

# Integrating systemic and locoregional therapies in a patient with advanced hepatocellular carcinoma (HCC)

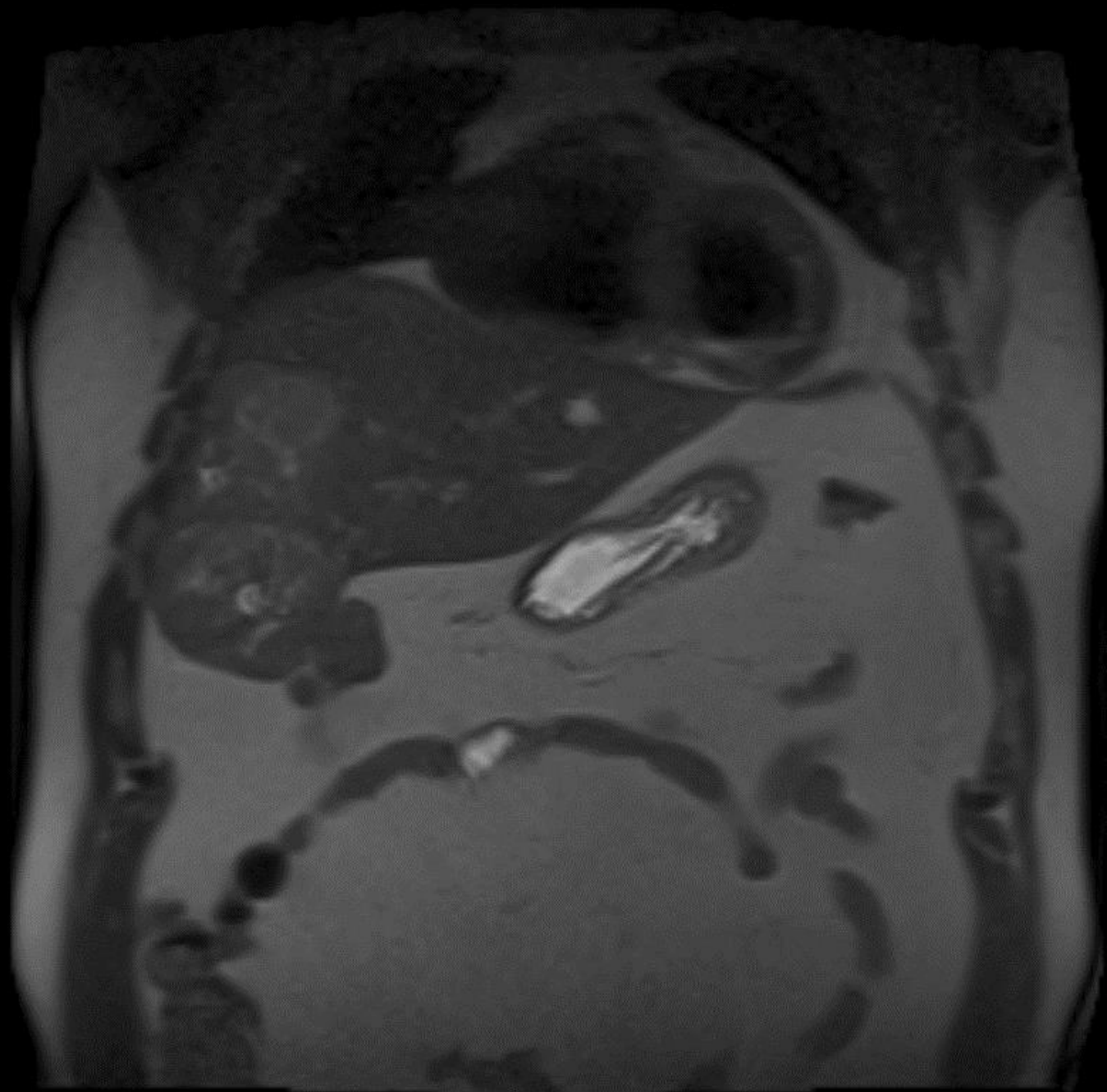
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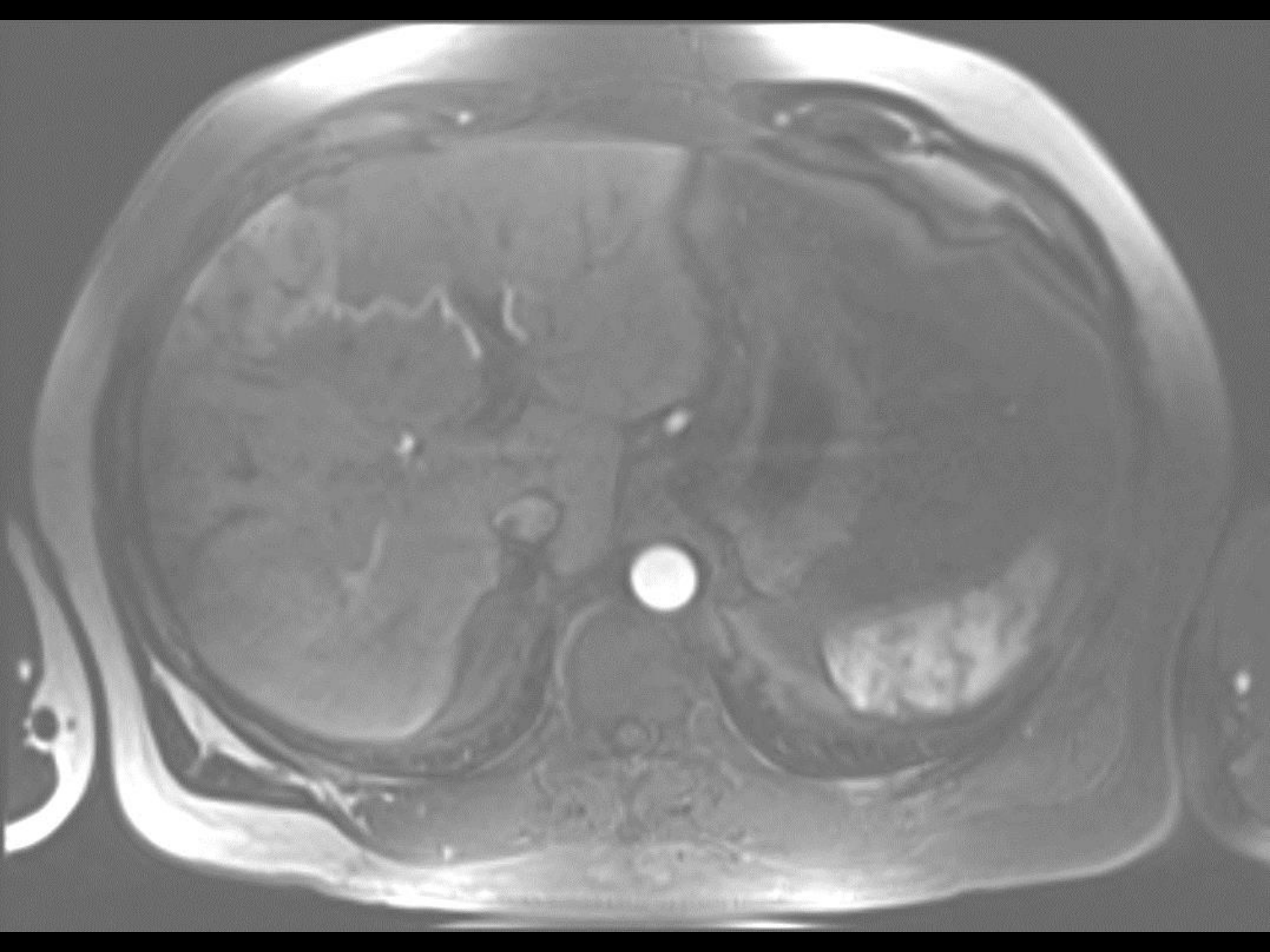
# Disclosures

- Ch. Verslype receives research funding from
  - Bayer
  - Sirtex

# Case 1: male patient, 47 yr

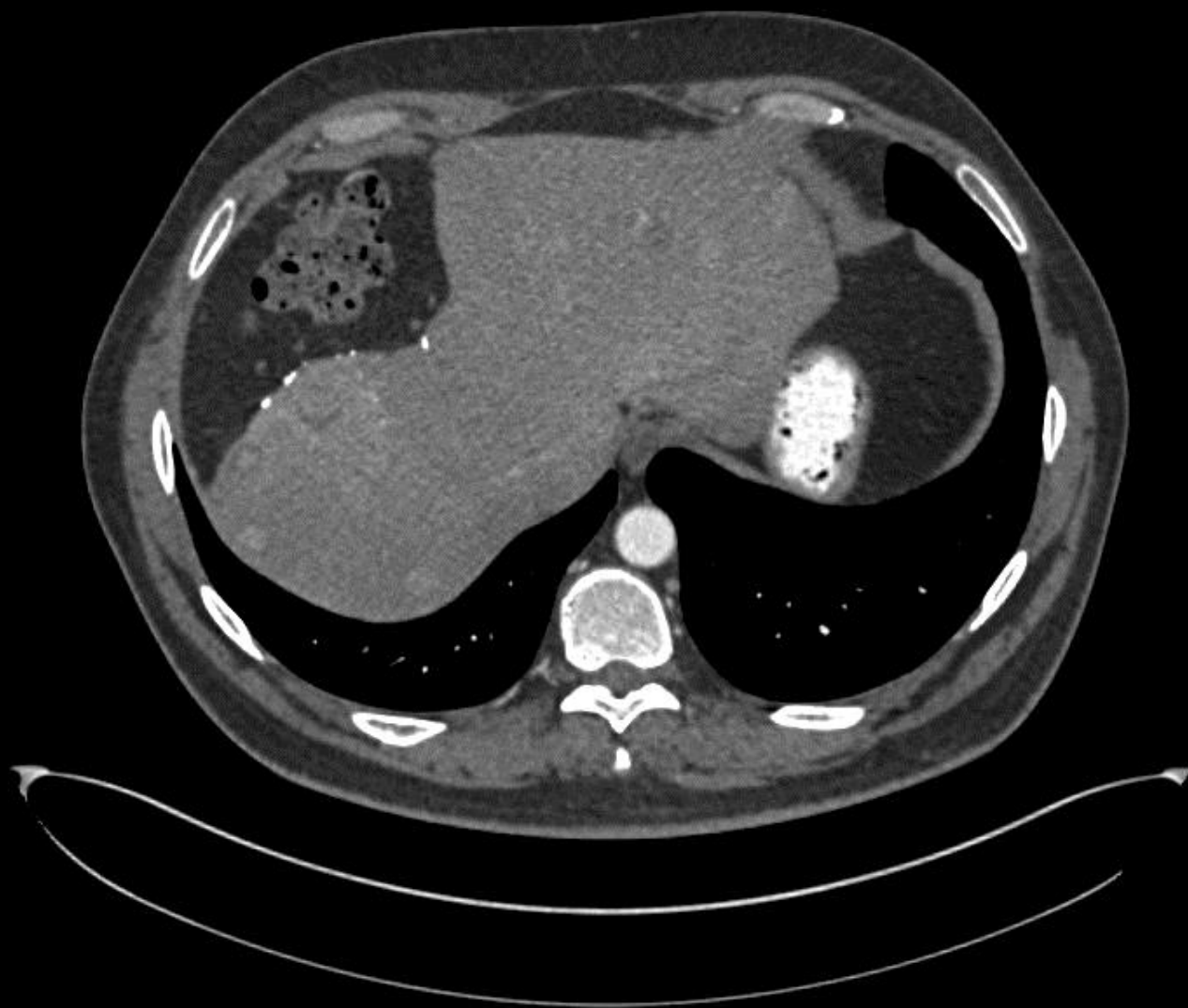
- 1/2013: abdominal pain, no signs of chronic liver disease
- Imaging: 2 hypervascular liver lesions (both > 5 cm)
- Excellent liver synthetic function
- Normal serum alfa-fetoprotein
- No portal hypertension





- 3/2013: central hepatectomy (s.4a + 4b + 5)
  - RO-resection
  - Well-differentiated HCC <  $\beta$ -catenin mutated adenoma?
  - Non-cirrhotic liver

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  - Non-cirrhotic liver
- 1/2014
  - rise in serum AFP
  - multifocal intrahepatic recurrence
  - no extra-hepatic spread



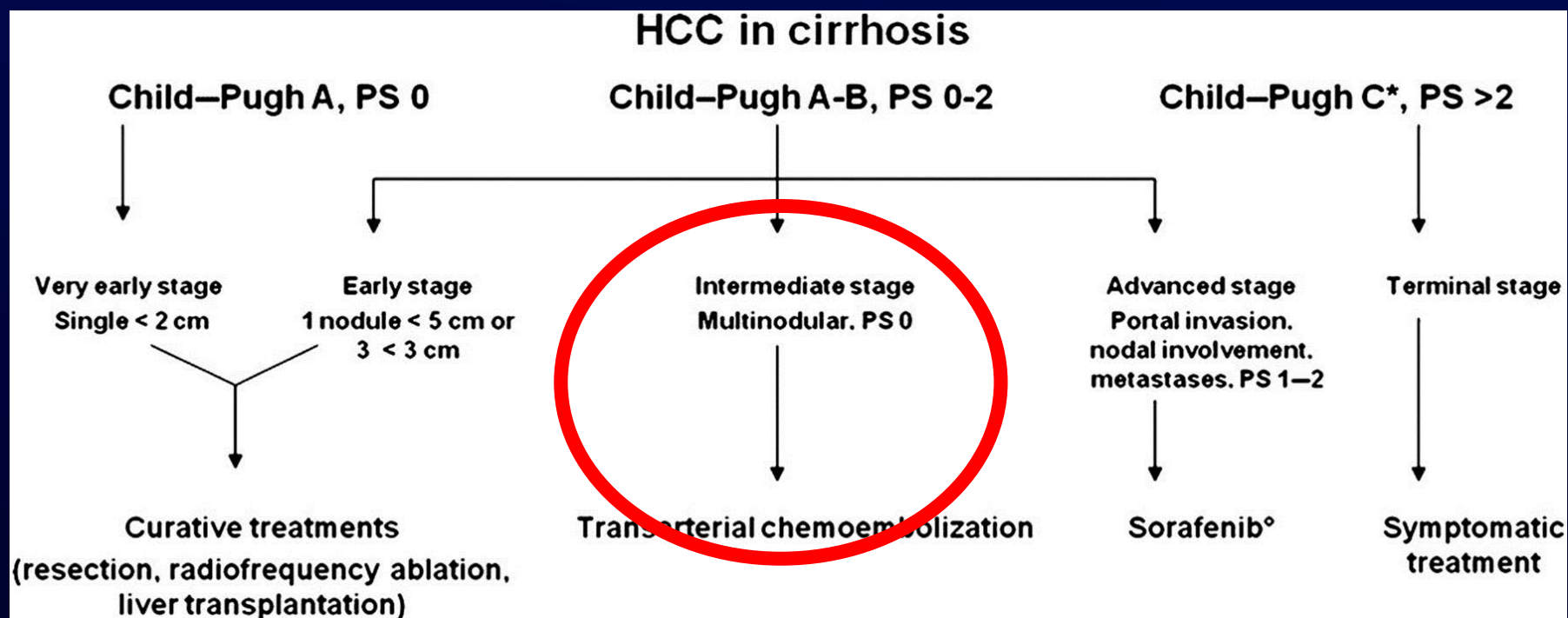
# Male patient, 47 yrs

- Multifocal bilobar recurrence of HCC
  - 1 year following central hepatectomy
  - No extrahepatic spread
  - Excellent liver function
- Therapeutic options?

# Male patient, 47 yrs

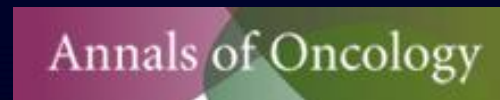
- Multifocal bilobar recurrence of HCC
  - 1 year following central hepatectomy
  - No extrahepatic spread
  - Excellent liver function
- Therapeutic options?
  1. Liver transplantation
  2. Transarterial chemoembolization
  3. Sorafenib
  4. Radioembolization
  5. Other

# Hepatocellular Carcinoma: ESMO Clinical Practice Guidelines for Diagnosis, Treatment, and Follow-up<sup>†</sup>



\* Poor liver synthetic function due to tumor involvement of the liver.

<sup>°</sup> Only Child-Pugh A.



# Guidelines versus clinical practice

- = 101 patients with newly diagnosed, previously untreated HCC in BCLC stage B
  - 55%: transarterial locoregional therapy
    - TACE/TAE: 38%
    - Y90-RE: 17 %
  - 35%: radical therapy
    - RFA: 4%
    - Resection: 9%
    - LTx: 25%
  - 5%: systemic therapy
  - 5%: best supportive care

# SORAMIC

## Imaging Sub-Study

### 1° endpoint

Non-inferiority (1<sup>st</sup> step) or  
superiority (2<sup>nd</sup> step) of Primovist-  
MRI vs. CE-CT

Contrast-  
enhanced CT

Primovist®-  
enhanced MRI

Assign to  
study arm

Off Study

- BCLC 0
- BCLC D

## Local Ablation Group

( $\leq 4$  tumours;  $\leq 5$  cm each)

RFA

Randomise  
1:1  
n = 290

## Palliative Group

Randomise  
n = 375

SIR-Spheres

## 1° endpoint

sorafenib

Time to Recurrence

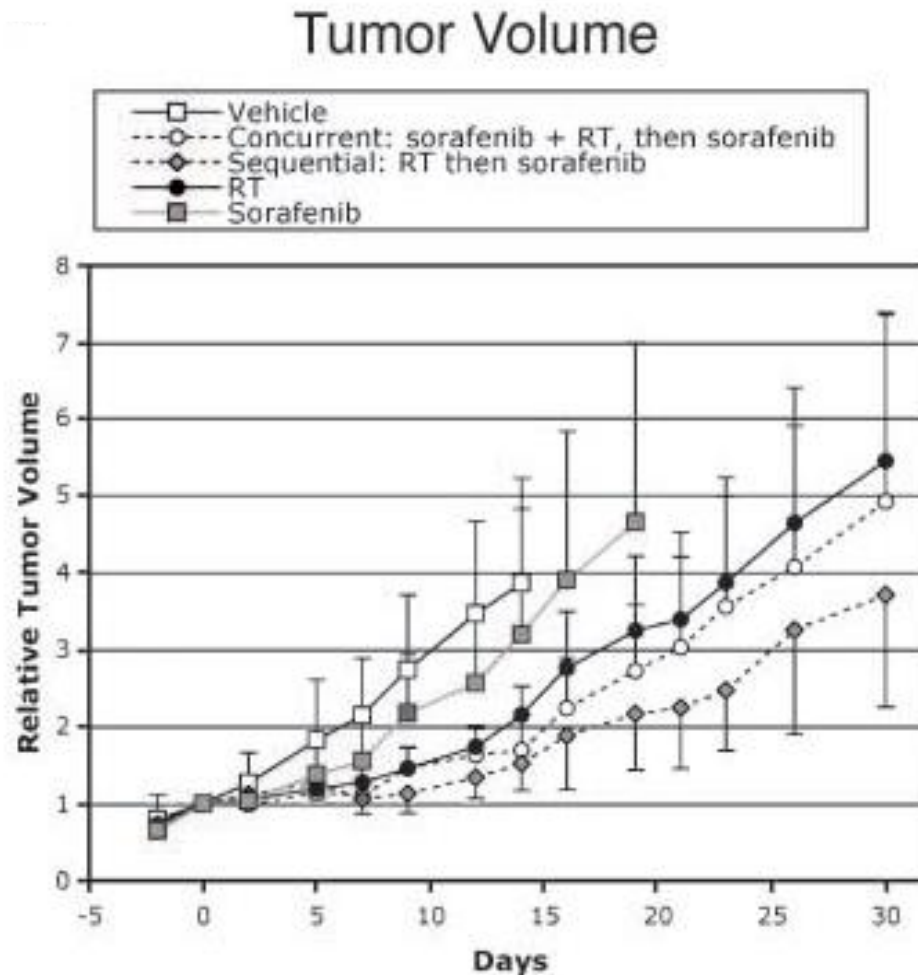
placebo

sorafenib

Overall Survival

sorafenib

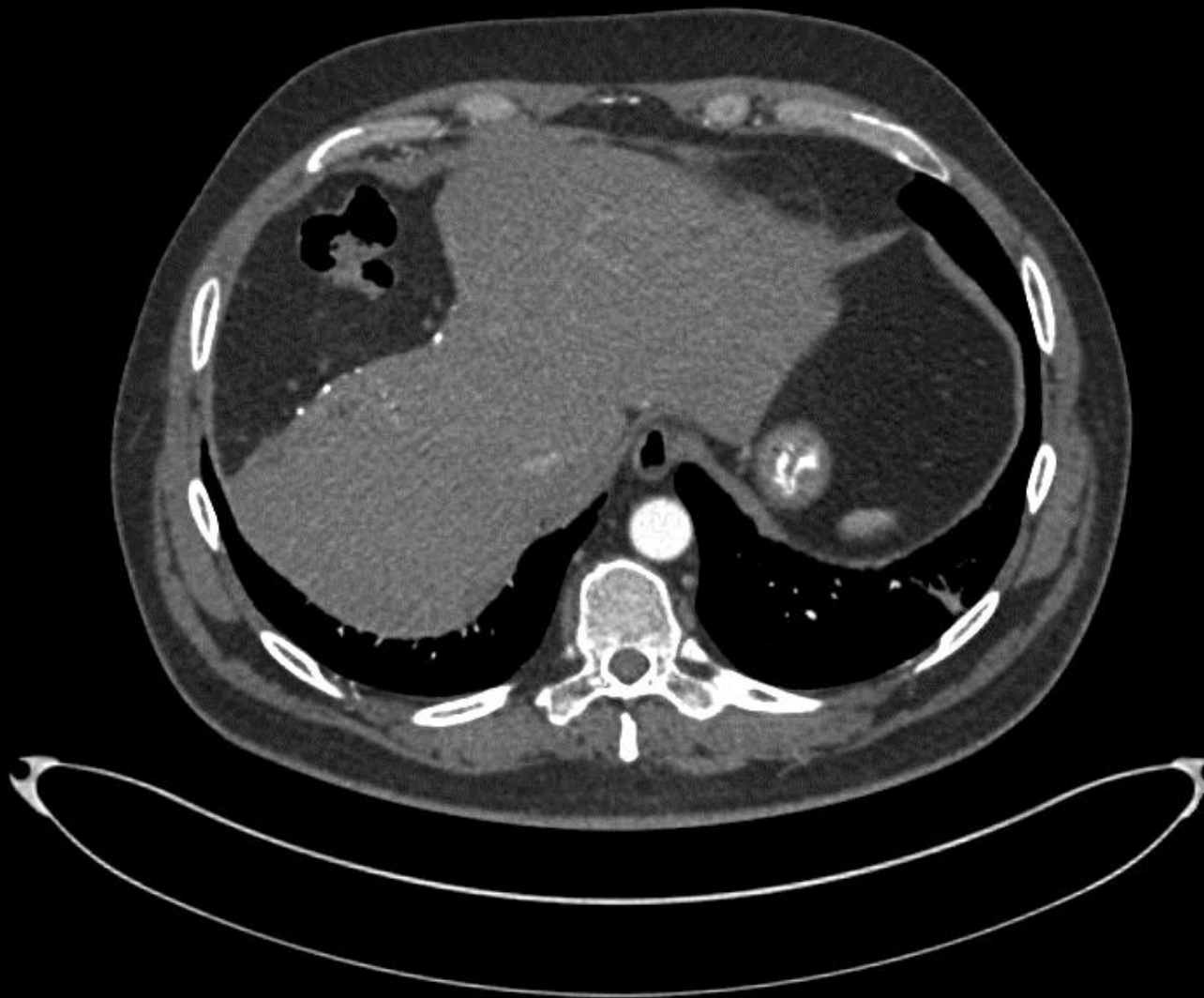
# HCT116 xenograft tumor growth delay: sorafenib alters radiation response



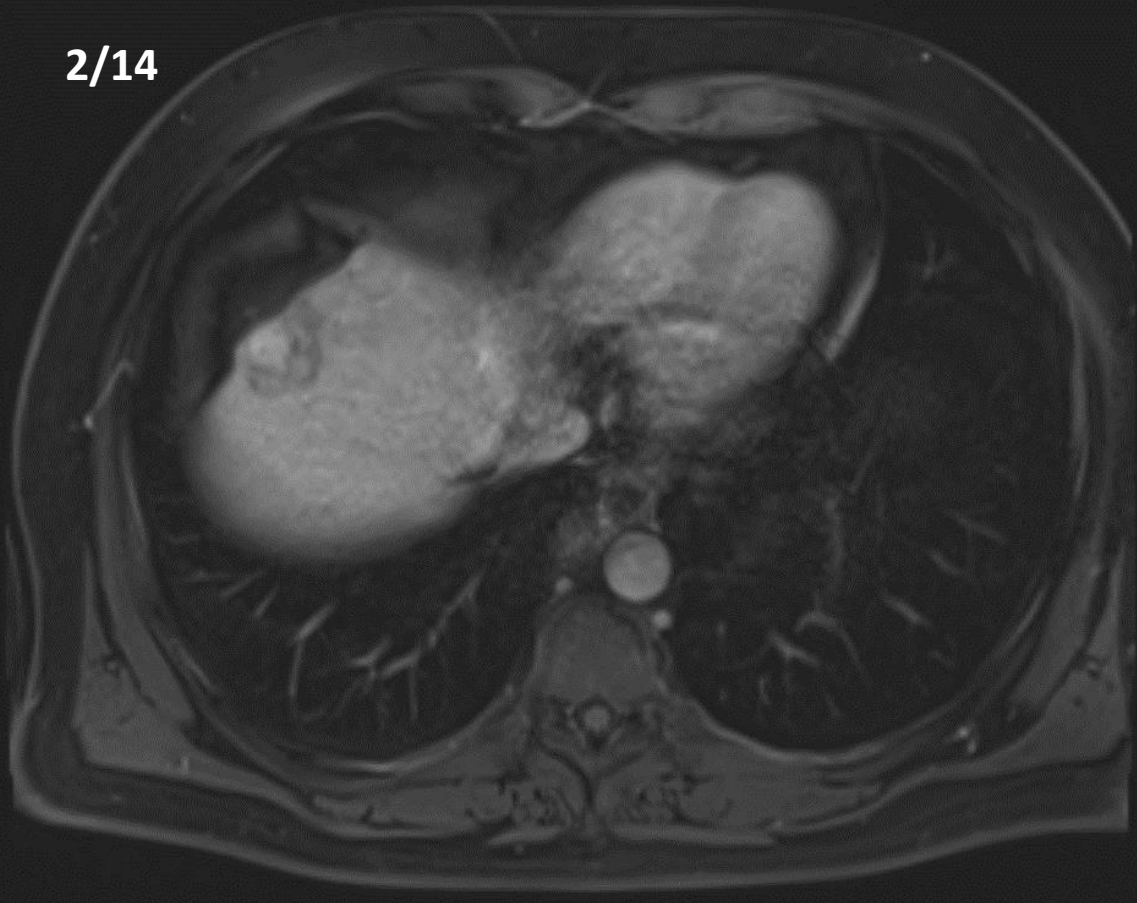
# Case 1 (continued)

- SORAMIC trial
  - randomized in combination arm
  - sequential treatment of right and left liver lobe with  $^{90}\text{Y}$ -resin microspheres
  - Day 3 post-SIRT, start sorafenib
    - Half dose (400 mg/day)
    - After 1 week: full dose (800 mg/day)
- Tolerance: grade 2 fatigue and skin rash

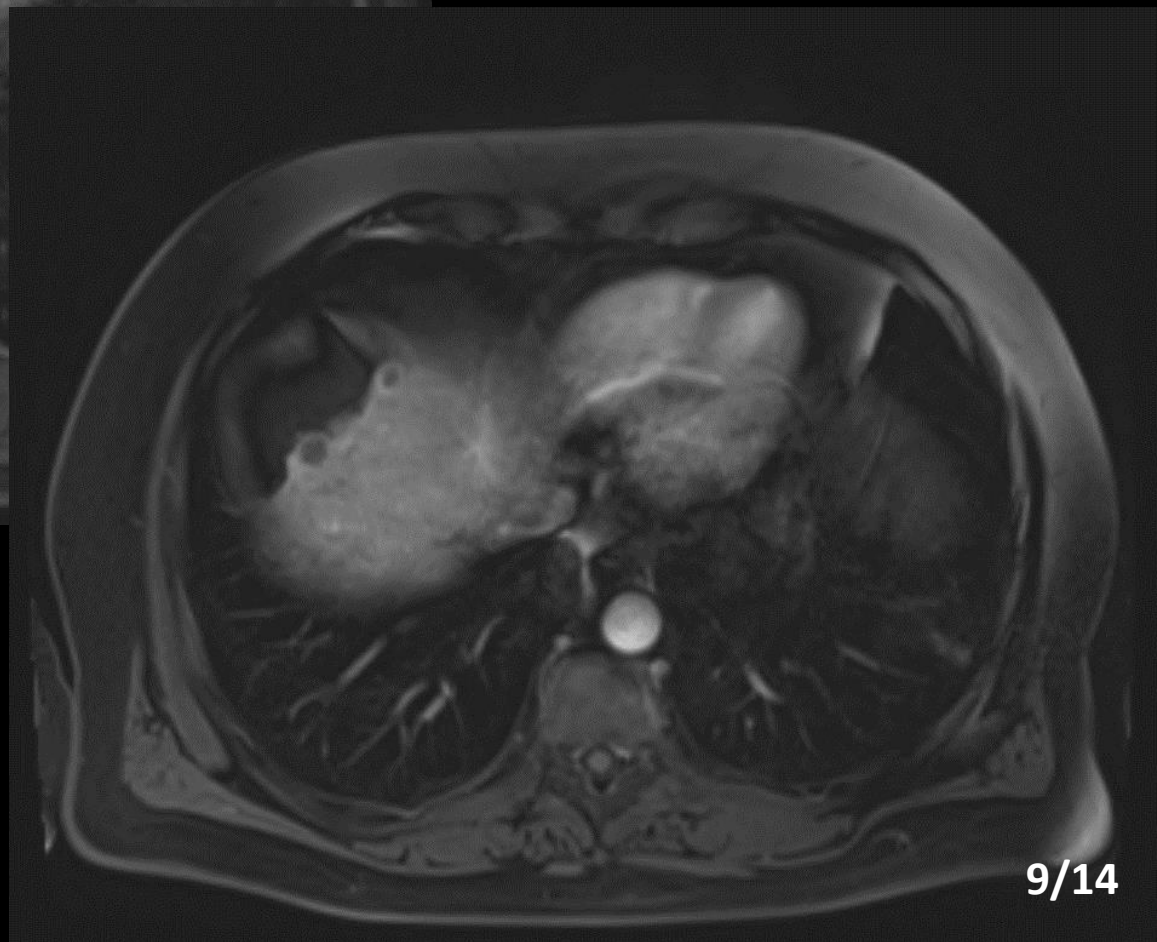
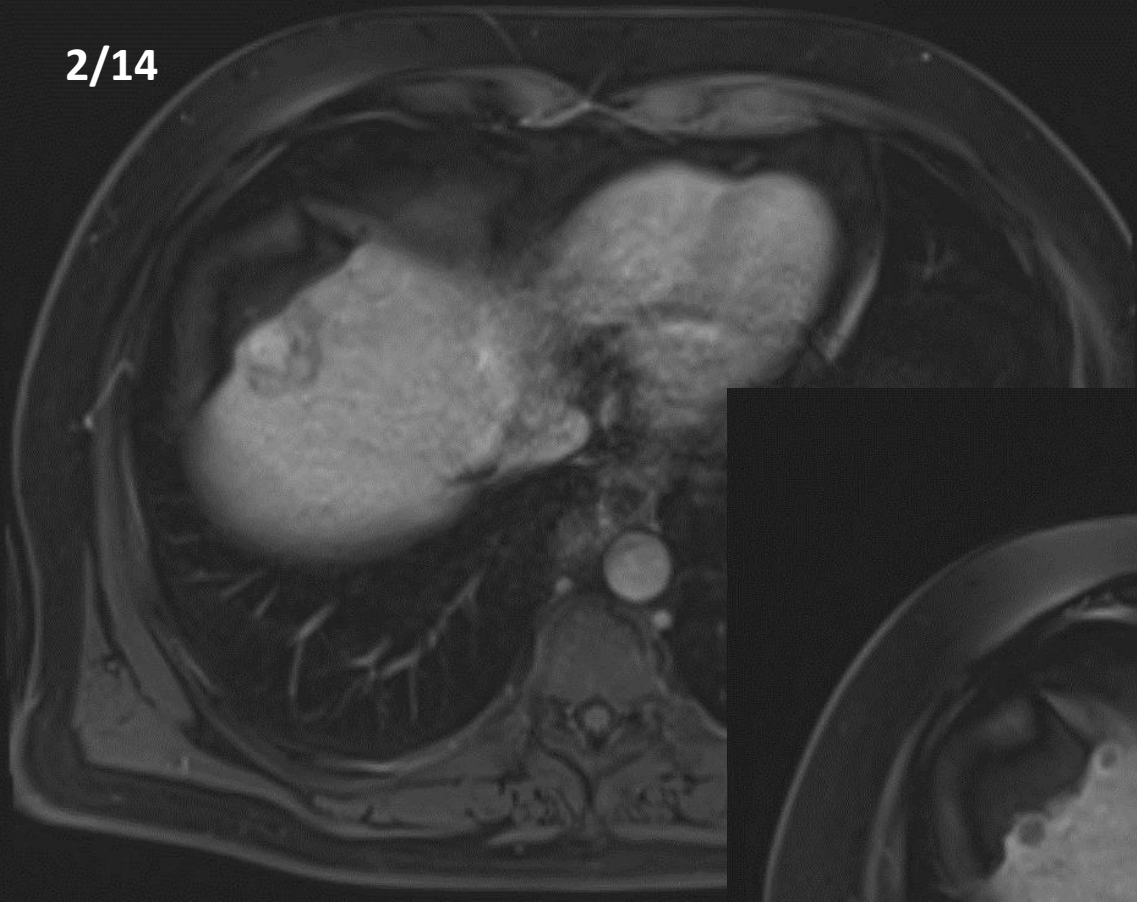
**2 months post SIRT + sorafenib**



2/14

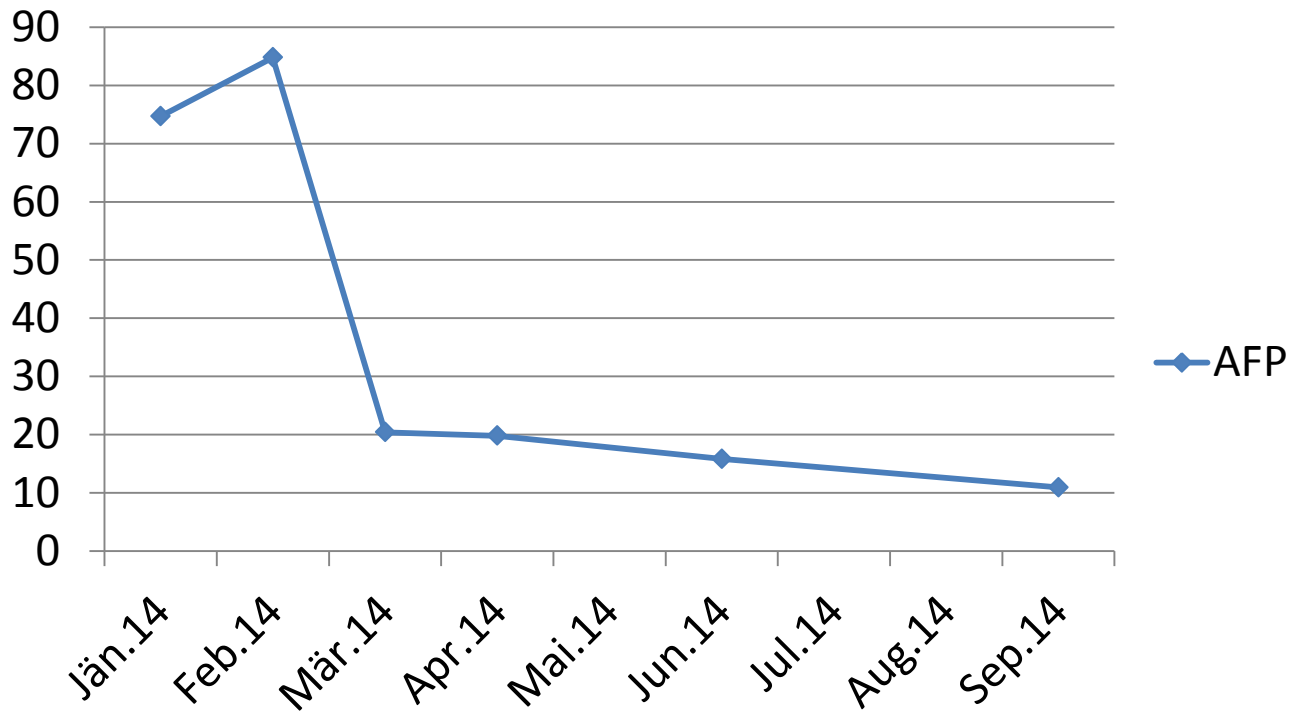


2/14



9/14

## AFP



↑  
SIRT  
R

↑  
SIRT  
L

↑  
sorafenib

LIVER CANCER

**Safety and toxicity of radioembolization plus Sorafenib in advanced hepatocellular carcinoma: analysis of the European multicentre trial SORAMIC**

Jens Ricke<sup>1</sup>, Karsten Bulla<sup>1</sup>, Frank Kolligs<sup>2</sup>, Markus Peck-Radosavljevic<sup>3</sup>, Peter Reimer<sup>4</sup>, Bruno Sangro<sup>5</sup>, Eckart Schott<sup>6</sup>, Kerstin Schütte<sup>7</sup>, Chris Verslype<sup>8</sup>, Jerzy Walecki<sup>9</sup> and Peter Malfertheiner<sup>7</sup> for the SORAMIC\* study group

# Planned safety analysis for the first 40 patients in the SORAMIC trial

**Table 2.** Treatment characteristics

Characteristic	Sorafenib + radioembolization	Sorafenib only	<i>P</i> value
Daily sorafenib dose, mg			
Mean	528	574	0.647
Median	614	557	
Range	45–793	284–792	
Duration of sorafenib treatment, months			
Mean	9.4	8.8	0.776
Median	8.5	9.6	
Activity RE total, GBq			
Median	1.87	n.a.	
Range	0.54–2.35	n.a.	

n.a., not applicable.

# Planned safety analysis for the first 40 patients in the SORAMIC trial

**Table 3.** Percentage patients with clinical and laboratory adverse events (listed in order of the most common grade  $\geq 3$  events)

Adverse event (%)	Sorafenib + RE		Sorafenib only		P Value	
	All Grade	Grade 3/4/5	All Grade	Grade 3/4/5	All Grade	Grade 3/4/5
Hypertension	74 (14 of 19)	21/0/0	89.5 (17 of 19)	26/0/0	0.405	1.000
Hand-foot skin reaction	35	20/0/0	35	15/0/0	1.000	1.000
Diarrhoea	55	20/0/0	55	20/0/0	1.000	1.000
Infection	10	5/0/0	50	20/0/0	0.014	0.342
Fatigue	40	15/5/0	40	10/0/0	0.748	0.661
Anorexia	5	0/0/0	30	10/0/0	0.092	0.487
Weight loss	70	5/0/0	68 (13 of 19)	5/0/0	1.000	1.000
Nausea	15	5/0/0	10	0/0/0	1.000	1.000
Vomiting	15	0/0/0	0	0/0/0	0.231	–
Rash/Desquamation	10	5/0/0	10	0/0/0	1.000	1.000
Haemorrhage	5	0/0/5	15	5/0/5	0.605	1.000
Laboratory-related events						
Elevated GGT	95	25/5/0	100	40/5/0	1.000	0.515
Elevated AST	90	0/0/0	90	15/0/0	1.000	0.231
Elevated ALT	60	0/0/0	65	10/0/0	1.000	0.487
Ascites	25	10/0/0	20	10/0/0	1.000	1.000
Hyperbilirubinaemia	40	5/0/0	45	10/0/0	1.000	1.000
Hypoalbuminaemia	45	0/0/0	37 (7 of 19)	5/0/0	0.748	1.000
Anaemia	60	5/0/0	70	10/0/0	0.741	1.000
Thrombocytopaenia	90	0/0/0	65	0/0/0	0.127	–
Increased INR	20	0/0/0	40 (7 of 18)	0/0/0	0.288	–

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase.

# Conclusions

- The benefits of combined systemic and liver-directed treatments in inoperable intermediate- or advanced-stage hepatocellular carcinoma (HCC) have yet to be defined
- Early safety analysis of SORAMIC study is promising