermann, MD • Arnaud Dieudonné, PhD • Maxime Ronot, MD, PhD • Manuel Sanchez, PhD • Helena Pereira, MSc • Gilles Chatellier, MD • Etienne Garin, MD • Laurent Castera, MD, PhD • Rachida Lebtahi, MD • Valérie Vilgrain, MD • For the SARAH Trial Group**

Key Results

- Tumor radiation–absorbed dose at technetium 99m (^{99m}Tc) macroaggregated human albumin (MAA) SPECT/CT was an independent predictor of prolonged survival for inoperable hepatocellular carcinoma treated with transarterial radioembolization with yttrium 90 (^{90}Y) (median, 14.1 months with ≥100 Gy vs 6.1 months with <100 Gy; $P < .001$).
- The longest survival (median, 24.9 months) and the best disease control rate (78%) after treatment with ^{90}Y were observed with both tumor radiation–absorbed dose greater than or equal to 100 Gy and optimal visual agreement among CT, ^{99m}Tc-MAA SPECT/CT, and ^{90}Y SPECT/CT or PET/CT ($P < .001$ and $P = .005$, respectively).

Radiology

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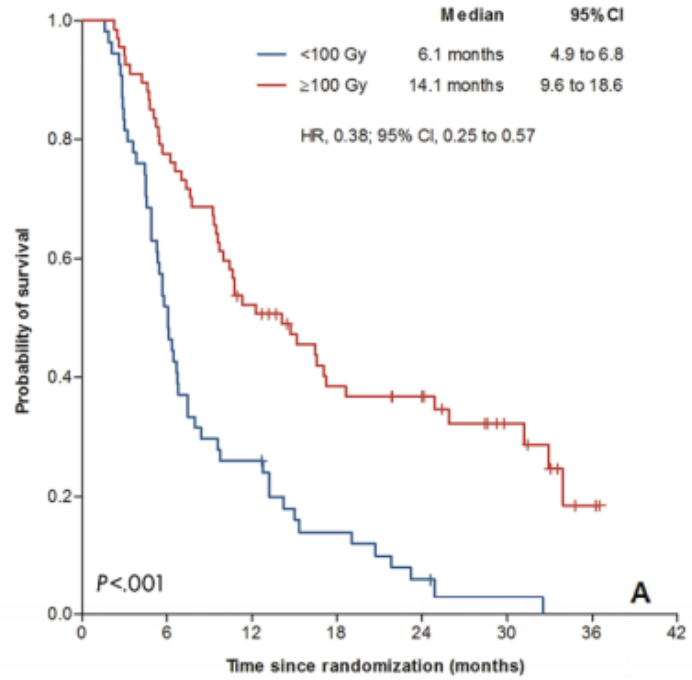
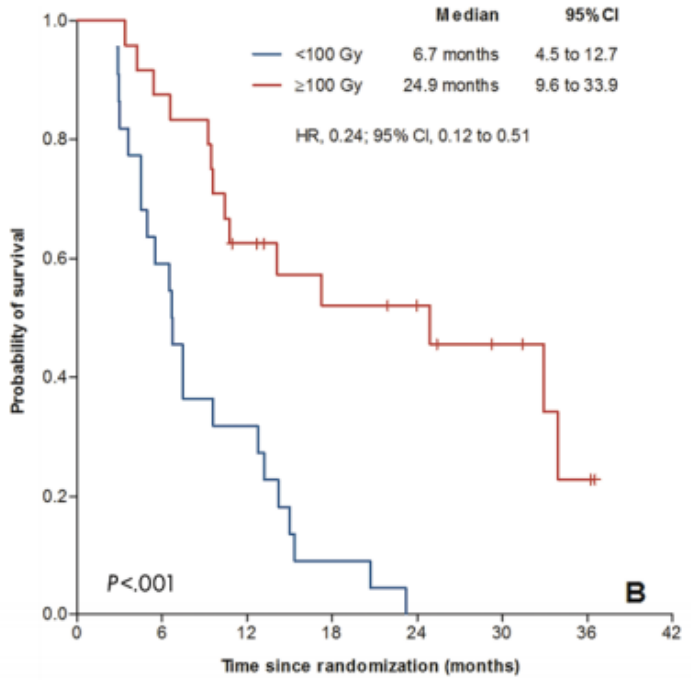
Relationship of Tumor Radiation–absorbed Dose in Survival and Response



Number at risk (number censored)

<100 Gy	54 (0)	28 (0)	14 (0)	7 (1)	3 (1)	1 (2)	0 (2)	
≥100 Gy	67 (0)	52 (0)	34 (1)	22 (5)	18 (8)	9 (15)	2 (19)	0 (21)



Number at risk (number censored)

<100 Gy	22 (0)	13 (0)	7 (0)	2 (0)	0 (0)			
≥100 Gy	24 (0)	21 (0)	14 (1)	10 (3)	8 (5)	5 (7)	2 (8)	0 (10)

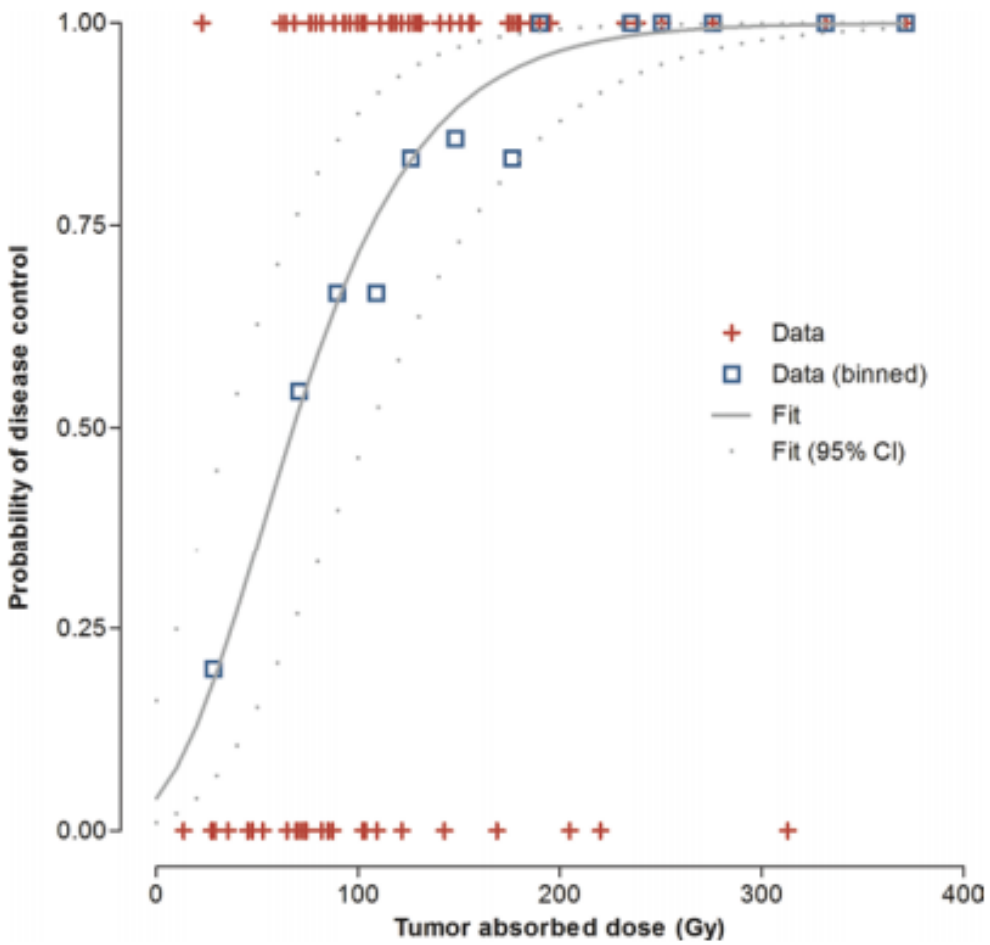


Figure 4: Dose–tumor response curve shows disease control probability (tumor control probability). Red crosses represent raw data (with optimal agreement), blue squares are data binned with 20-Gy intervals, gray curve is fit of linear quadratic model of Lea and Catcheside (24), and gray dots represent 95% confidence intervals of fit. CI = confidence interval.

Journal of Clinical Oncology®
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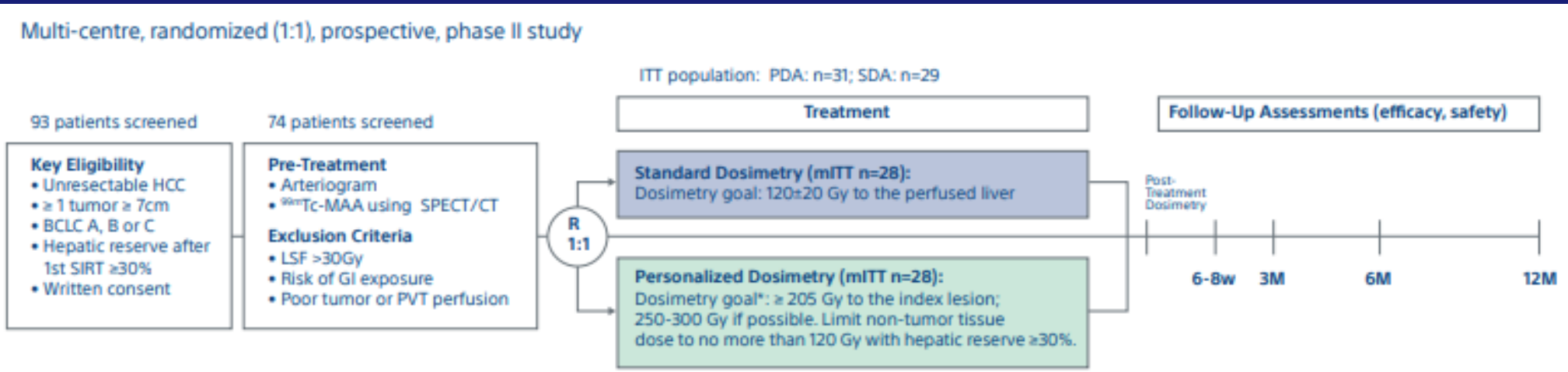
HEPATOBILIARY CANCER

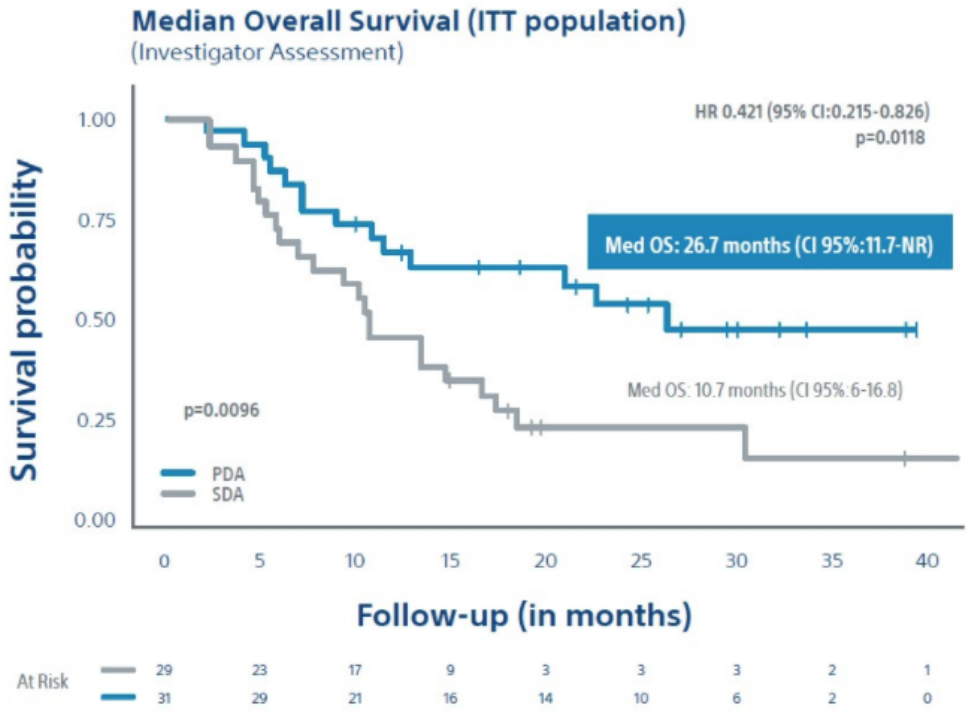
Major impact of personalized dosimetry using 90Y loaded glass microspheres SIRT in HCC: Final overall survival analysis of a multicenter randomized phase II study (DOSISPHERE-01).

Etienne Garin, Lambros Tzelikas, Boris Guiu, Julia Chalaye, Julien Edeline, Thierry De Baere, ...

Show More

DOSISPHERE 01 STUDY





PDA: Personalized dosimetry

SDA: Standard, single-compartment dosimetry

Garin, et al ASCO GI 2019

HEPATOLOGY

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

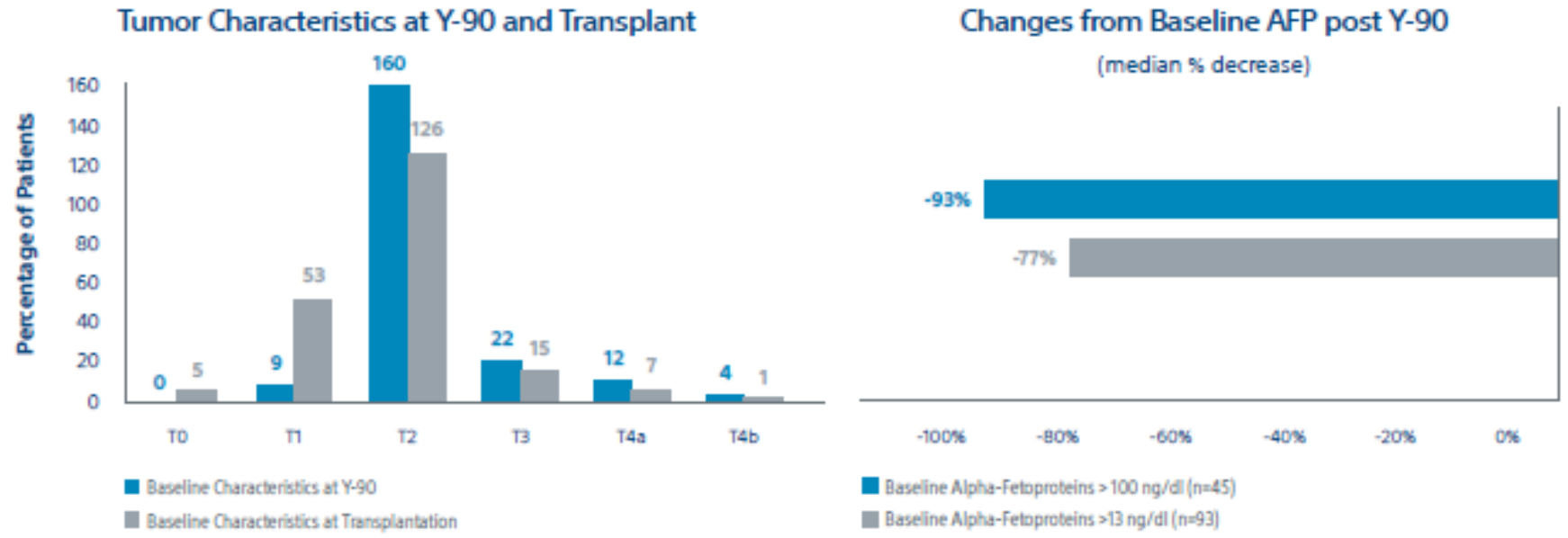
ORIGINAL ARTICLE | Full Access

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

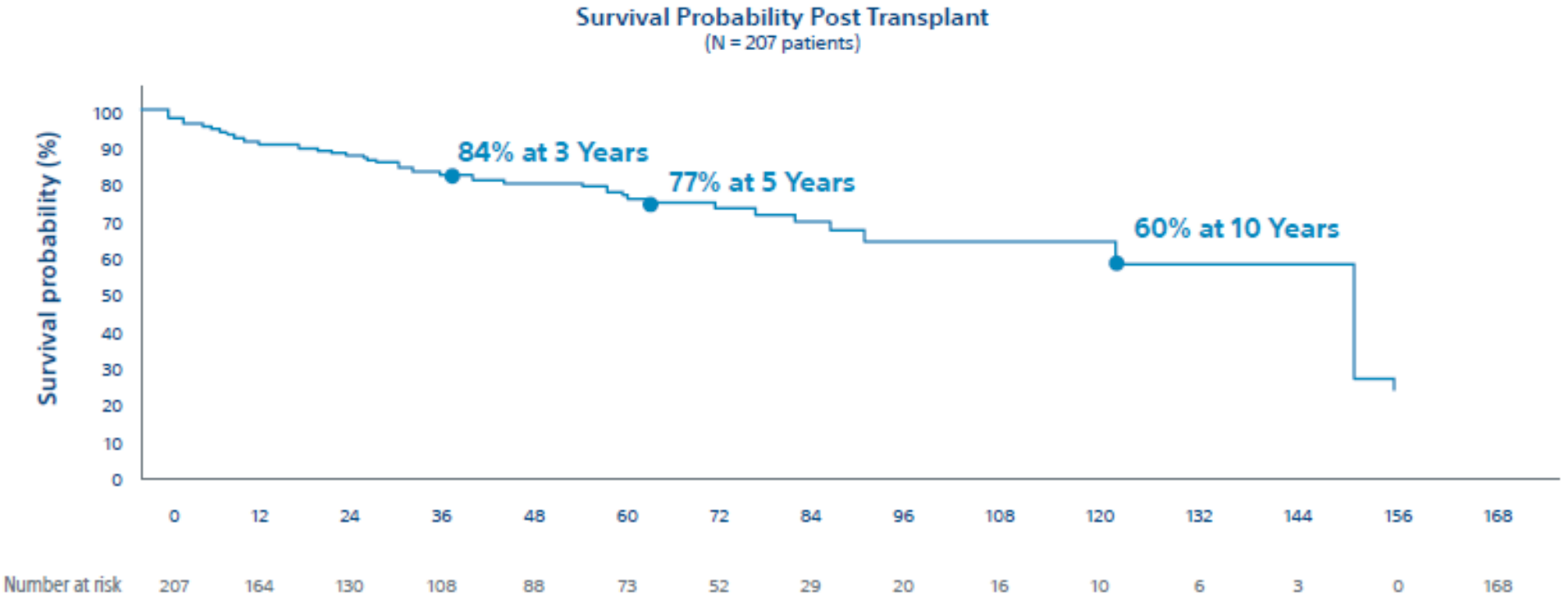
Ahmed Gabr, Laura Kulik, Samdeep Mouli, Ahsun Riaz, Rehan Ali, Kush Desai, Ronald A Mora, Daniel Ganger, Haripriya Maddur, Steven Flamm, Justin Boike, Christopher Moore ... See all authors

First published: 16 May 2020 | https://doi.org/10.1002/hep.31318

169 Patients were Bridged and 38 Patients were Downstaged to T2 for Liver Transplant
Median Time to LT was 7.5 Months



Y90 BRIDGE TO TRANSPLANT



BRIDGE TO TRANSPLANT : PATH OUTCOMES

- 45% complete necrosis
- 29% extensive necrosis
- 26% partial necrosis

Gabr et al. Hepatology 2020

Research Article

EASL JOURNAL OF HEPATOLOGY

Stereotactic body radiotherapy *vs.* TACE or RFA as a bridge to transplant in patients with hepatocellular carcinoma. An intention-to-treat analysis

Gonzalo Sapisochin[1,2,*], Aisling Barry[3], Mark Doherty[4], Sandra Fischer[5], Nicolas Goldaracena[1,2], Roizar Rosales[1], Moises Russo[3], Rob Beecroft[6], Anand Ghanekar[1,2], Mamatha Bhat[1], James Brierley[3], Paul D. Greig[1,2], Jennifer J. Knox[4], Laura A. Dawson[3,†], David R. Grant[1,2,†]

[1]*Multi-Organ Transplant, Toronto General Surgery, Canada;* [2]*Department of General Surgery, University of Toronto, Canada;* [3]*Radiation Medicine Program, Princess Margaret Cancer Centre, Department of Radiation Oncology, University of Toronto, Canada;* [4]*Department of Medical Oncology, University of Toronto, Canada;* [5]*Department of Pathology, University of Toronto, Canada;* [6]*Division of Interventional Radiology, University of Toronto, Canada*

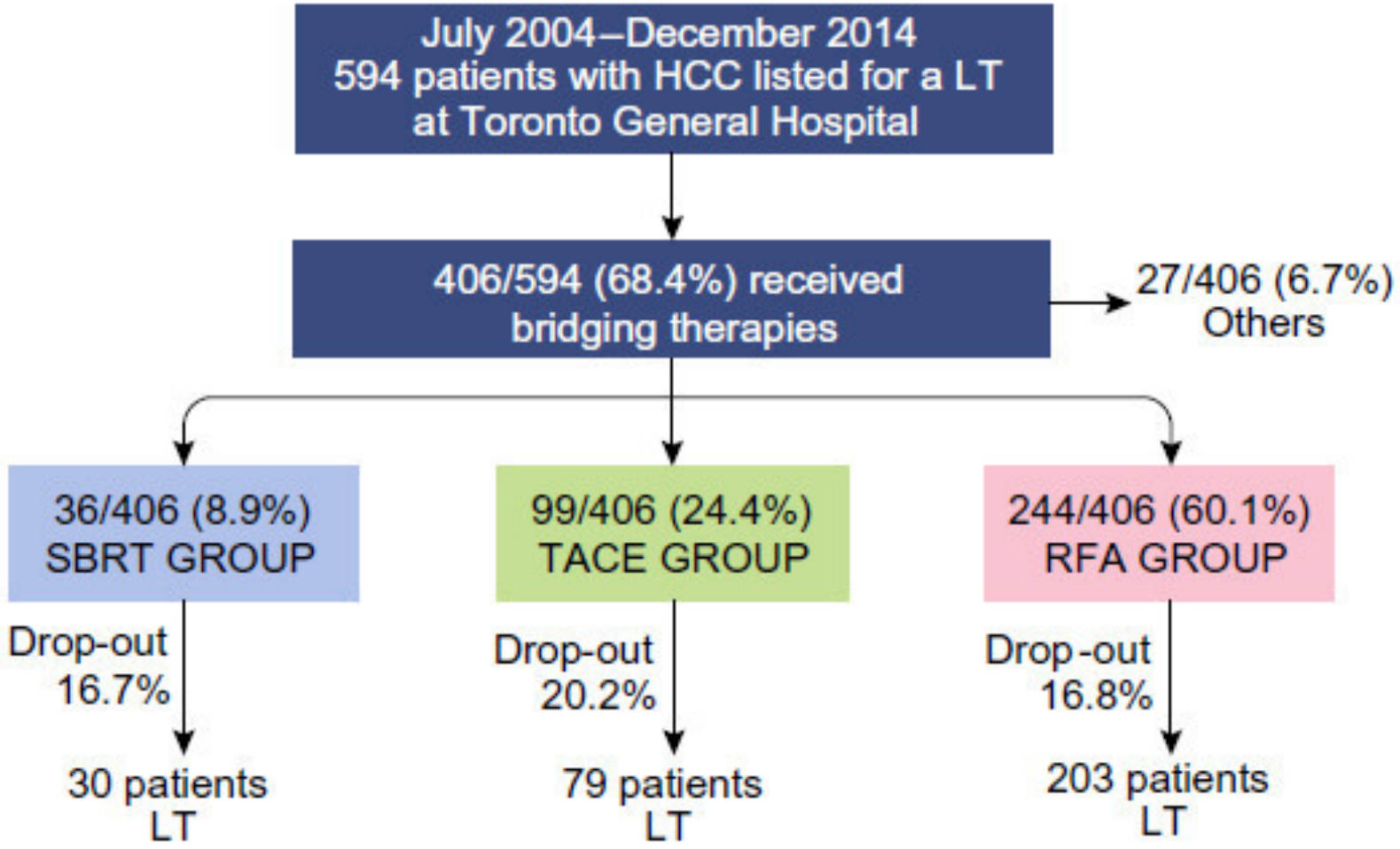


Fig. 1. Patient distribution. (This figure appears in colour on the web.)

Explant pathology characteristics	SBRT group (n = 30)	TACE group (n = 79)	RFA group (n = 203)	*p* value
Median number of tumors	3 (1–6)	4 (2–9)	2 (1–4)	0.001
Median maximum tumor size (cm)	3.7 (2.5–4.9)	4.5 (3–6)	3.2 (2.5–4)	<0.001
Tumor necrosis*				<0.001
None	3 (10%)	6 (8.6%)	7 (4%)	
Mild (1–49%)	11 (36.7%)	29 (41.4%)	58 (32.8%)	
Significant (50–99%)	12 (40%)	18 (25.7%)	25 (14.1%)	
Complete (100%)	4 (13.3%)	17 (24.3%)	87 (49.2%)	
Tumor differentiation				<0.001

CONCLUSIONS

- Radiation segmentectomy emerging as curative intent option in early stage disease
- Refinements in dosimetry have improved results across stages
- Safety and efficacy of radioembolization as a bridge to transplant