Selective Internal Radiotherapy (SIRT) for liver lesions

Clinical workshop

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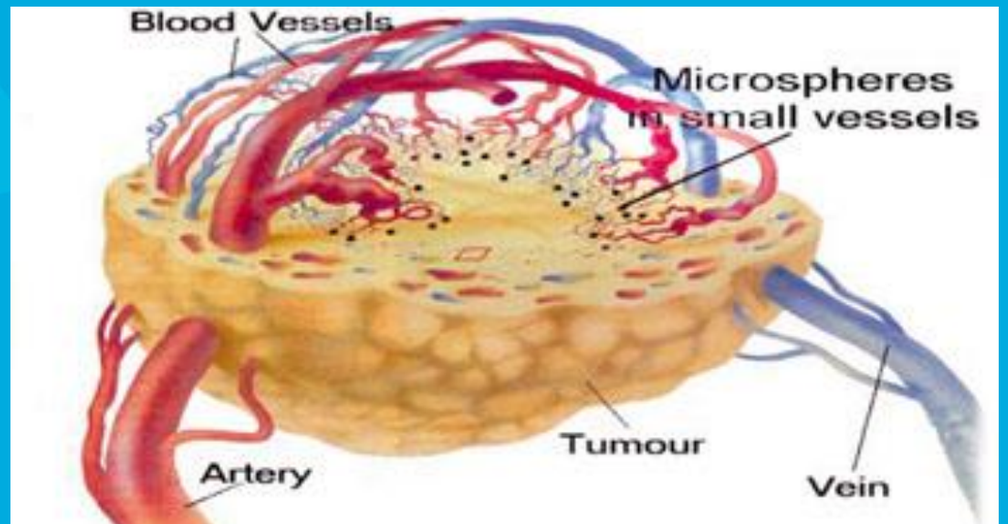
Introduction

- Definition, rationale & physics
- SIRT-procedure
  - Work-up
  - Therapy
- Clinical data
- Current place of SIRT in HCC treatment algorithm

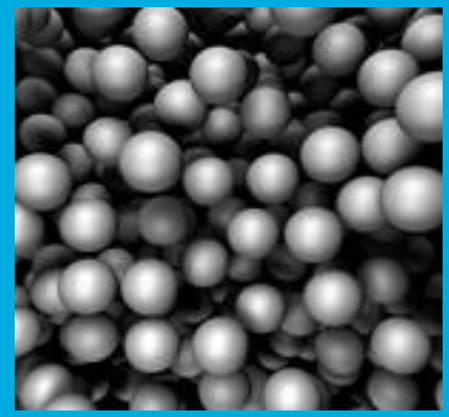
Definition, rationale & physics

- Selective Internal (transarterial approach) Radiation Therapy (SIRT)
  - Preferential (90%) hepatic arterial supply of HCC & liver metastases
  - Residual ‘normal’ liver parenchyma : mostly (70-80%) supported by portal venous system



Rationale & physics

- Radio-active microspheres
  - Small resin-based (29-35 micron) – glass-based (25 +/- 10 micron) microspheres
  - Y90 : active element
    - Pure Beta-emitter (937 KeV)
    - Decays to Zirconium-90
    - Half-life: 64.2 h
    - Average tissue penetration: 2.5 mm (maximum of 10 mm)
    - < 3 GBq delivery in the liver (cave REILD)
  - Average activity:
    - 40 Bq (resin) – 2500 Bq (glass)
    - 40 – 80 million resin-microspheres >< 1 – 8 million glass-microspheres



SIRT procedure : patient selection

- Clinical (ECOG)
- Biochemical
- Imaging (CT – MR)

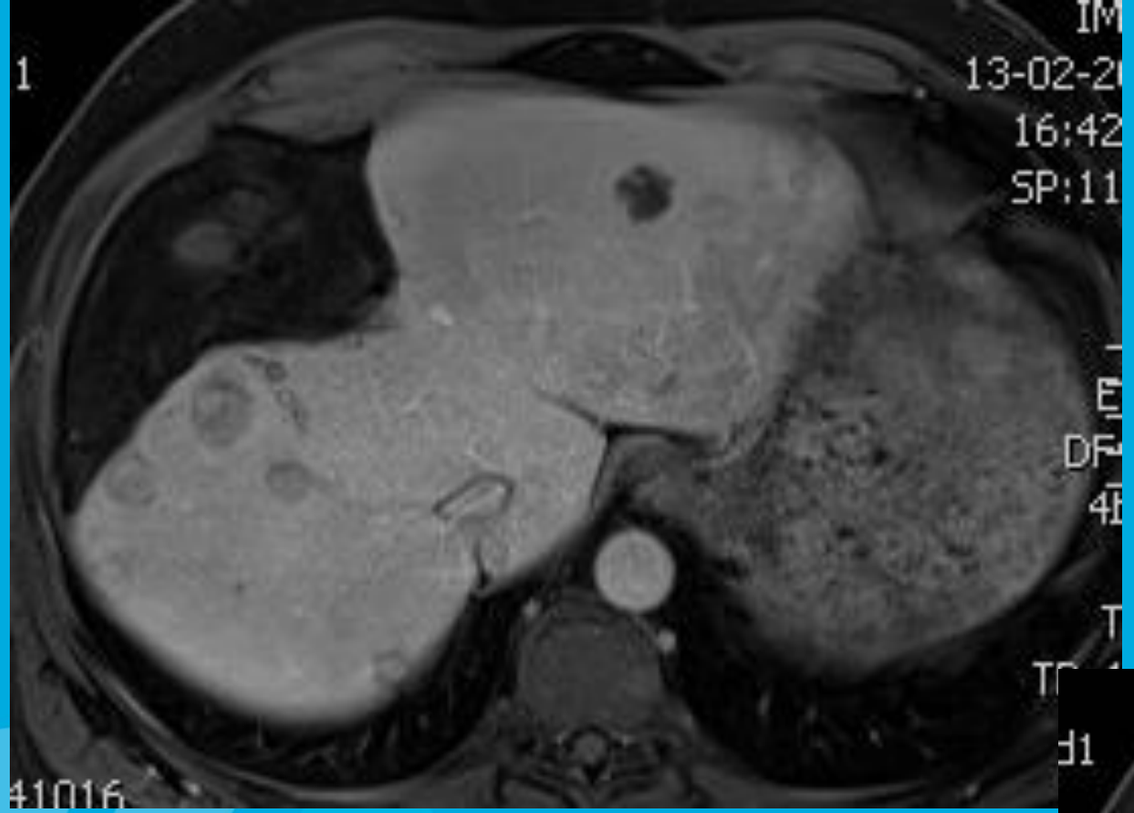
multidisciplinary tumor board

- Palliative versus curative intention

Biochemical considerations

- Liver function
  - Total bilirubin < 1.5 mg/100ml (total liver infusion)
  - Serum albumine > 3.0 g/dL
  - AST, ALT, alkaline phosphatase : < 4 x upper limit of normal
- Renal function
  - Creatinine < 1.5 X normal values
  - creatinine clearance > 50 ml/min
- Hemostatic parameters
  - Platelet count > 100.000/mm

- Cosimelli et al. Br J Cancer 2010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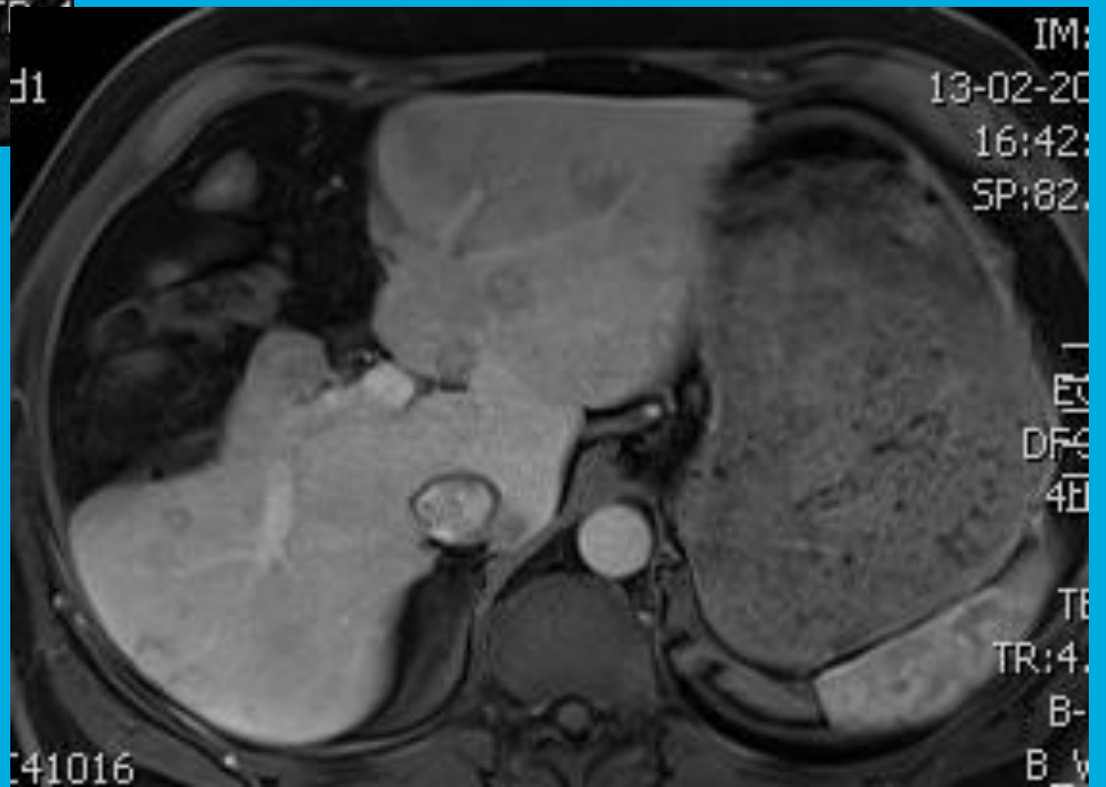
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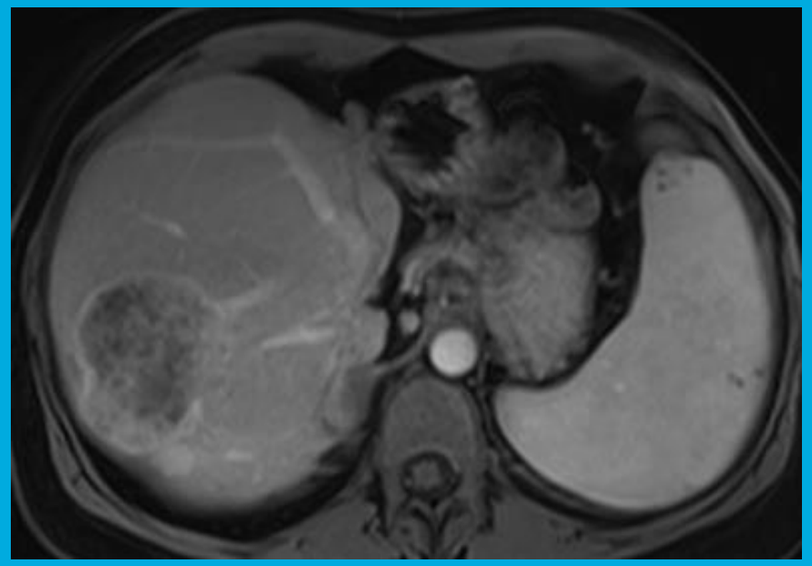

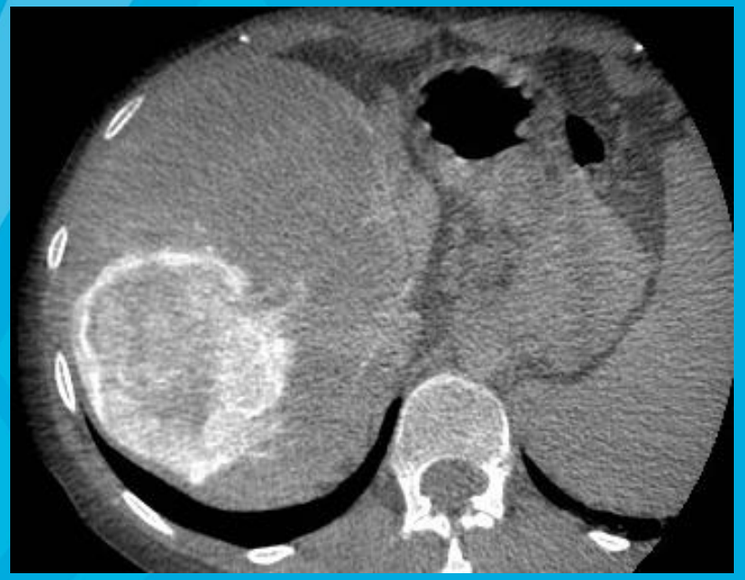

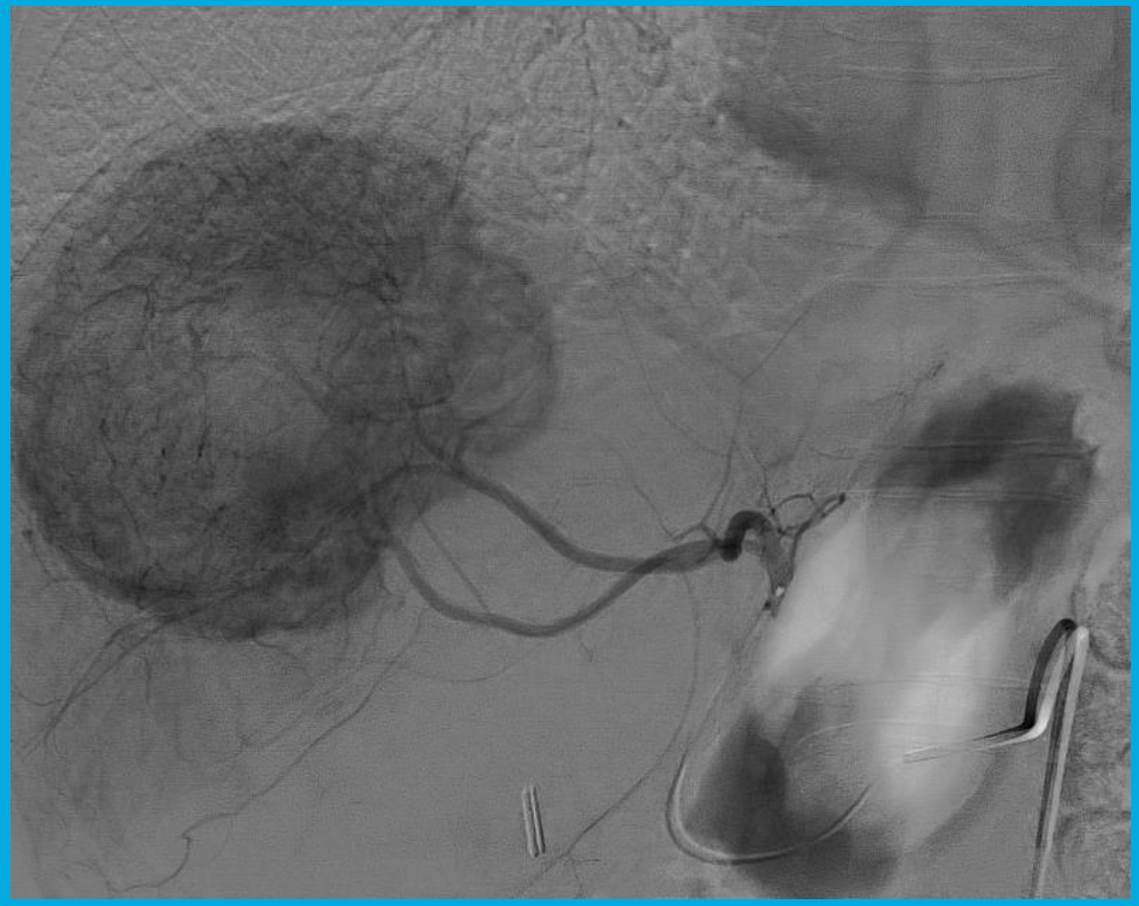

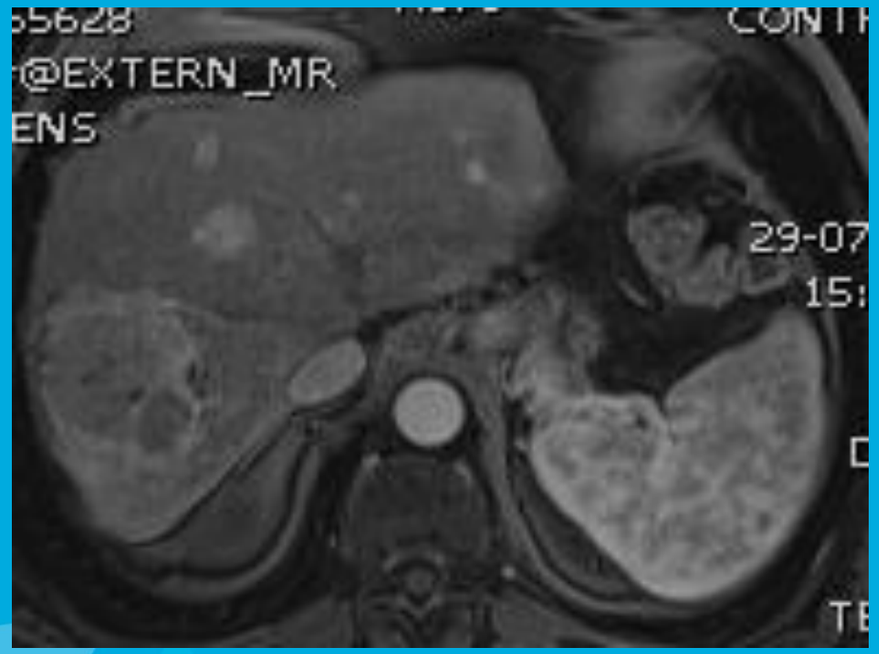
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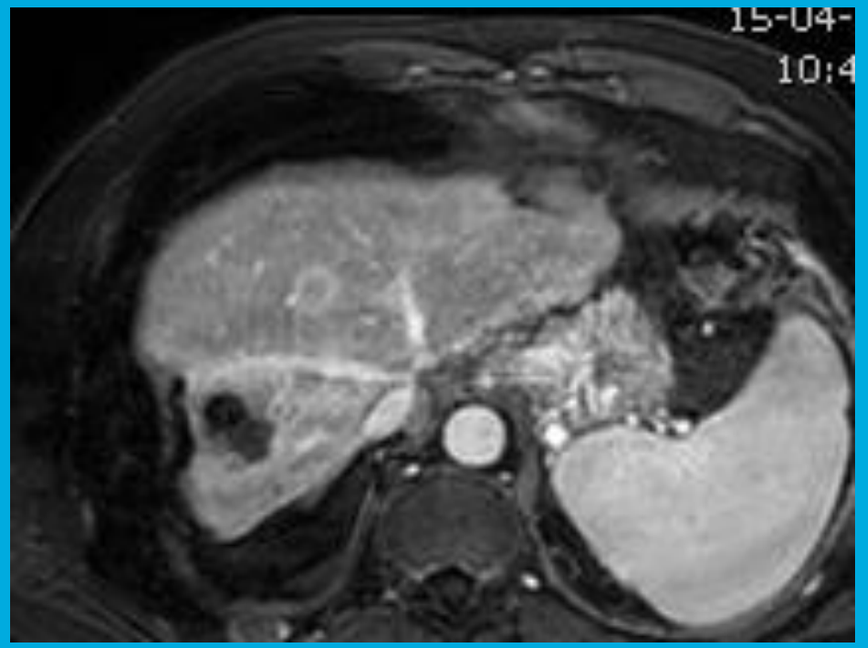
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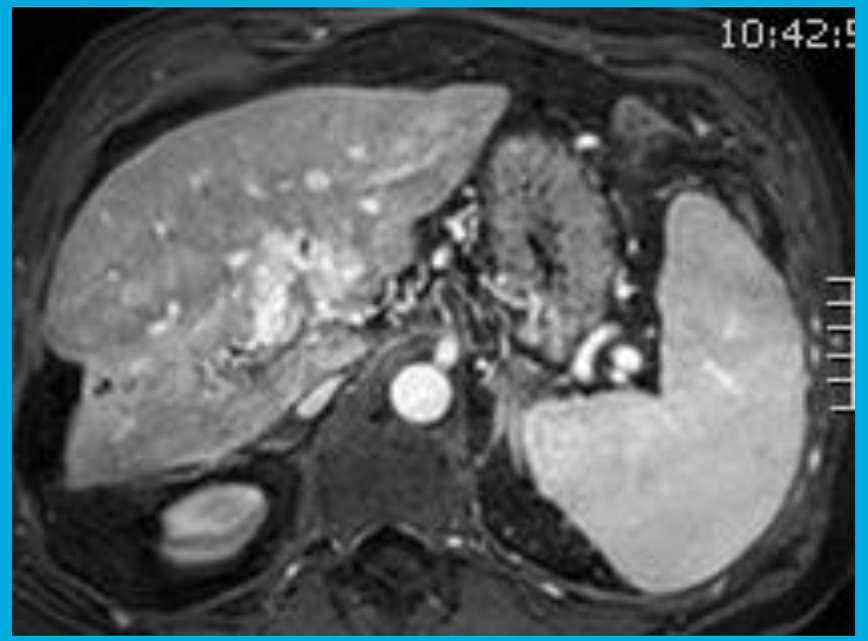
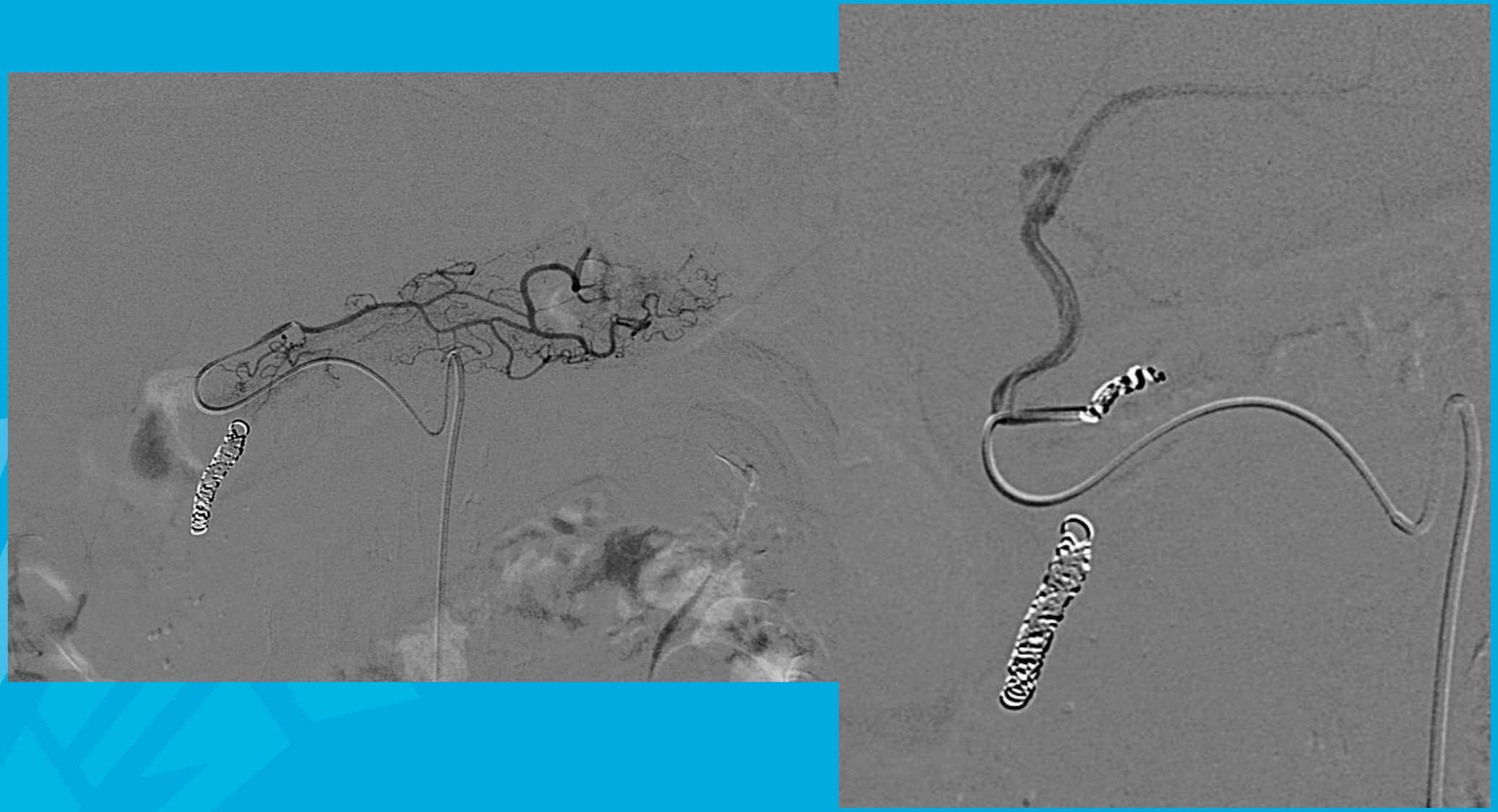


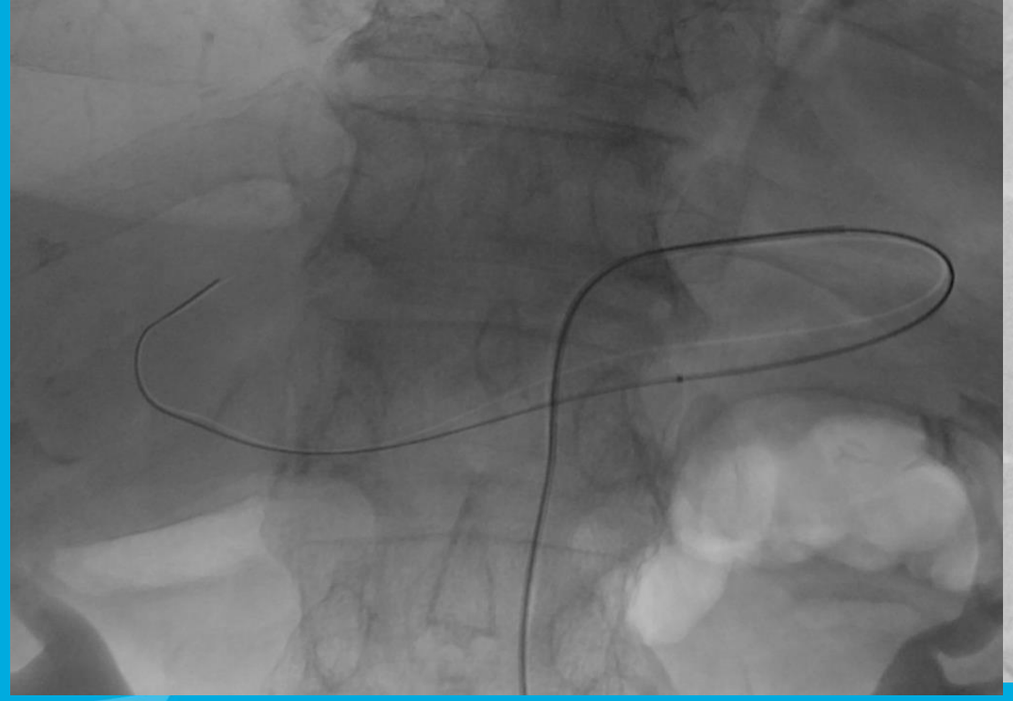
SIRT work-up (catheter-based)

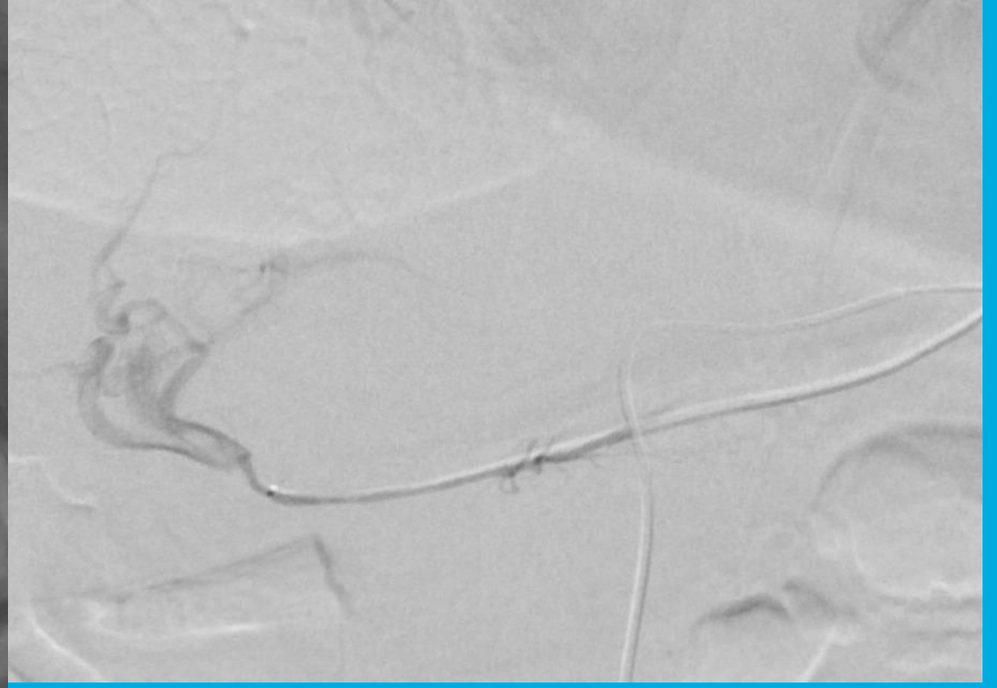
- Vascular mapping
- Identification of HCC-lesions (cone-beam CT)
- Coil / plug embolization of non-hepatic vessels if needed
- Intra-arterial Tc-99-MAA injection
- Transfer to NucMed for SPECT-CT

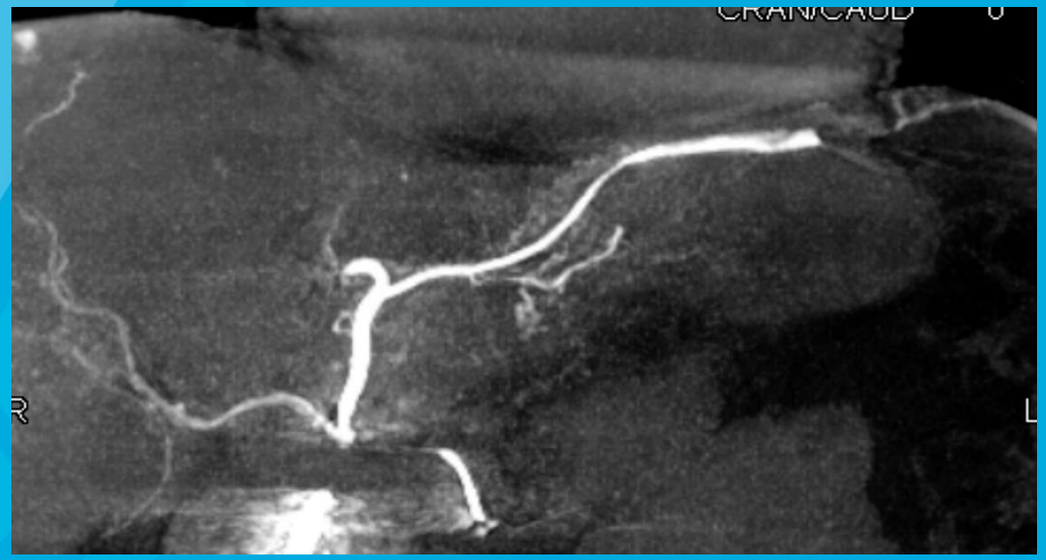
Work-up: coil-embolization





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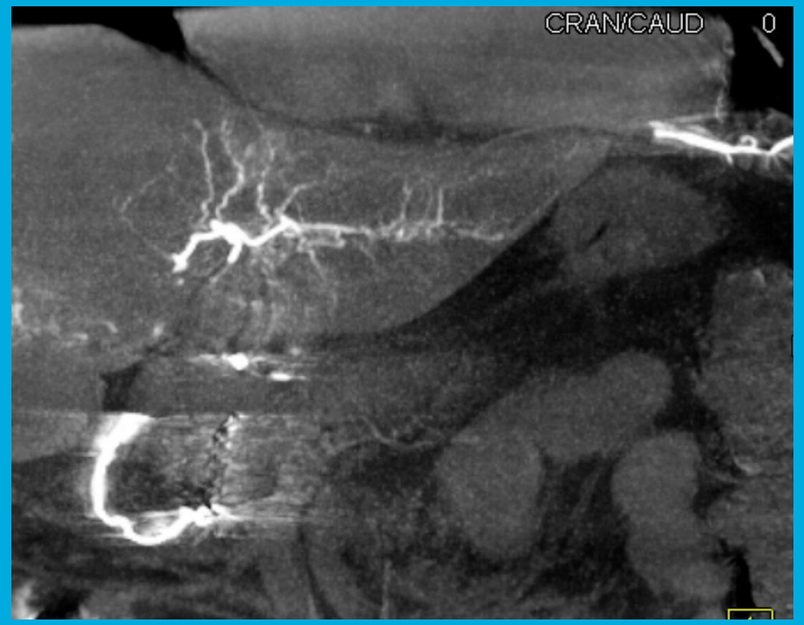
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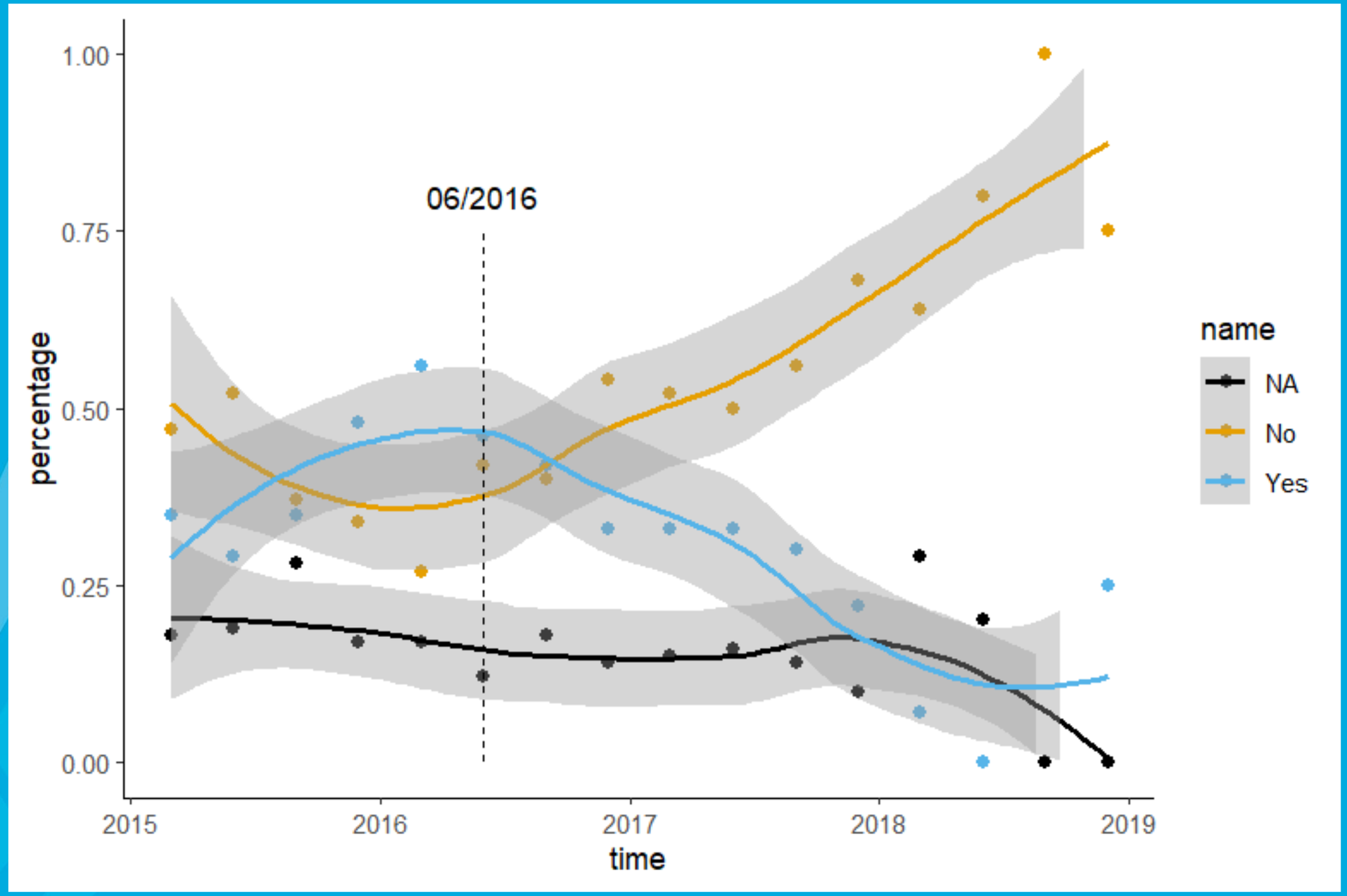
Study1
Study2
1-2
Full
4View
Splash
MIP
Left
Posterior
Left
Anterior
Poster
65 / 128
Right
Left
44 / 128
Head
Feet
35 / 81
10 fps
1 / 32
Fusion
Posterior
258 / 512
134 / 512
96 / 214
HERMES



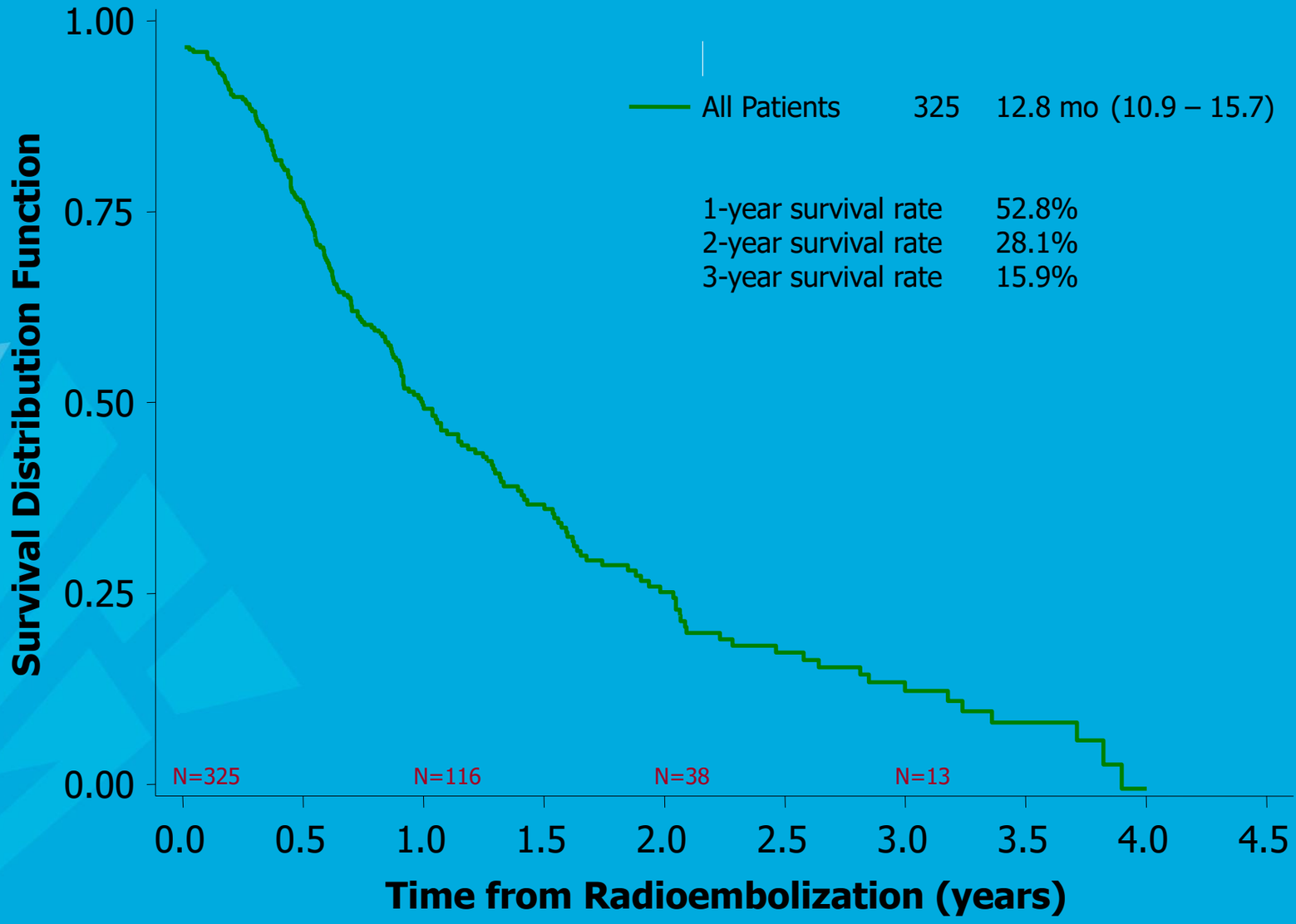
Maleux et al. Cardiovasc Intervent Radiol 2022 in press

SIRT therapy

Clinical data

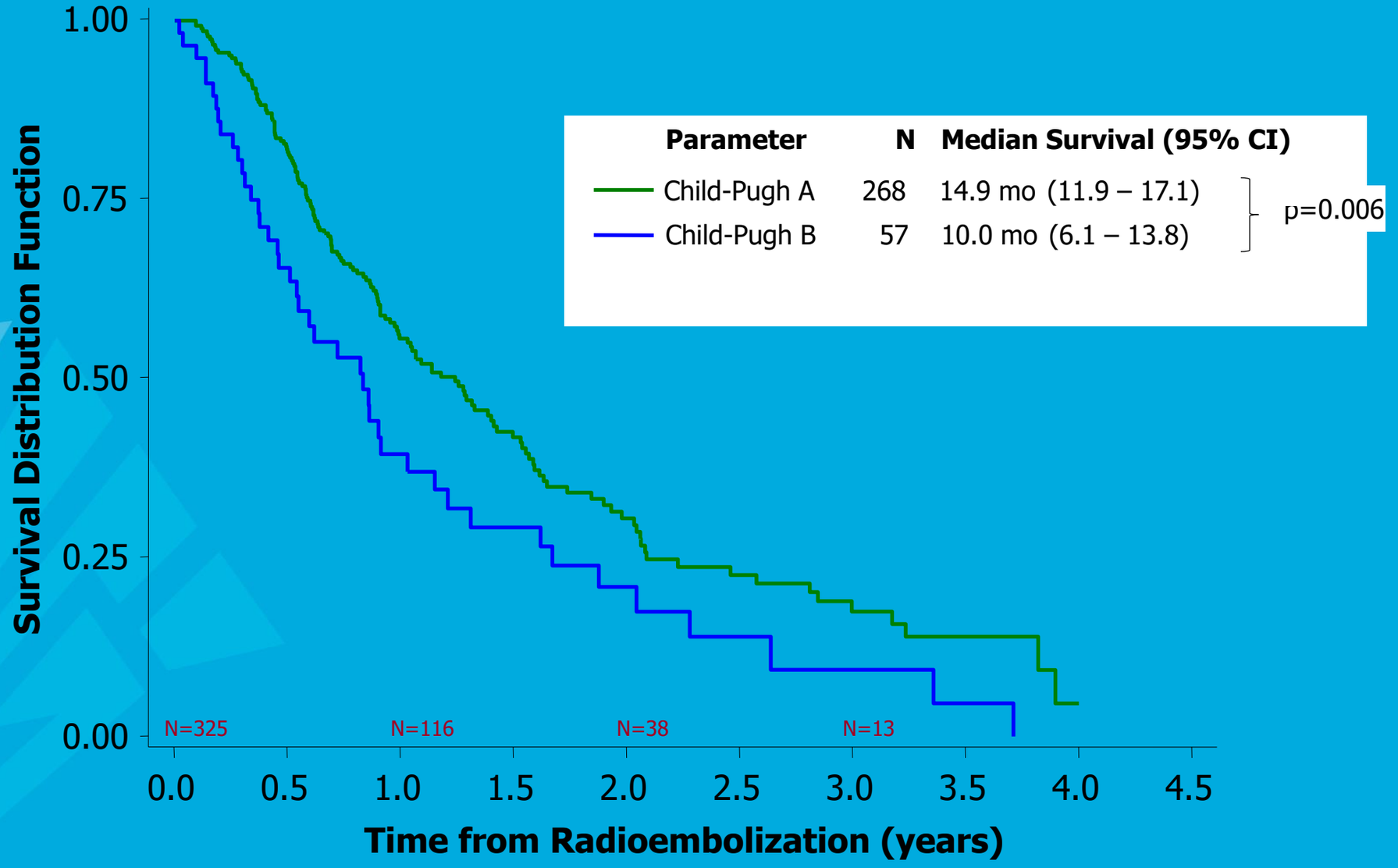
- Retro- & prospective studies
- RCT (Y90 vs Sorafenib)
  - SARAH
  - SORAMIC
- Focal lesions vs multifocal (bilobar) disease
- Y90-radioembolization vs chemo-embolization

ENRY trial : multicentric, retrospective

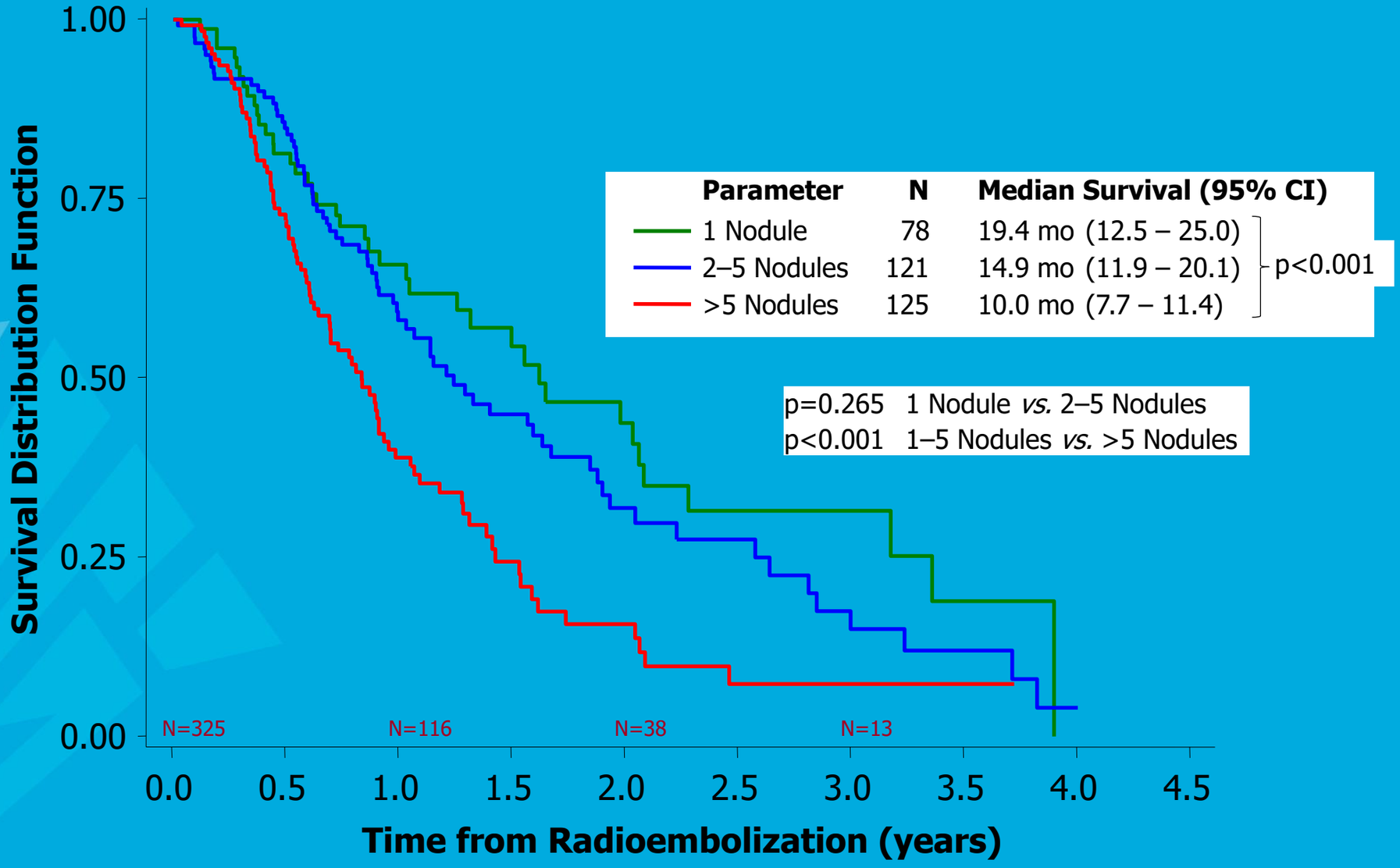


Sangro et al. J Hep 2011

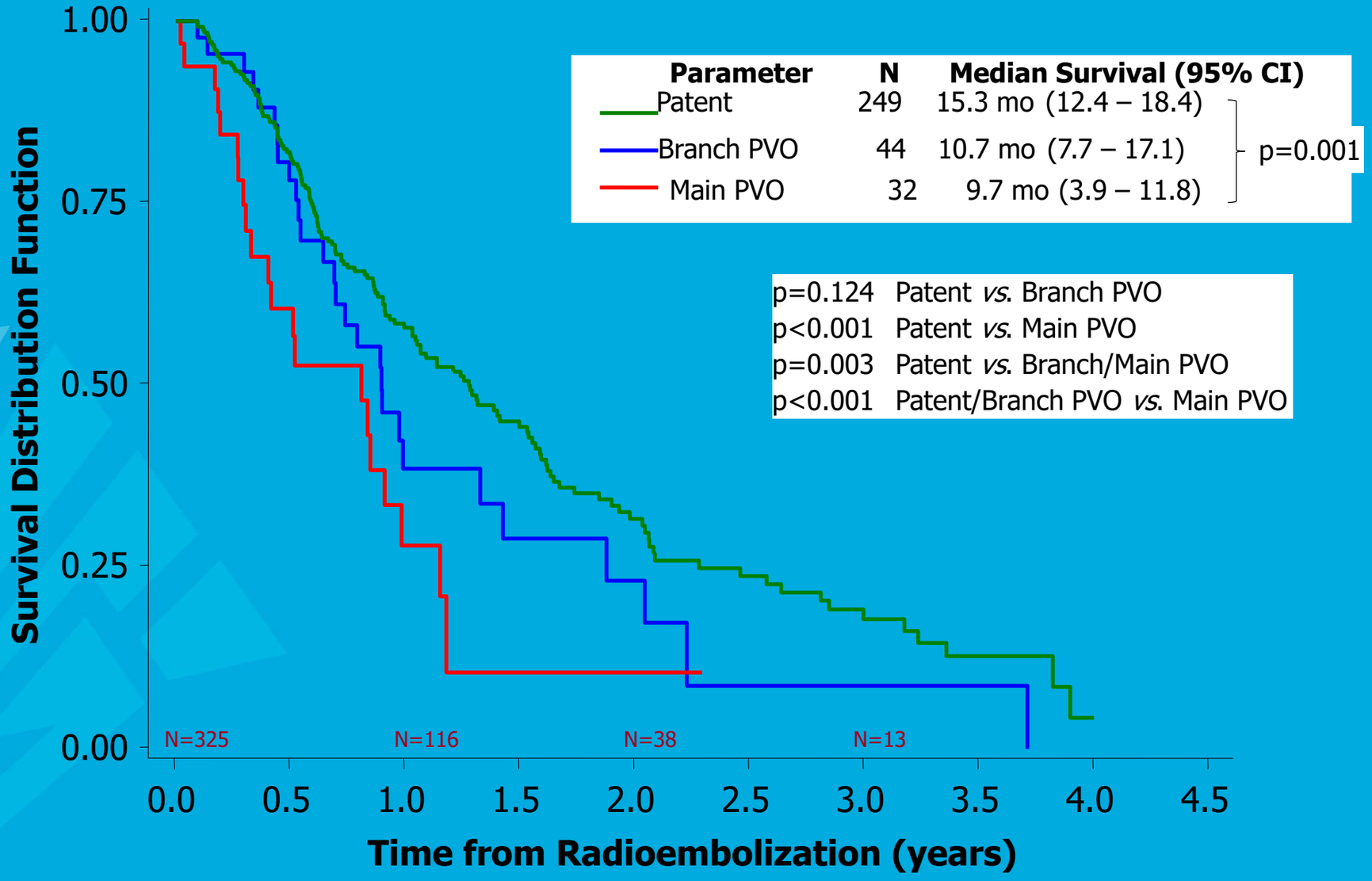
Kaplan-Meier Survival of HCC Patients Treated with ^{90}Y Microspheres Stratified by Child-Pugh Class



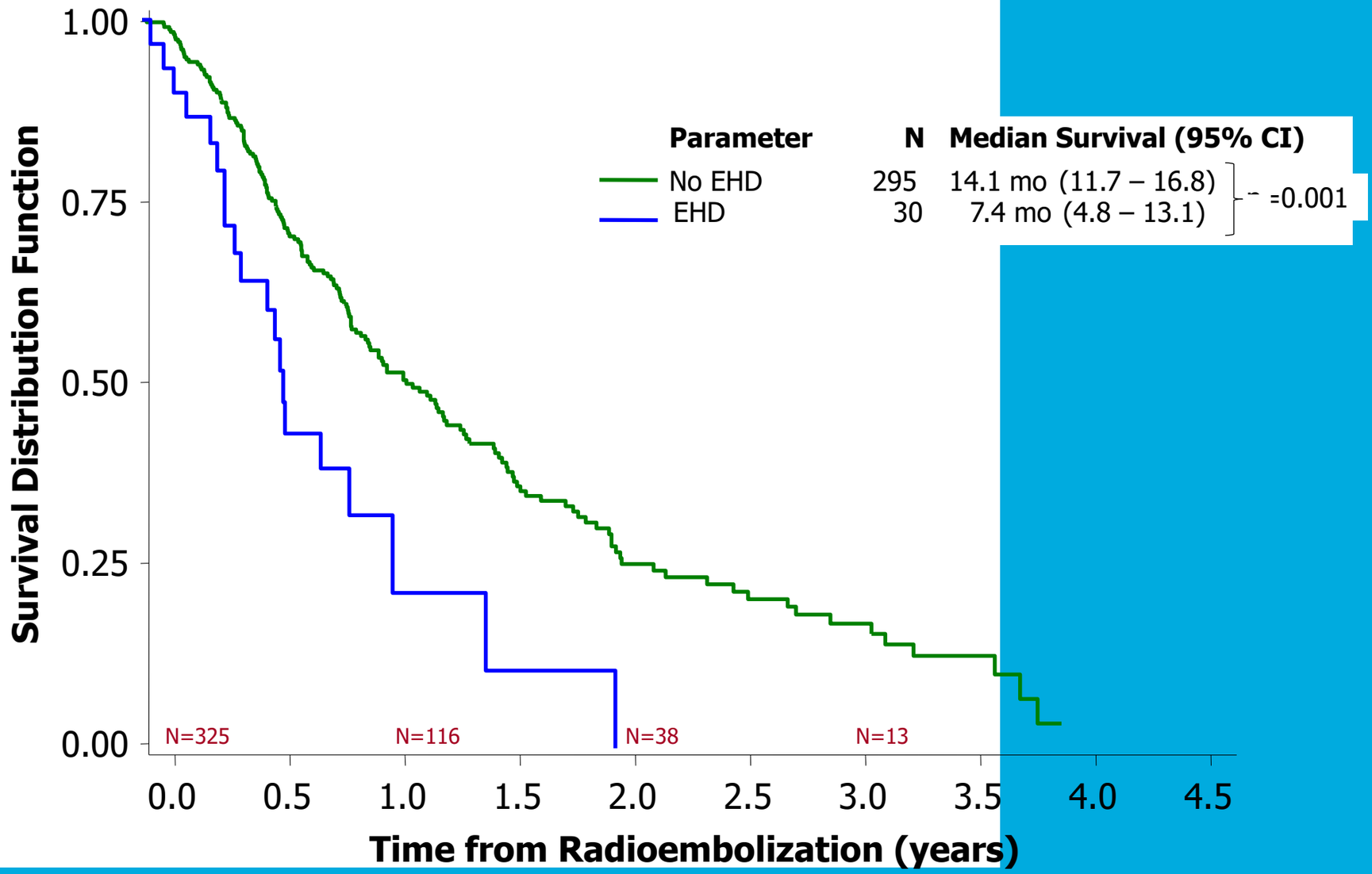
Kaplan-Meier Survival of HCC Patients Treated with ^{90}Y Microspheres Stratified by Tumour Burden



Kaplan-Meier Survival of HCC Patients Treated with ^{90}Y Microspheres Stratified by Portal Vein Involvement



Kaplan-Meier Survival of HCC Patients Treated with ^{90}Y Microspheres Stratified by Extra-Hepatic Disease (EHD)



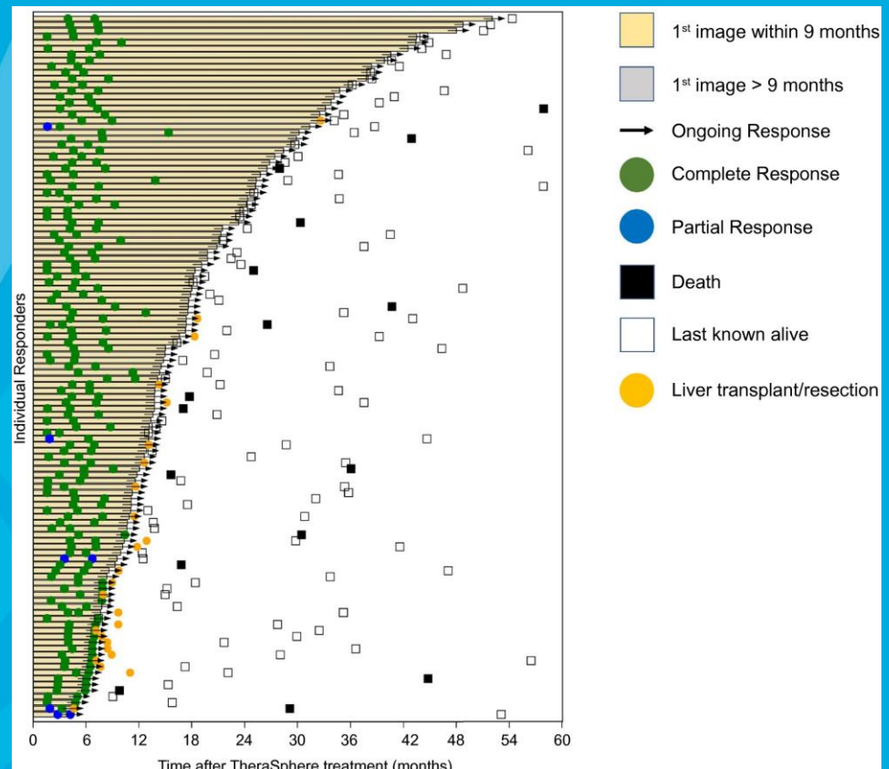
HEPATOLOGY

AASLD

HEPATOLOGY, VOL. 68, NO. 4, 2018

Institutional Decision to Adopt Y90 as Primary Treatment for Hepatocellular Carcinoma Informed by a 1,000-Patient 15-Year Experience

Riad Salem,[1-3] Ahmed Gabr,[1] Ahsun Riaz,[1] Ronald Mora,[1] Rehan Ali,[1] Michael Abecassis,[3] Ryan Hickey,[1] Laura Kulik,[4] Daniel Ganger,[4] Steven Flamm,[4] Rohi Atassi,[1] Bassel Atassi,[1] Kent Sato,[1] Al B. Benson,[2] Mary F. Mulcahy,[2] Nadine Abouchaleh,[1] Ali Al Asadi,[1] Kush Desai,[1] Bartley Thornburg,[1] Michael Vouche,[1] Ali Habib,[1] Juan Caicedo,[3] Frank H. Miller,[5] Vahid Yaghmai,[5] Joseph R. Kallini,[1] Samdeep Mouli,[1] and Robert J. Lewandowski[1-3]



Salem et al. Hepatology 2018
Salem et al. Hepatology 2022 (LEGACY)

RCT : SARAH

SIR-Spheres® Y-90 resin microspheres

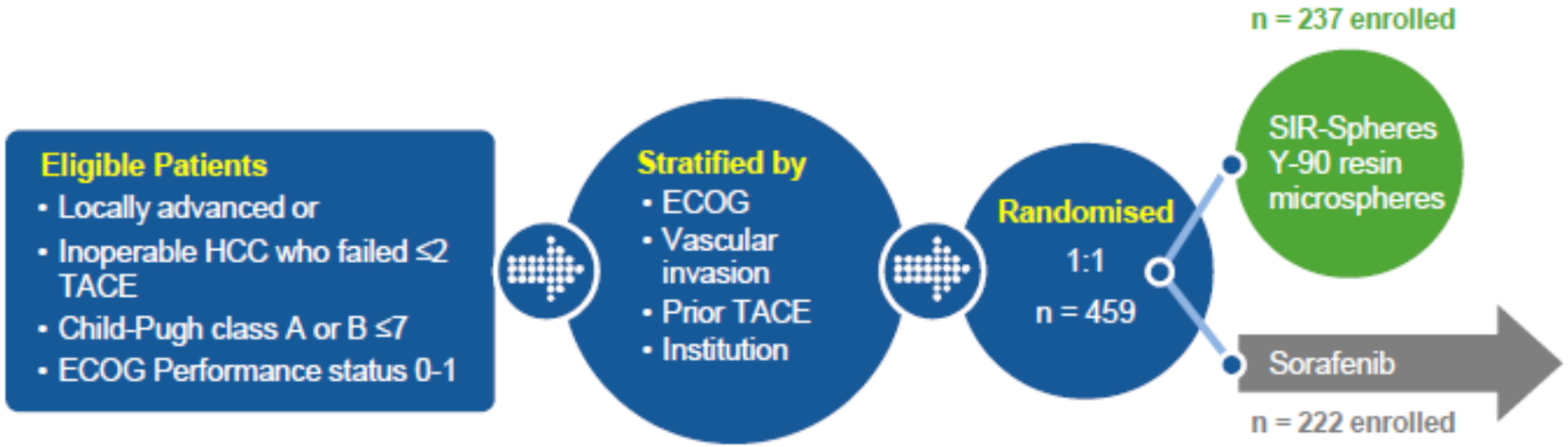
SARAH

The SARAH study design

Prospective open-label multi-centre French national RCT

Primary endpoint: Overall survival
Secondary endpoints: Safety/tolerability, PFS, ORR, HRQoL, healthcare costs

SARAH study endpoints | Key eligibility criteria



Vilgrain et al. Lancet Oncol 2017

SIR-Spheres® Y-90 resin microspheres

SARAH

SIR-Spheres Y-90 resin microspheres leads to similar overall survival compared to sorafenib

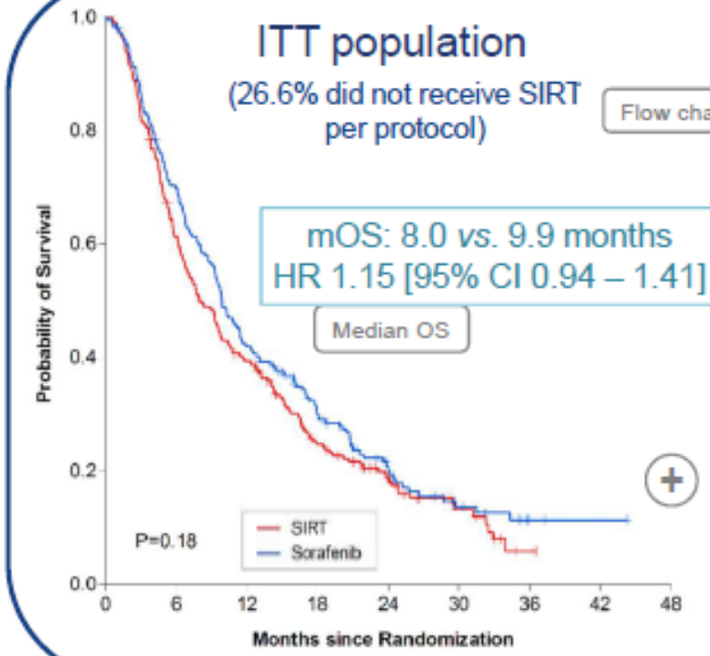
ITT population

(26.6% did not receive SIRT per protocol)

Flow chart

mOS: 8.0 *vs.* 9.9 months
HR 1.15 [95% CI 0.94 – 1.41]

Median OS

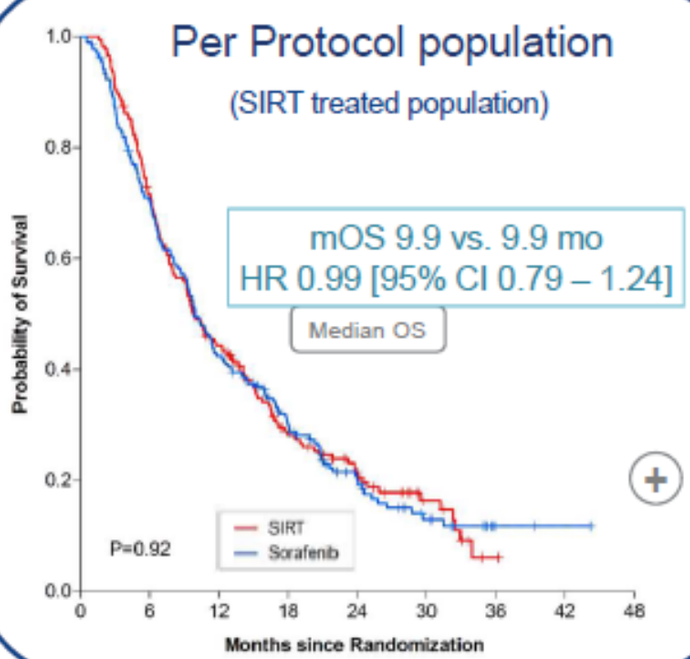


Per Protocol population

(SIRT treated population)

mOS 9.9 vs. 9.9 mo
HR 0.99 [95% CI 0.79 – 1.24]

Median OS



Vilgrain V *et al. J Hepatol* 2017; 66 (Suppl 1): Abs. GS-012.

REF

Improving Quality of Survival for patients with inoperable HCC

SIR-Spheres® Y-90 resin microspheres

SIRveNIB

SARAH AEs

Significantly reduced frequency and severity of side effects (2/2)

Common adverse events (%)	SIR-Spheres Y-90 resin microspheres (n=130)		Sorafenib (n=162)		p value	
	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3
Respiratory, thoracic, mediastinal disorders						
Cough	6.2%	0%	4.9%	0%	0.7969	-
Skin and subcutaneous tissue disorders						
Alopecia	**0%**	**0%**	**9.9%**	**0%**	**<0.0001**	-
Palmar-plantar erythrodysaesthesia syndrome	**0.8%**	**0%**	**38.3%**	**16.7%**	**<0.0001**	**<0.0001**
Rash	**0%**	**0%**	**11.1%**	**0%**	**<0.0001**	-
Vascular disorders						
Hypertension	**0%**	**0%**	**13.6%**	**1.2%**	**<0.0001**	0.5043
Portal hypertension	0%	0%	0%	0.6%	-	1.0000
Metabolism and nutrition and disorders						
Decreased appetite	8.5%	0%	12.3%	0.6%	0.3412	1.0000
Hypoalbuminaemia	4.6%	0.8%	4.3%	0.6%	1.0000	1.0000

Back

Includes adverse events which were experienced by at least 5% of treated subjects in either arm and have onset date on or after study treatment start date. P values were computed for comparison between treatment arms using the Fisher's exact test.

Chow PKH *et al. J Clin Oncol* 2017; 35 (Suppl): Abs 4002.

REF

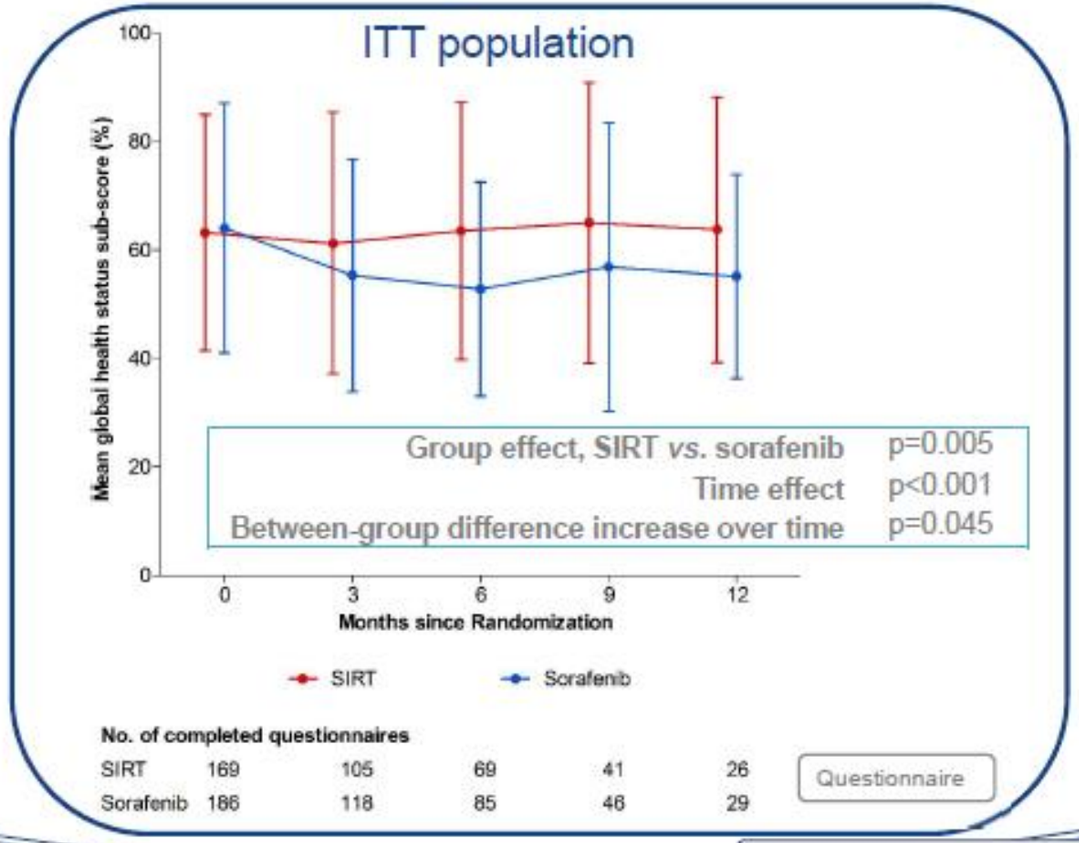
Improving Quality of Survival for patients with inoperable HCC

SIR-Spheres® Y-90 resin microspheres

SARAH

SIR-Spheres Y-90 resin microspheres provided significantly better Quality of Life*

Per Protocol population

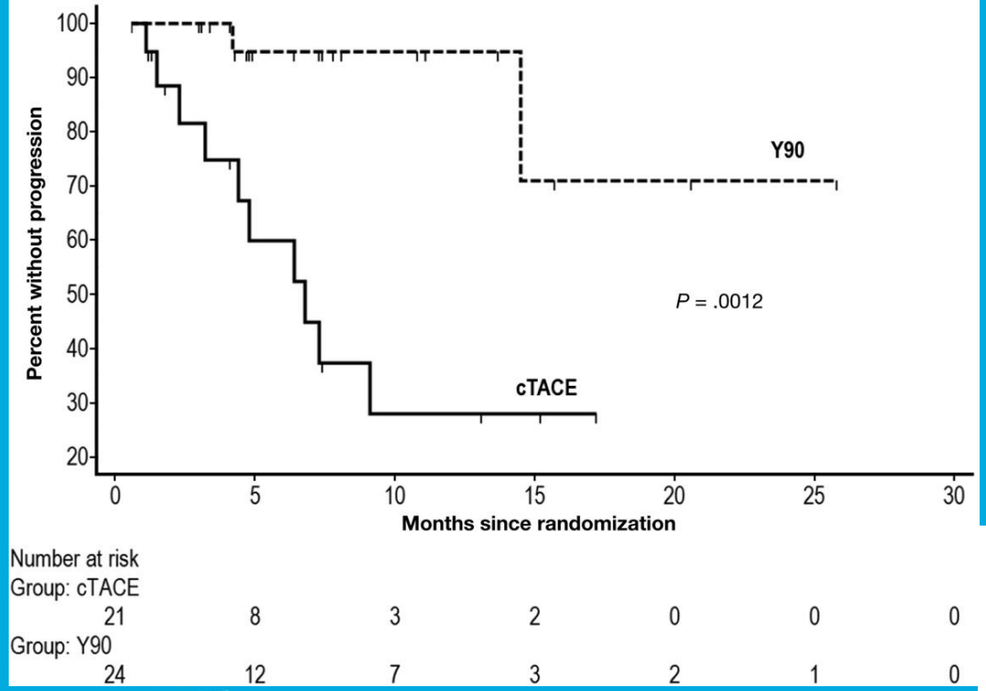


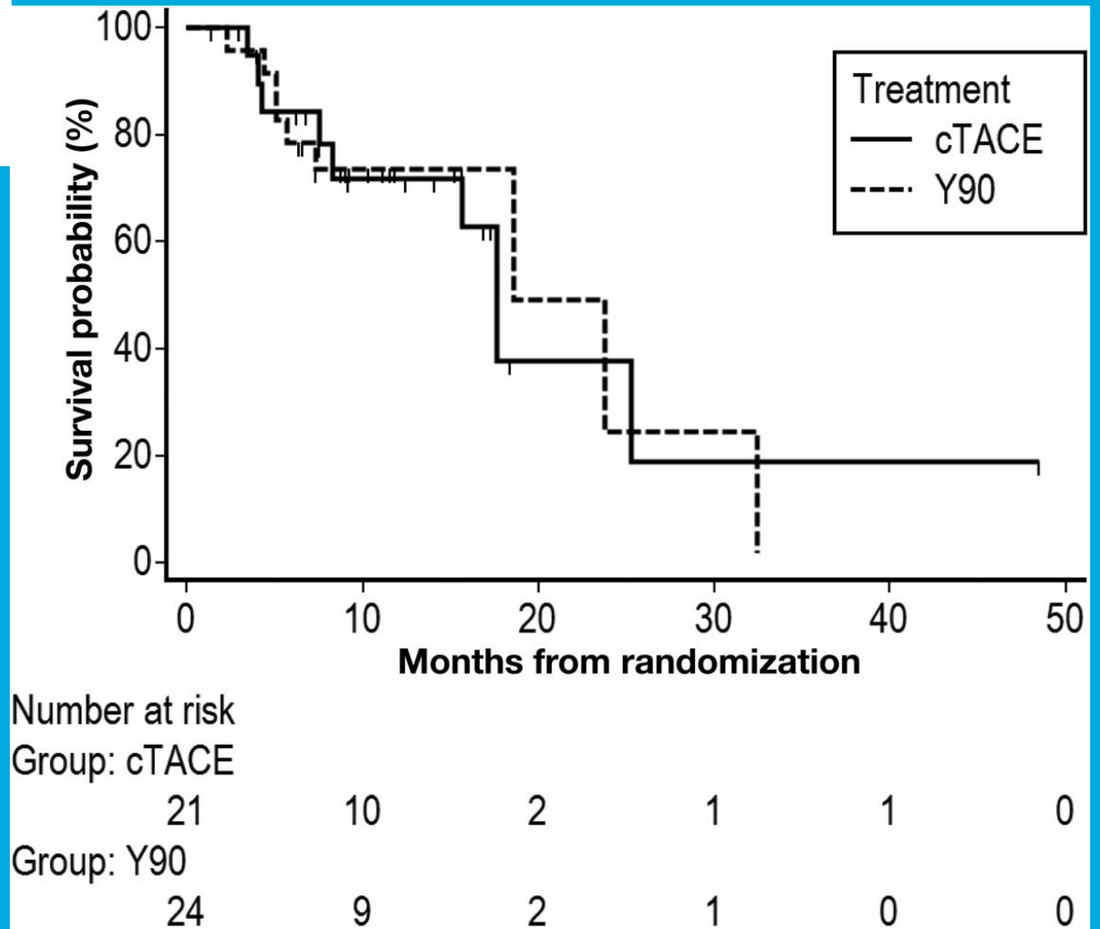
*Quality of Life by Global Health Status sub-score of EORTC QLQ-C30

Vilgrain V *et al. J Hepatol* 2017; 66 (Suppl 1): Abs. GS-012.

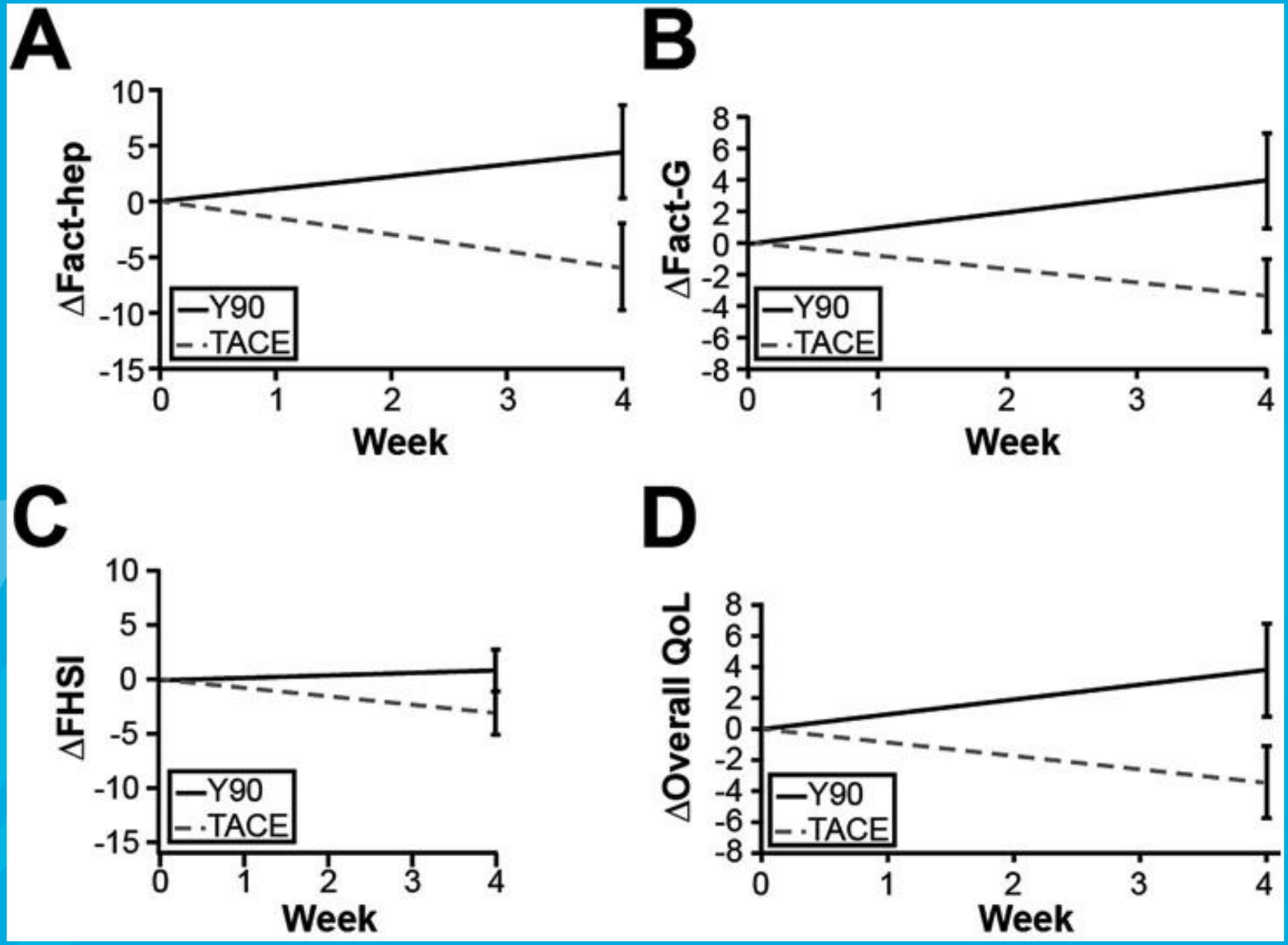
REF

Improving Quality of Survival for patients with inoperable HCC

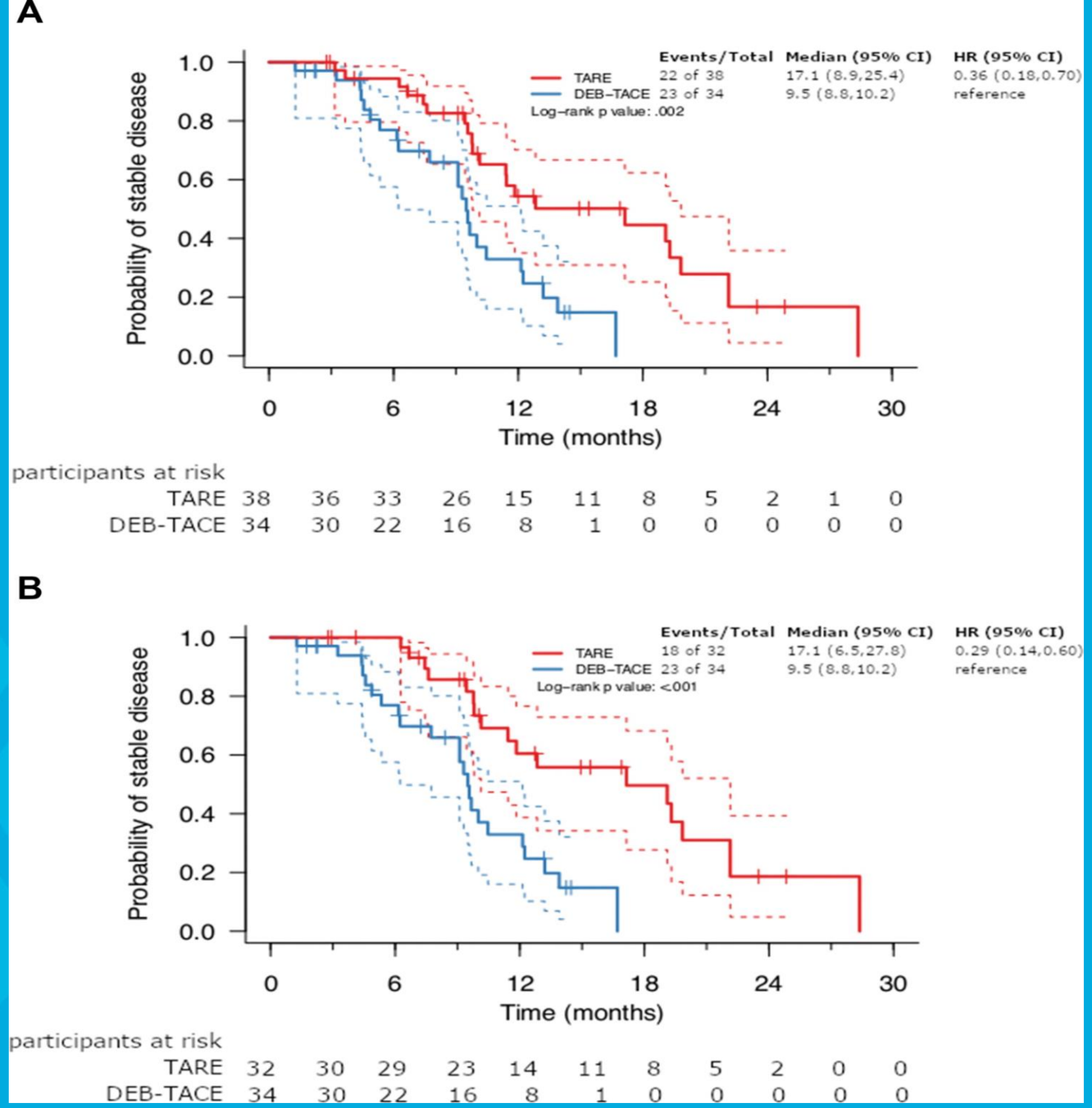




Salem, Gastroenterol 2016



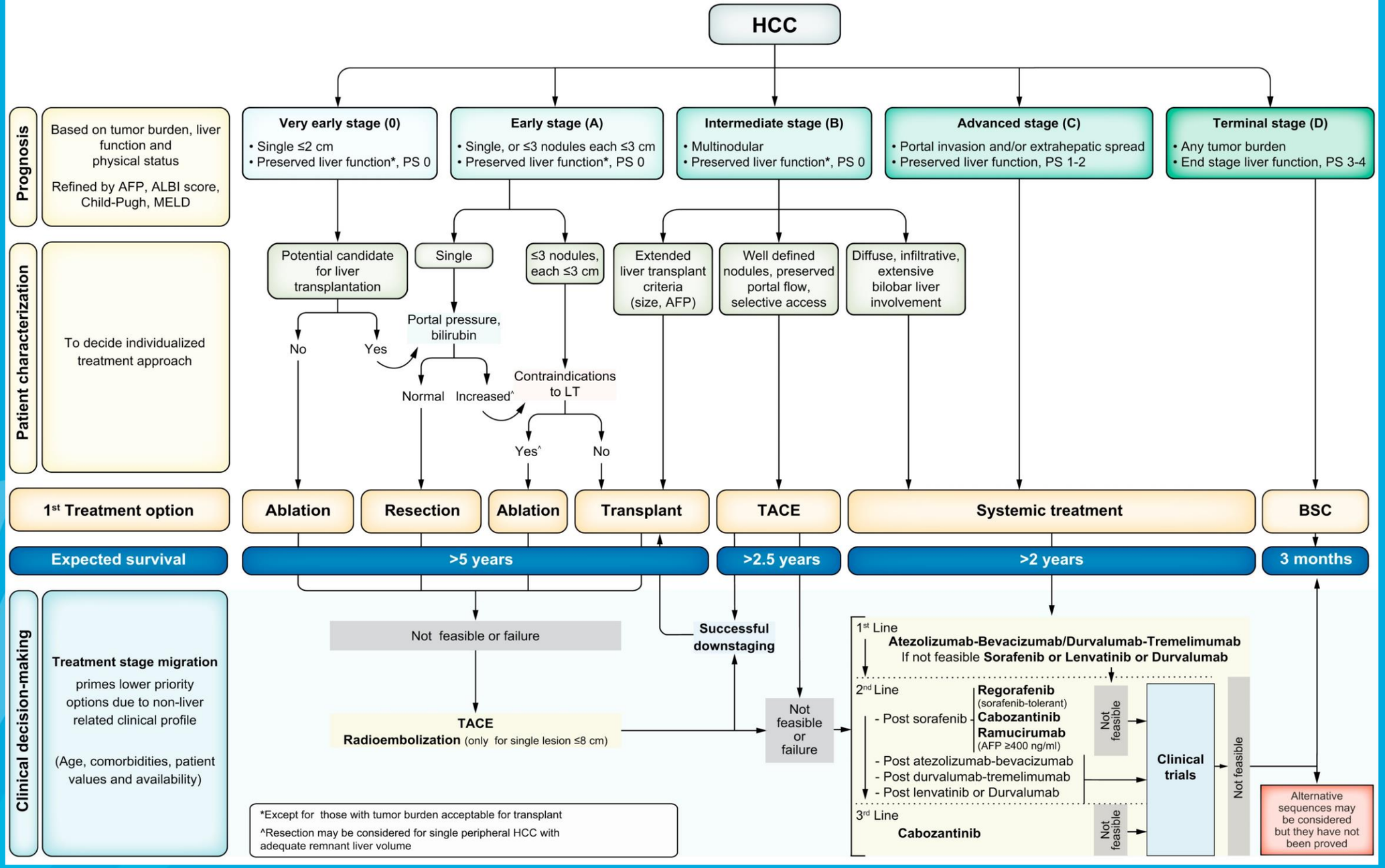
Salem et al. Clin Gastroenterol Hepatol 2016



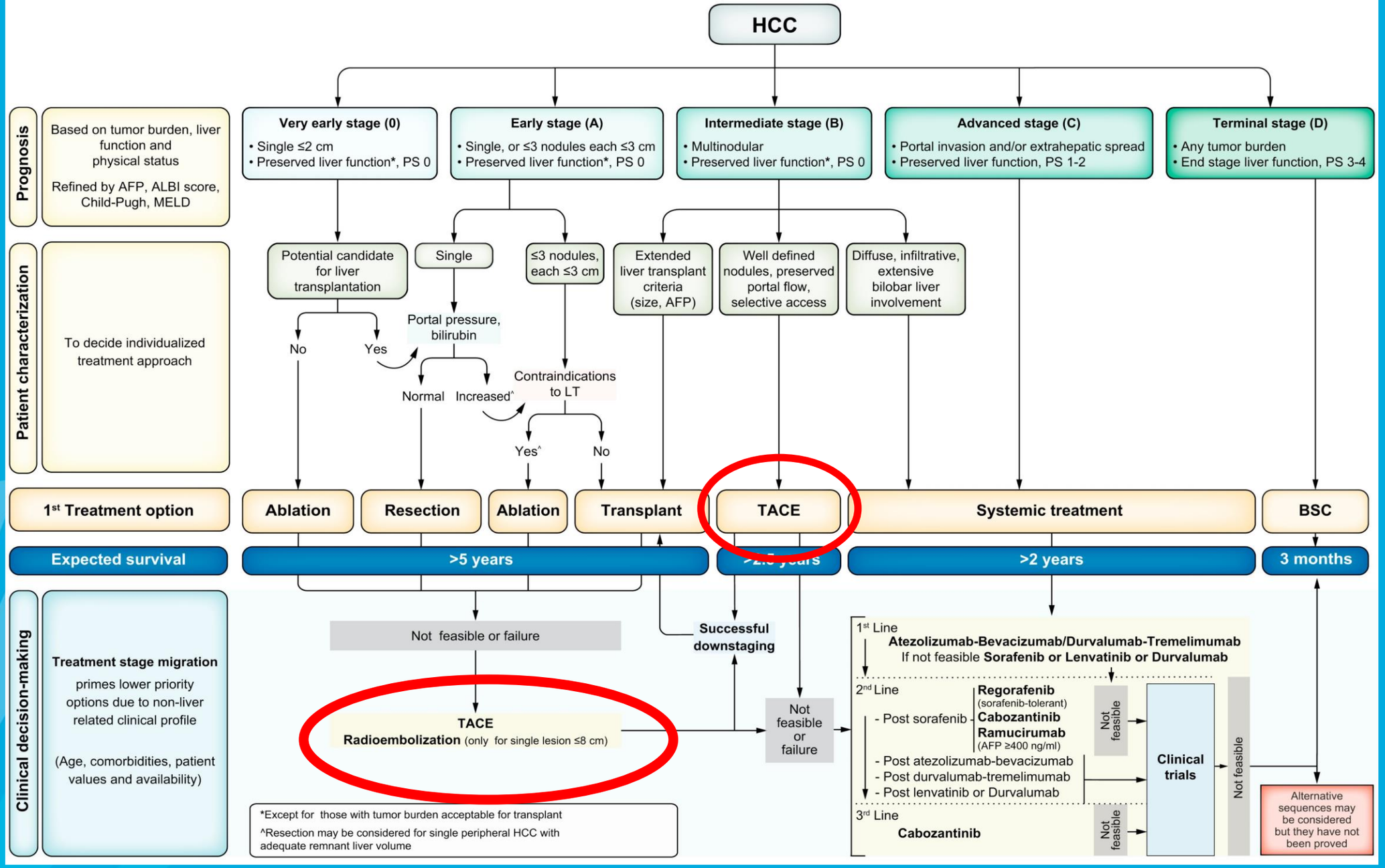
Dhondt et al. Radiology 2022

Conclusions : Radioembolization for HCC

- Safe & efficacious
- Unifocal > multifocal
- Unifocal = curative intent
- Multifocal = palliative & better toxicity profile & QoL (>< Sorafenib)
- Y90-radioembolization > chemo-embolization



Reig et al. J Hep 2022



Reig et al. J Hep 2022

- Thank you for your attention

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