Sirtex Medical Limited

SARAH Clinical Study Results Investor Presentation

Nigel Lange, Interim CEO

Dr David N. Cade, CMO

24 April 2017

Agenda

- Summary of Results
- SARAH Study Presentation from EASL/ILC
- Key Opinion Leader (KOL) Feedback
- Conclusions – SARAH Study Findings
- Sirtex Strategies
- Q&A

Summary of Results

- SARAH was the largest ever clinical study directly comparing SIR-Spheres® Y-90 resin microspheres with sorafenib (Nexavar®) in hepatocellular carcinoma (HCC)
- First ever large randomised controlled study with Level I evidence in a liver-directed therapy to show comparable survival to sorafenib
- However, the Primary Endpoint of an Overall Survival (OS) benefit (superiority) for SIR-Spheres versus sorafenib was not met

SARAH

SorAfenib versus Radioembolization in Advanced Hepatocellular carcinoma

SIRTeX

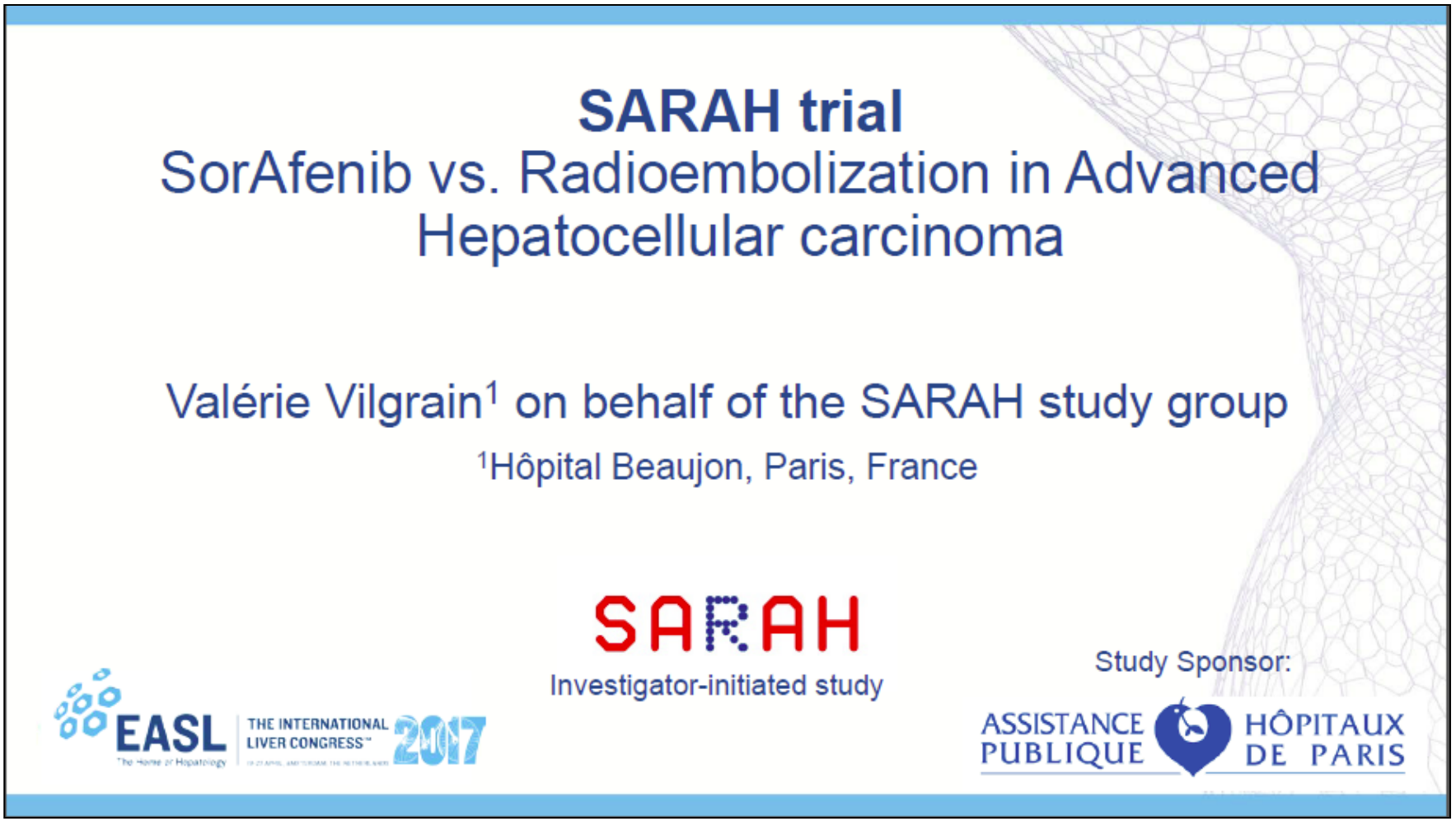
Summary of Results

- Overall Survival was similar (not statistically different) between treatments in the following key sub-groups of interest: TACE, PVT, BCLC, ECOG status, Child Pugh status

- SIR-Spheres offers a higher tumour response, a better tolerance, with less treatment related adverse events and a better quality of life over time than sorafenib

- Quality of Life (QoL) assessments showed patients treated with SIR-Spheres maintained their health status over the duration of the SARAH study, whereas patients receiving sorafenib reported a significant and sustained decline

SARAH Study Presentation from EASL/ILC



NB - Sirtex comment(s) on presentation slides are in green

SARAH Study Presentation from EASL/ILC

Disclosures

- Guerbet : Study investigator, Speaker fees
- SIRTEX : Speaker fees, Funding of the SARAH Trial
- Supersonic : Speaker fees
- Toshiba : Speaker fees

EASL THE INTERNATIONAL LIVER CONGRESS™ 2017

SIRTeX

SARAH Study Presentation from EASL/ILC

Rationale

- Treatment of HCC depends on tumour size and extension, severity of liver disease, and general performance
- The reference treatment of **advanced HCC** is sorafenib (SHARP trial), a multikinase inhibitor (targeted therapy) that established *vs*. placebo mOS: 10.7 *vs*. 7.9 months [1]
- The reference treatment of **intermediate HCC** is transarterial chemoembolization (TACE)
  - Increase life expectancy (2 RCTs [2,3] and 2 meta-analyses [4,5])
  - Treatment efficacy related to technique and tumour size and some patients failed even after several rounds of TACE
- Radioembolization (selective internal radiation therapy, SIRT) has demonstrated efficacy in large cohorts [6,7]

[1] Llovet JM *et al. N Engl J Med*. 2008;359:378-90.
[2] Llovett JM *et al. Lancet* 2002;359:1734–9.
[3] Lo CM *et al. Hepatology* 2002;35:1164–71.
[4] Llovett JM *et al. Hepatology* 2003;37:429–42.
[5] Oliveri RS *et al. Cochrane Database Syst Rev* 2011;(3):CD004787.
[6] Sangro B *et al. Hepatology* 2011;54:868–78.
[7] Salem R *et al. Gastroenterology* 2010;138:52–64.

SIRTeX

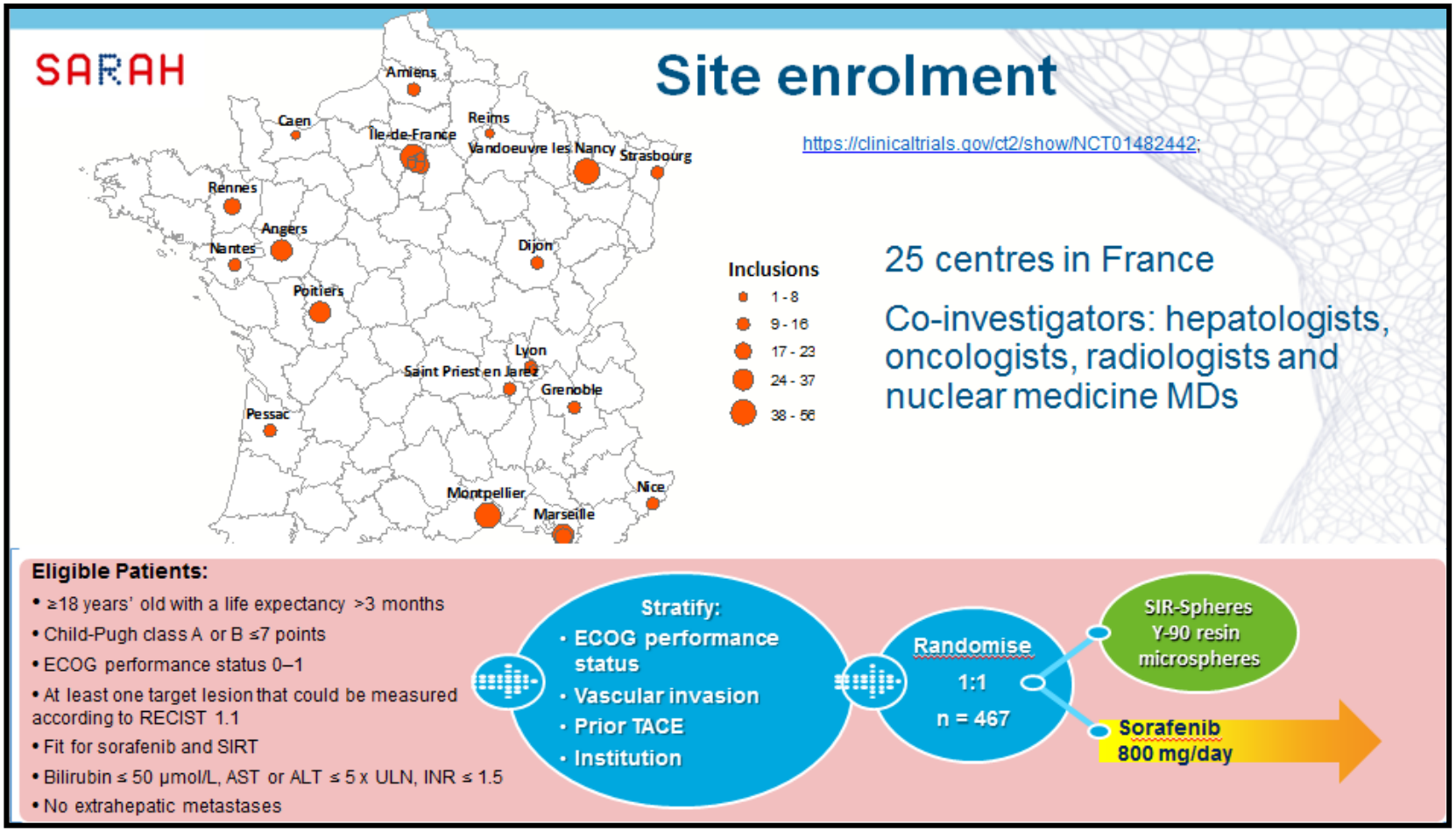
SARAH Study Presentation from EASL/ILC

Aims of SARAH

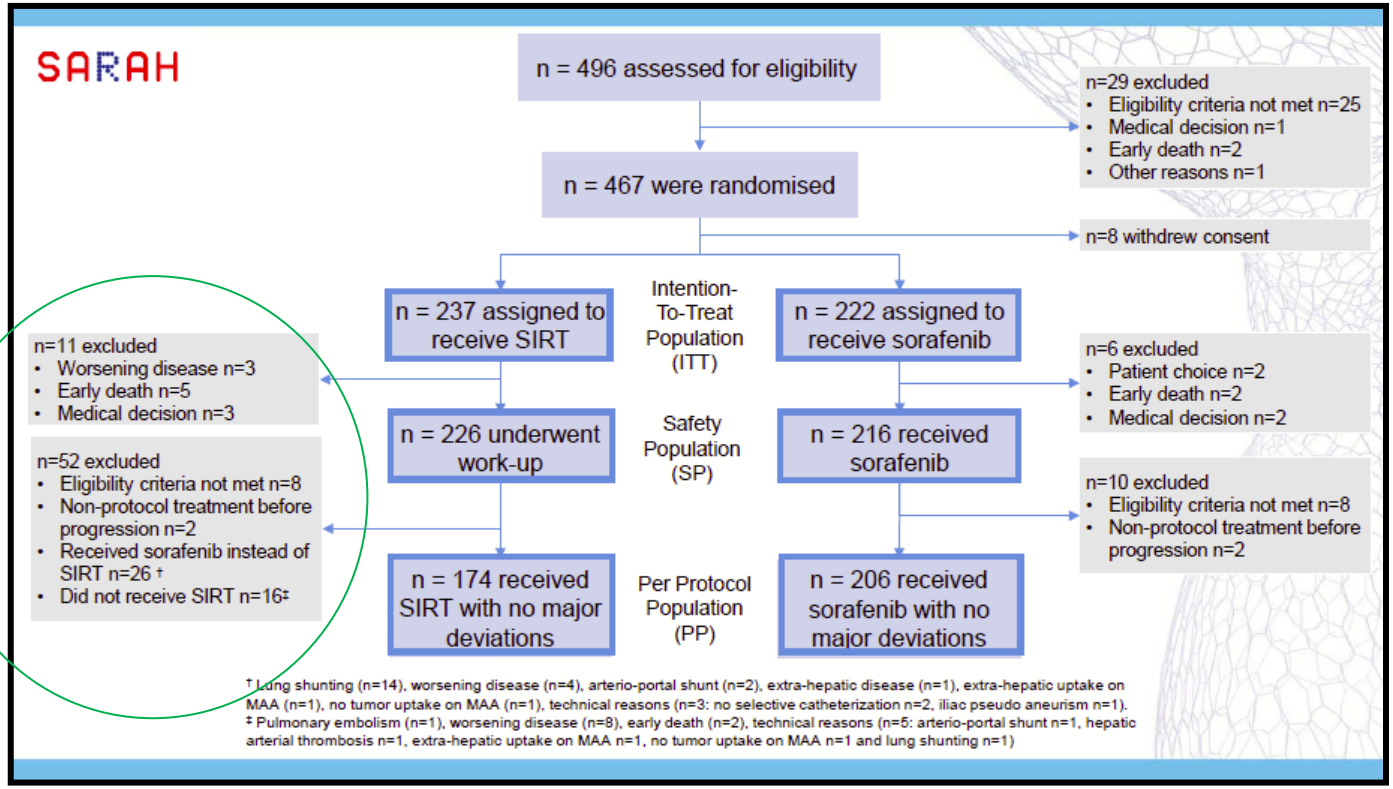
- Prospective open-label, phase 3, multi-center, RCT in locally advanced HCC and inoperable HCC who failed after two rounds of TACE
- Primary endpoint
  - Overall survival in patients with SIRT vs. Sorafenib
- Secondary endpoints
  - Progression free survival (*CT imaging every 3 months*)
  - Incidence of intrahepatic and extrahepatic progression (*competing risk*)
  - Tumour response rate (*RECIST 1.1, BOR*)
  - Safety and tolerability (*NCI-CTCAE 4.0*)
  - Quality of life (*global health status sub-score, QLQ-C30*)

SIRTeX

SARAH Study Presentation from EASL/ILC



SARAH Study Presentation from EASL/ILC



- **26.6% of pts randomised to SIR-Spheres, did not receive SIR-Spheres v 2.7% for sorafenib**
- **Per-Protocol population probably offers more useful insights into therapeutic effect of each treatment**

Per-Protocol (PP) *analysis is a comparison of treatment groups that includes only those patients who completed the treatment originally allocated.*

Intention-To-Treat (ITT) *analysis is where all patients who were enrolled and randomly allocated to treatment are included in the analysis and are analysed in the groups to which they were randomised.*

SARAH Study Presentation from EASL/ILC

SARAH Main baseline characteristics

	SIRT (n=237)	Sorafenib (n=222)
Age, years; mean ± SD	65.8 ± 9.4	64.6 ± 9.4
Gender (male)	89.5%	91.0%
Cirrhosis	89%	90.5%
Alcohol / HCV / NASH	68.7% / 25.7% / 22.9%	61.4% / 24.3% / 29.7%
ECOG 0 / 1	61.2% / 38.8%	62.6% / 37.4%
Child-Pugh class/score: A / B7	82.7% / 16.5%	84.2% / 15.8%
BCLC stage A / B / C	3.8% / 27.8% / 68.4%	5.4% / 27.5% / 67.1%
TACE failure	44.7%	42.3%
Multiple tumours	53.6%	56.8%
Tumor burden (% volume; median)	18%	18%
Tumor involvement: unilobar / bilobar	78.9% / 21.1%	84.2% / 15.8%
Macrovascular invasion (main portal vein)	62.9% (34.3%)	57.7% (32.2%)

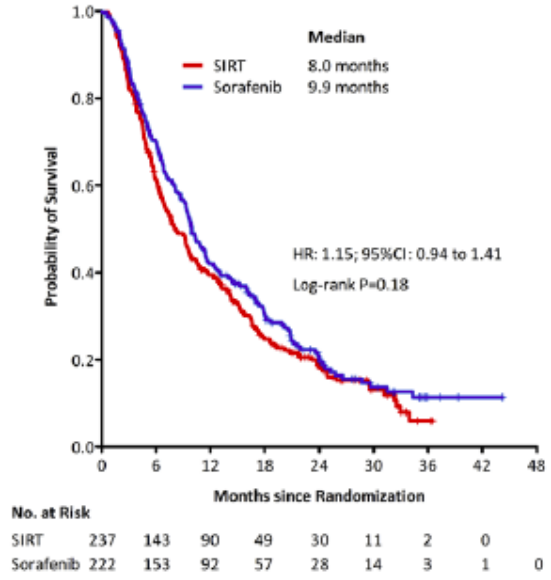
SIRTeX

SARAH Study Presentation from EASL/ILC

SARAH

Overall survival

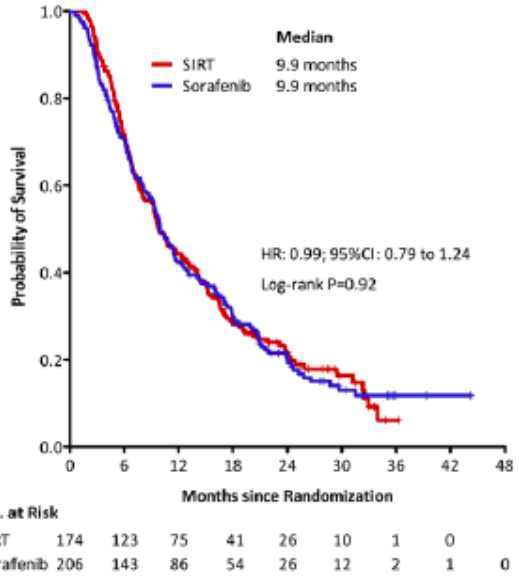
Intention-To-Treat population
N=459



No. at Risk

SIRT	237	143	90	49	30	11	2	0
Sorafenib	222	153	92	57	28	14	3	1	0

Per-Protocol population
N=380



No. at Risk

SIRT	174	123	75	41	26	10	1	0
Sorafenib	206	143	86	54	26	12	2	1	0

No significant difference in overall survival between groups

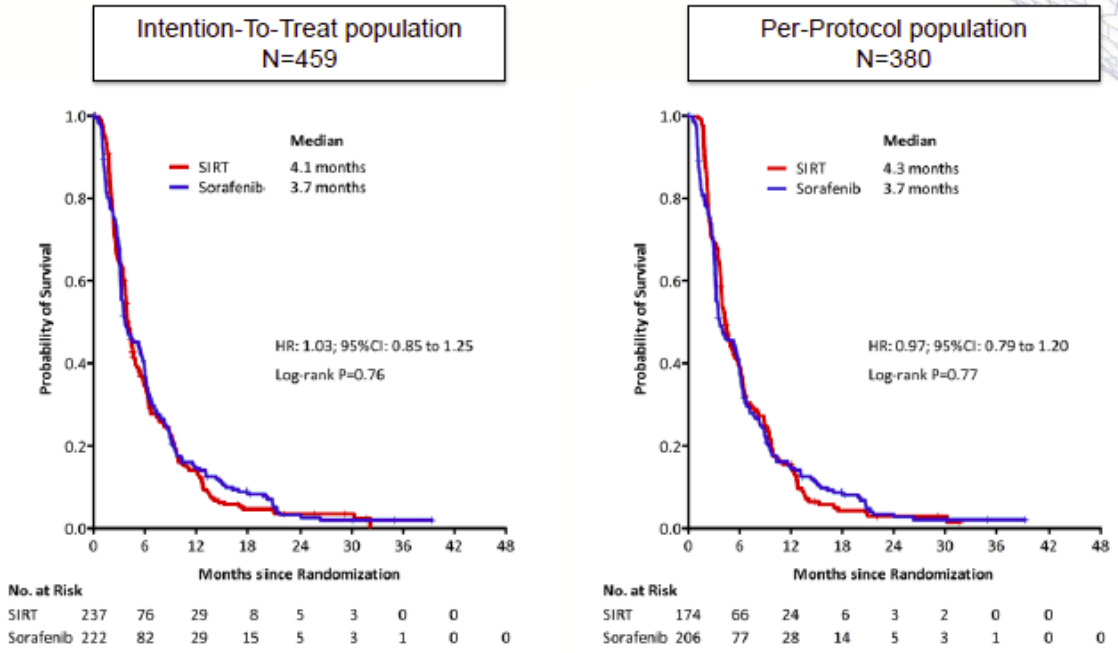
26.6% of patients didn't get SIRT & 7.2% sorafenib per protocol

SIRTeX

SARAH Study Presentation from EASL/ILC

SARAH

Progression-free survival



No significant difference in PFS between groups

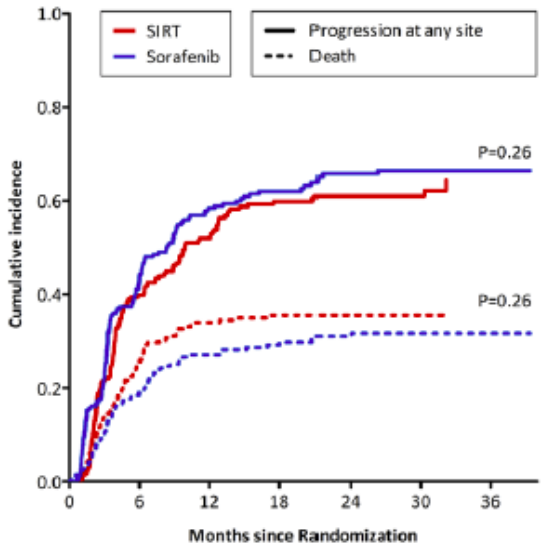
SIRTeX

SARAH Study Presentation from EASL/ILC

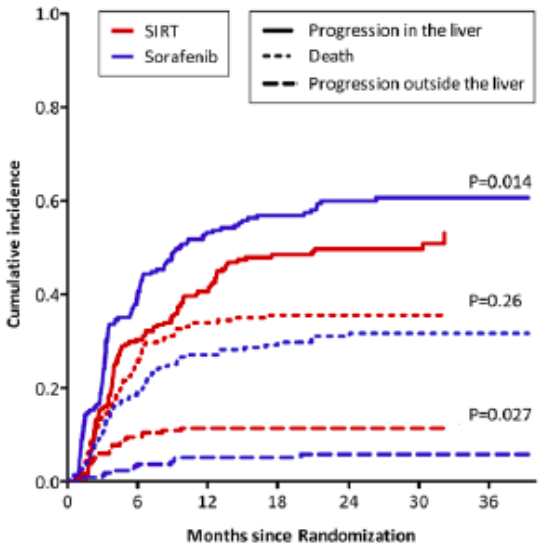
SARAH

Radiologic Progression in ITT

ITT: Progression at any site



ITT: Progression in the liver as first site



Progression in the liver as first site was significantly lower in the SIRT group (p values correspond to Gray test)

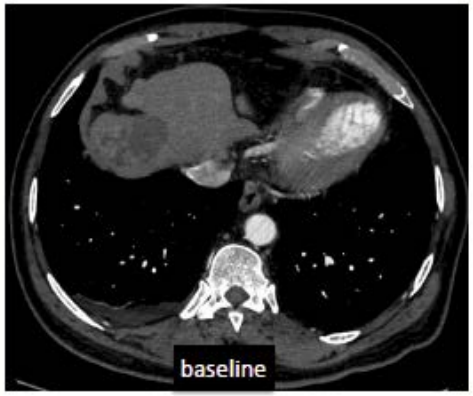
SIRTeX

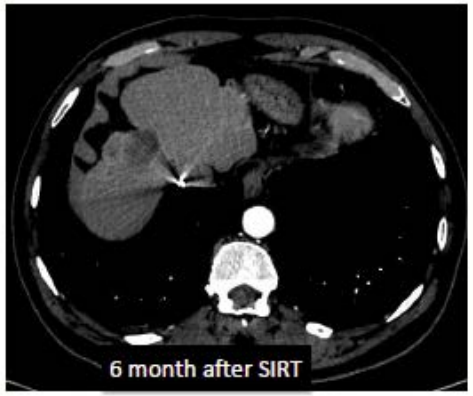
SARAH Study Presentation from EASL/ILC

SARAH

Tumor response by RECIST 1.1

	SIRT (n=190)	Sorafenib (n=198)	P value
Objective response [CR + PR]	36 (19.0%)	23 (11.6%)	0.042





Tumor response (CR+PR) rate was significantly better in the SIRT group than in sorafenib

SIRTeX

SARAH Study Presentation from EASL/ILC

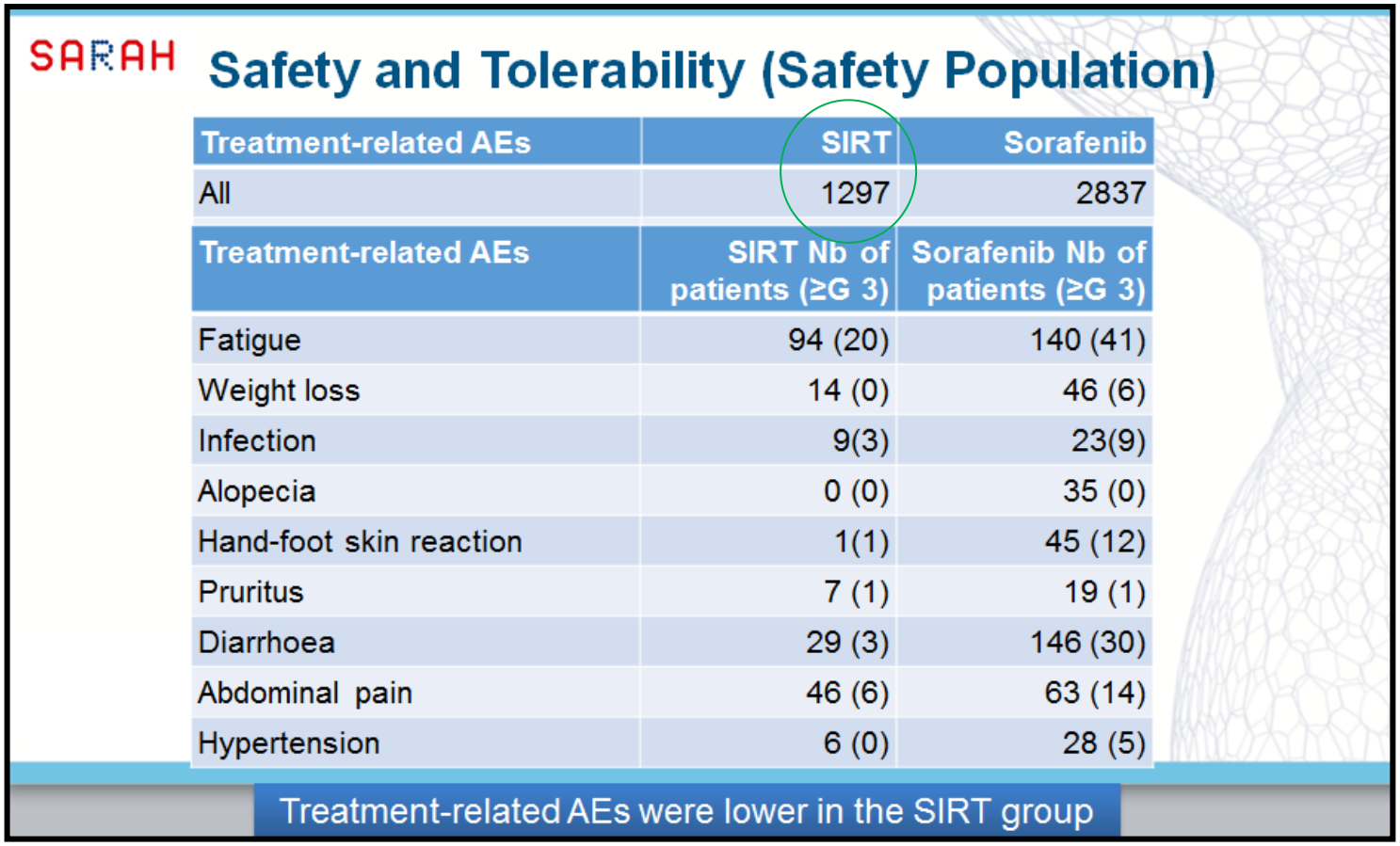
SARAH

Subgroup analysis

- Overall survival was similar between treatments in the following subgroups:
  - Demographic characteristics: age, sex
  - Severity of the disease: ECOG score, cirrhosis, BCLC classification, Child Pugh score, TACE failure
  - Tumor characteristics
  - Laboratory exams: alpha-fetoprotein, albumin, alkaline phosphatase and bilirubin

SIRTeX

SARAH Study Presentation from EASL/ILC



- Includes the 26 pts in the SIR-Spheres arm who received sorafenib

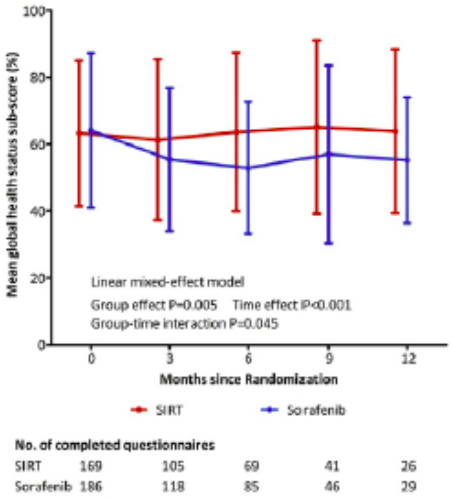
SIRTeX

SARAH Study Presentation from EASL/ILC

SARAH

Quality of life (QoL)

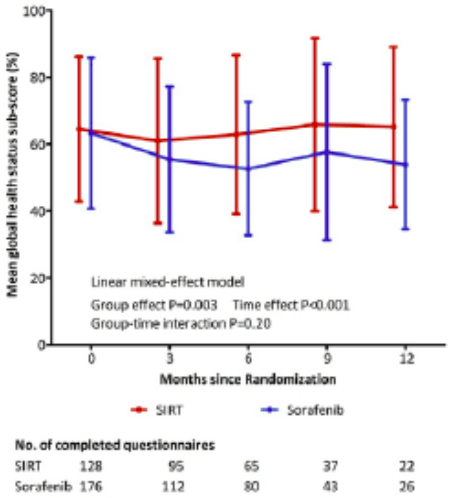
Intention To Treat population
N=459



No. of completed questionnaires

SIRT	169	105	69	41	26
Sorafenib	186	118	85	46	29

Per-Protocol population
N=380



No. of completed questionnaires

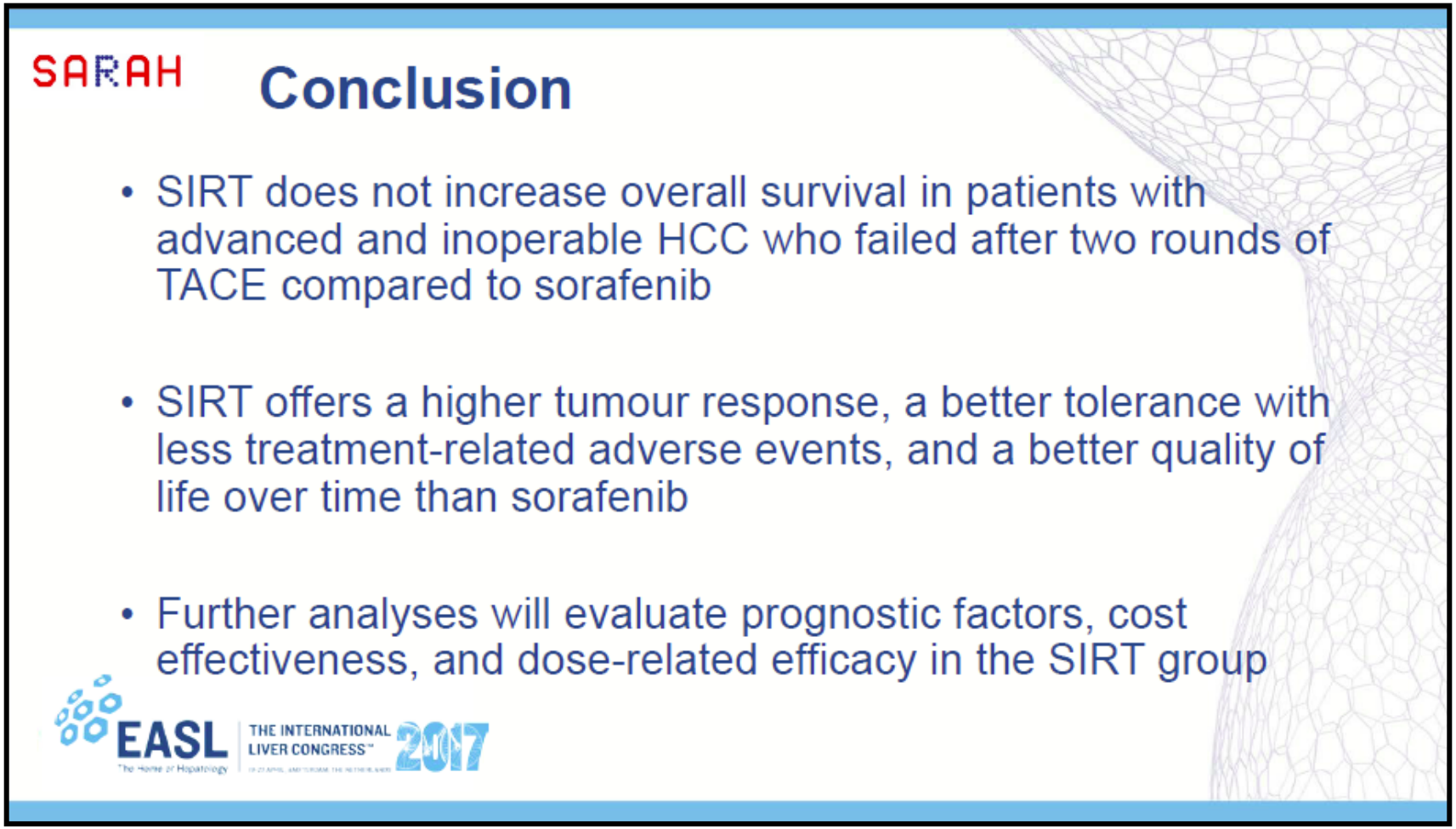
SIRT	128	95	65	37	22
Sorafenib	176	112	80	43	26

Global Heath Status sub-score EORTC QLQ-C30

QoL was significantly better in the SIRT group than sorafenib over time

SIRTeX

SARAH Study Presentation from EASL/ILC



SARAH Study Presentation from EASL/ILC

SARAH

Acknowledgements

The authors thank:

- The patients who took part in the SARAH study and their families
- The multi-disciplinary team of investigators, study co-ordinators, nurses and staff who participated in the SARAH study
- Assistance-Publique – Hôpitaux de Paris, the study sponsor
- Sirtex Medical Limited, for funding the study

EASL THE INTERNATIONAL LIVER CONGRESS™ 2017

SIRTeX

SARAH Study Presentation from EASL/ILC

Treatment characteristics

SIRT arm

Time from randomisation to treatment, median (IQR) days		29 (23-36) *
Number of treatments per patient:		
	1: Unilobar	115
	2 : Ipsi-lateral / Contra-lateral	21 / 37
	3 : Ipsi-lateral / Contra-lateral	2 / 9
Treatment type:	Lobe	71.7%
	Sector	17.8%
	Segment	10.5%
Cumulative lung dose per patient (Gy)		2.6 [1.2–4.8]
Activity delivered per session (MBq)		952.5 [628.0–1223.5]
Activity delivered per patient (MBq)		1394.5 [993.5–1847.5]

Sorafenib arm

Time from randomisation to treatment, median (IQR) days	7 (3-9) *
Sorafenib Dose Intensity, median (IQR) mg	800 (585–800)
Cumulative Time of Sorafenib Intake, median (IQR) months	2.8 (1.0–5.8)
Permanent Discontinuation Rate [PDR], %	61.1%
including those discontinuing sorafenib prior to tumour progression, %	37.1%

The dose intensity (DI) of sorafenib was defined as the amount of drug delivered per unit of time
The permanent discontinuation of sorafenib was defined as the interruption of sorafenib with no resumed treatment

* p<0.001

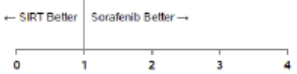
- **Current market practice for time from treatment decision to SIR-Spheres is approx. 10 days in most markets**

SIRTeX

SARAH Study Presentation from EASL/ILC

Forest plot in the ITT population

Subgroup	No. of Patients (%)	HR (95% CI)	P Value
Overall survival	459 (100.0)	1.15 (0.94-1.41)	
Age (years)			0.44
<=65	227 (49.5)	1.24 (0.93-1.65)	
>65	232 (50.5)	1.06 (0.79-1.41)	
Sex			0.24
Male	414 (90.2)	1.19 (0.96-1.48)	
Female	45 (9.8)	0.82 (0.42-1.58)	
Functional ECOG score			0.14
0	284 (61.9)	1.30 (1.00-1.69)	
1	175 (38.1)	0.94 (0.68-1.29)	
Cirrhosis			0.55
No	47 (10.2)	1.49 (0.74-2.97)	
Yes	412 (89.8)	1.12 (0.90-1.39)	
BCLC classification			0.36
A+B	148 (32.2)	1.00 (0.69-1.44)	
C	311 (67.8)	1.22 (0.95-1.56)	
Child Pugh score			0.66
A	383 (83.8)	1.13 (0.90-1.41)	
B	74 (16.2)	1.23 (0.75-2.03)	
Involvement			0.71
Unilobar	374 (81.5)	1.16 (0.93-1.46)	
Bilobar	85 (18.5)	1.09 (0.69-1.72)	
Tumor type			0.52
Nodular	241 (53.8)	1.09 (0.81-1.45)	
Infiltrative	207 (46.2)	1.23 (0.91-1.65)	
Tumor number			0.72
Single	206 (44.9)	1.18 (0.87-1.61)	
Multiple	253 (55.1)	1.12 (0.85-1.47)	
Tumor burden (%)			0.19
<=25	303 (66.0)	1.07 (0.83-1.39)	
>25	156 (34.0)	1.34 (0.96-1.88)	
Macroscopic vascular invasion			0.49
No	182 (39.7)	1.05 (0.75-1.47)	
Yes	277 (60.3)	1.19 (0.92-1.54)	
Portal venous invasion			0.60
Main portal vein	87 (33.3)	1.39 (0.88-2.19)	
Other	174 (66.7)	1.20 (0.87-1.67)	
Pattern occlusion in the main portal vein*			0.48
Complete	36 (41.9)	1.66 (0.81-3.40)	
Incomplete	50 (58.1)	1.14 (0.63-2.08)	
TACE failure			0.14
No	259 (56.4)	1.31 (1.00-1.71)	
Yes	200 (43.6)	0.98 (0.71-1.34)	
Alpha fetoprotein (ng/mL)			0.73
<=400	260 (62.5)	1.15 (0.87-1.52)	
>400	156 (37.5)	1.07 (0.76-1.51)	



Forest plot in the Per-Protocol population

Subgroup	No. of Patients (%)	HR (95% CI)	P Value
Overall survival	380 (100.0)	0.99 (0.79-1.24)	
Age (years)			0.39
<=65	188 (49.5)	1.08 (0.78-1.49)	
>65	192 (50.5)	0.89 (0.65-1.23)	
Sex			0.17
Male	344 (90.5)	1.04 (0.82-1.31)	
Female	36 (9.5)	0.62 (0.29-1.31)	
Functional ECOG score			0.06
0	236 (62.1)	1.17 (0.87-1.56)	
1	144 (37.9)	0.75 (0.52-1.07)	
Cirrhosis			0.84
No	39 (10.3)	1.12 (0.52-2.40)	
Yes	341 (89.7)	0.98 (0.77-1.24)	
BCLC classification			0.48
A+B	123 (32.4)	0.89 (0.59-1.33)	
C	257 (67.6)	1.06 (0.81-1.39)	
Child Pugh score			0.66
A	329 (86.8)	1.01 (0.79-1.29)	
B	50 (13.2)	0.88 (0.48-1.62)	
Involvement			0.75
Unilobar	311 (81.8)	0.99 (0.77-1.28)	
Bilobar	69 (18.2)	0.95 (0.57-1.58)	
Tumor type			0.75
Nodular	200 (53.8)	0.97 (0.71-1.34)	
Infiltrative	172 (46.2)	1.04 (0.74-1.45)	
Tumor number			0.74
Single	172 (45.3)	1.02 (0.73-1.43)	
Multiple	208 (54.7)	0.96 (0.71-1.30)	
Tumor burden (%)			0.43
<=25	262 (68.9)	0.97 (0.74-1.28)	
>25	118 (31.1)	1.12 (0.75-1.67)	
Macroscopic vascular invasion			0.70
No	152 (40.0)	0.95 (0.65-1.37)	
Yes	228 (60.0)	1.02 (0.77-1.36)	
Portal venous invasion			0.74
Main portal vein	66 (31.0)	1.18 (0.70-1.98)	
Other	147 (69.0)	1.06 (0.74-1.52)	
Pattern occlusion in the main portal vein*			0.09
Complete	28 (43.1)	2.44 (1.01-5.88)	
Incomplete	37 (56.9)	0.78 (0.39-1.55)	
TACE failure			0.23
No	202 (53.2)	1.13 (0.83-1.54)	
Yes	178 (46.8)	0.86 (0.62-1.20)	
Alpha fetoprotein (ng/mL)			0.21
<=400	227 (66.0)	1.07 (0.80-1.43)	
>400	117 (34.0)	0.79 (0.53-1.18)	

SARAH Study Presentation from EASL/ILC

Key eligibility criteria

- Unresectable, non-transplantable or non-ablatable HCC
- BCLC stage C or
- BCLC stage A/B
  - New lesions post radical therapy and unsuitable for further radical therapy or
  - No objective response after ≤2 TACE sessions
- Child-Pugh class A or B ≤7 points
- ECOG performance status 0 – 1
- Bilirubin ≤ 50 µmol/L, AST or ALT ≤ 5 x ULN, INR ≤ 1.5
- At least one measurable target lesions according to RECIST 1.1
- Fit for sorafenib and SIRT
- No extrahepatic disease

SIRTeX

SARAH Study Presentation from EASL/ILC

Safety and Tolerability (Safety Population)

Tx-Related Adverse Event	SIRT (n=226) †		Sorafenib (n=216)		p value	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AE	1297	230	2837	411		
Patients with ≥1 AE, n (%)	173 (76.5%)	92 (40.7%)	203 (94.0%)	136 (63.0%)	**<0.001**	**<0.001**
AEs per patient, Median [IQR]	5.0 [2.0–9.0]	2.0 [1.0–3.0]	10.0 [5.0–17.0]	2.0 [1.0–4.0]	**<0.001**	0.10

EASL THE INTERNATIONAL LIVER CONGRESS™ 2017

† Includes 26 patients receiving only sorafenib instead of SIRT

SIRTeX

SARAH Study Presentation from EASL/ILC

Safety and Tolerability (Safety Population): 1/3

Tx-Related Adverse Event	SIRT (n=226) †		Sorafenib (n=216)		p value	
N AEs (% patients with ≥1 AE)	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Constitutional symptoms						
Infection	9 (4.0%)	3 (1.3%)	47 (10.6%)	18 (4.2%)	**0.007**	0.08
Fever	15 (5.8%)	0 (0%)	28 (8.8%)	4 (1.4%)	0.22	0.12
Fatigue	128 (41.6%)	20 (8.8%)	268 (64.8%)	45 (19.0%)	**<0.001**	**0.002**
Weight loss	16 (6.2%)	0 (0%)	63 (21.3%)	6 (2.8%)	**<0.001**	**0.013**
Dermatologic events						
Alopecia	0 (0%)	0 (0%)	36 (16.2%)	0 (0%)	**<0.001**	-
Hand-foot skin reaction	1 (0.4%)	1 (0.4%)	78 (20.8%)	13 (5.6%)	**<0.001**	**0.001**
Rash or desquamation	4 (1.3%)	1 (0.4%)	21 (9.3%)	0 (0%)	**<0.001**	1.00
Pruritus	8 (3.1%)	1 (0.4%)	20 (8.8%)	1 (0.5%)	**0.011**	1.00
Dry skin	2 (0.9%)	0 (0%)	61 (18.5%)	3 (1.4%)	**<0.001**	0.12
Other dermatological events	4 (1.8%)	0 (0%)	77 (24.5%)	6 (2.8%)	**<0.001**	**0.013**

† Includes 26 patients receiving only sorafenib instead of SIRT

SIRTeX

SARAH Study Presentation from EASL/ILC

Safety and Tolerability (Safety Population): 2/3

Tx-Related Adverse Event	SIRT (n=226) †		Sorafenib (n=216)		p value	
N AEs (% patients with ≥1 AE)	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Gastro-intestinal (GI) disorders						
Anorexia	34 (13.3%)	7 (3.1%)	132 (32.4%)	11 (4.6%)	**<0.001**	0.40
Diarrhoea	37 (12.8%)	3 (1.3%)	316 (67.6%)	37 (13.9%)	**<0.001**	**<0.001**
Nausea/vomiting	40 (11.5%)	1 (0.4%)	88 (23.1%)	5 (2.3%)	**0.001**	0.11
Abdominal pain	65 (20.4%)	6 (2.7%)	113 (29.2%)	16 (6.5%)	**0.032**	**0.05**
GI ulceration ‡	7 (1.8%)	5 (1.3%)	1 (0.5%)	1 (0.5%)	0.37	0.62
GI bleeding	12 (4.0%)	11 (4.0%)	17 (6.5%)	10 (3.7%)	0.24	0.88
Liver disorders						
Ascites	39 (12.4%)	15 (4.9%)	31 (10.6%)	11 (4.2%)	0.57	0.72
Liver dysfunction	75 (17.3%)	28 (9.3%)	100 (21.8%)	34 (12.5%)	0.23	0.28
Radiation hepatitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-

† Includes 26 patients receiving only sorafenib instead of SIRT; ‡ One patient had a radiation-induced GI ulcer

- **SIR-Spheres almost completely mitigates the known toxicities of sorafenib, while not inflicting any additional toxicities of its own**

SARAH Study Presentation from EASL/ILC

Safety and Tolerability (Safety Population): 3/3

Tx-Related Adverse Event	SIRT (n=226) †		Sorafenib (n=216)		p value	
N AEs (% patients with ≥1 AE)	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Hypertension	7 (2.7%)	0 (0%)	53 (13.0%)	5 (2.3%)	**<0.001**	**0.027**
Cardiac failure congestive	32 (12.4%)	3 (1.3%)	45 (14.8%)	13 (5.1%)	0.46	**0.029**
Non-GI haemorrhage	6 (2.7%)	1 (0.4%)	29 (9.7%)	2 (0.9%)	**0.002**	0.62
Pulmonary embolism	0 (0%)	0 (0%)	1 (0.5%)	0 (0%)	0.49	-
Laboratory abnormalities						
Hyperbilirubinemia	56 (11.9%)	8 (3.1%)	48 (12.5%)	12 (4.2%)	0.86	0.55
Other increased blood liver tests	255 (24.8%)	23 (8.4%)	217 (21.8%)	28 (7.4%)	0.45	0.7
Haematologic biological abnormalities	195 (21.2%)	33 (10.2%)	298 (31.0%)	58 (13.4%)	**0.019**	0.29
Increased creatinine level	63 (11.1%)	4 (1.8%)	80 (18.1%)	13 (5.1%)	**0.037**	**0.07**
Hyponatremia	23 (4.9%)	5 (0.9%)	41 (10.2%)	6 (1.9%)	**0.034**	0.44

† Includes 26 patients receiving only sorafenib instead of SIRT.

SIRTeX

Key Opinion Leader Feedback

Comments on the significance of the SARAH results and impact on clinical practice

Professor Valérie Vilgrain MD, PhD, Principal Investigator of the SARAH study, Head of Department of Radiology, Beaujon Hospital, AP-HP and Professor at the Université Paris Diderot, Sorbonne Paris Cité, France

"Neither sorafenib nor SIR-Spheres Y-90 resin microspheres produced a statistically significant difference in Overall Survival (OS) of the patients we studied. Despite 26.6% of patients in the SIRT arm not receiving SIR-Spheres per protocol, Overall Survival by intention-to-treat [ITT] was not significantly different (median 8.0 vs. 9.9 months; p=0.18). Moreover, if we look at the patients who received SIR-Spheres or sorafenib according to the SARAH protocol, ***median OS was identical (9.9 vs. 9.9 months; p=0.92).***"

"In terms of what matters for patients, the findings from this first large head-to-head comparison of liver-directed Selective Internal Radiation Therapy (SIRT) and systemic chemotherapy with sorafenib also show clearly that ***liver-directed procedures with SIR-Spheres result in a significantly better tolerance of treatment and quality of life. I believe this consideration should be a critical factor in selecting first-line treatment for this patient population in the future."***

SIRTeX

Key Opinion Leader Feedback

Comments on clinical practice and implications for treatment guidelines

Professor Bruno Sangro, MD, PhD, Director of the Liver Unit at Clinica Universitaria de Navarra, Professor of Medicine at the University of Navarra School of Medicine, and senior researcher in the National Biomedical Research Network Center for Liver and Digestive Diseases

*"**SARAH provides confirmation in a multi-centre study setting that SIRT is safe and reliable, even for the most advanced patients**. SIR-Spheres may provide patients with an alternative option to an effective systemic therapy that is often not well tolerated. **The results will reassure current users and get the attention of those non-users concerned about the potential safety of SIRT in cirrhotic patients.** The SARAH study results will increase the presence of this technology in multi-disciplinary team discussions."*

"Treatment guidelines: There is a good chance that SIRT will appear in the EASL guidelines that are currently being revised. The AASLD guidelines already discuss SIRT as an option for patients, so these are unlikely to change; There is also a good chance that the EORTC and ESMO guidelines would consider including SIRT in their revised guidelines; The APASL guidelines are currently being published so inclusion would have to await the next revision."

Key Opinion Leader Feedback

Comments on impact of SARAH results in clinical practice

Professor Jens Ricke, MD, PhD, Principal Investigator of the SORAMIC study, University of Munich, Germany

"The favourable toxicity profile seen in the SARAH study for SIR-Spheres resin microspheres will have a compelling impact on clinical practice. *Toxicity makes a difference when speaking with patients, as they are concerned about the impact of side effects such as fatigue, hand-foot syndrome or diarrhoea."*

"For inoperable HCC patients in the out-patient setting, side effects of any therapy are very important. I believe it is a very compelling argument when discussing options with patients and families to start with Y90 which has a highly favourable toxicity profile – and add the systemic option as soon as needed."

"In patients with liver-limited inoperable HCC, the question now is, why not start treatment with SIR-Spheres / this technology, and reserve sorafenib for progressive disease – until we know from SORAMIC if a direct combination is even more favourable?"

SIRTeX

Key Opinion Leader Feedback

Comments on safety and Quality of Life benefits of SIR-Spheres

Professor Chris Verslype, MD, PhD, Professor of Digestive Oncology and Hepatology, University of Leuven, Belgium

"Previously, when we discussed the potential outcomes of treating patients with SIRT, we could only say that while we could provide benefit to a proportion of patients, we thought we risk harming others. Now with the SARAH study, we have real-world data where we can have a discussion with the patient and be confident that in those patients where we do not achieve down-staging, we know are not going to be doing any harm."

*"**The toxicities as a consequence of treatment and the Quality of Life of patients are important considerations for patients. Now we have the SARAH data, which can help us put the treatment choices into perspective for our patients.** With the SARAH data, we can look at what determines the Quality of Life for patients; we can see the effect of decreasing symptoms from treatment and now the SARAH investigators can look at what other factors are affected – is it the physical or the mental well-being of patients? We can see what really matters for patients and we haven't seen this maintenance of Quality of Life with sorafenib."*

SIRTeX

Conclusions – SARAH Study Findings

- Sirtex is pleased with the outcome of the SARAH study and initial KOLs response to the results have been positive
- SIR-Spheres provides a new treatment option for clinicians to consider for their first-line HCC patients
- For patients who received SIR-Spheres or sorafenib according to the SARAH protocol, median OS was identical
- SIR-Spheres has demonstrated significant safety, toxicity and tolerability benefits to patients versus sorafenib across a range of parameters
- Patients treated with SIR-Spheres maintained their health status over the duration of the SARAH study, whereas patients receiving sorafenib reported a significant and sustained decline in Quality of Life

Sirtex Strategies

- Sirtex will immediately commence sales and marketing activities on the SARAH result across EMEA, APAC, Latin America and Canada
- Engage in negotiations with European and country specific treatment guideline panels for HCC
- Negotiate with government/private payers on reimbursement for HCC where limited or no reimbursement exists
- Submit for additional regulatory approvals in the USA during 2H CY17

Sirtex Strategies – Commercial Opportunity

Excluding

179,000 (1)
Annual incidence of hepatocellular carcinoma in Sirtex's **current** markets

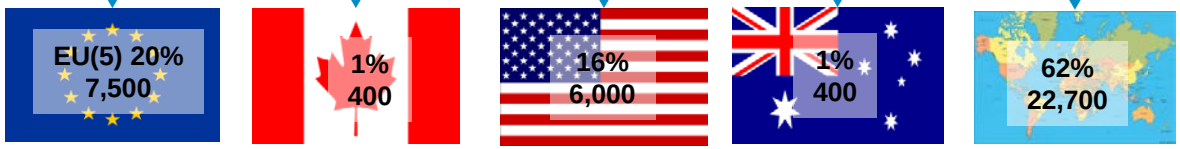
89,500 (50%) (2)
Intermediate to advanced stage disease

76,000 (85%)
Receive palliative treatment:
- TACE
- Sorafenib
- SIR-Spheres microspheres

30,000 (40%) (3)
Eligible for TACE

46,000 (60%) (3)
Ineligible for TACE

37,000 (80%) (4)
Eligible for SIR-Spheres microspheres



- SARAH data now provides an attractive option for clinicians to consider SIR-Spheres as a first-line treatment
- SARAH data now shows that SIR-Spheres offers the same OS benefit vs. sorafenib for those who failed prior TACE – extended commercial opportunity
- Asian market potential contingent on SIR*ve*NIB (ASCO – June) and potentially VESPRO data (2H CY17)

(1) Sirtex markets – see previous slides
(2) Llovet et. al. Design and endpoints of clinical trials in hepatocellular carcinoma. J Natl Cancer Inst 2008.
(3) Geschwind et. al. Use of Transarterial Chemoembolization (TACE) and Sorafenib in Patients with Unresectable Hepatocellular Carcinoma: US Regional Analysis of the GIDEON Registry. Liver Cancer 2016
(4) Sirtex data and analysis.
Globocan http://globocan.iarc.fr/Pages/fact_sheets_population.aspx [EU(5) includes the UK]. * Please refer to important footnote on slide 94 when examining data

Thank you