ASX / MEDIA RELEASE **2nd March 2017**

Sirtex Medical Clinician Lunch and Learn Briefing

Sydney, Australia; 2nd March 2017 – Sirtex Medical Limited (ASX:SRX) today is hosting analysts and investors at the Sofitel Sydney Wentworth for a Clinician Lunch and Learn Briefing. Attached is a copy of the management and invited speaker presentations to be given at lunch time.

Furthermore, a live webcast of the briefing, commencing at 12:30 p.m., can be viewed by clicking on the following link or pasting it into your browser: http://webcast.openbriefing.com/3300/.

A recording of the webcast and slide presentation will be made available in the 'Investors' section of the Company website following the conclusion of the briefing at: http://www.sirtex.com/au/investors/

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Sirtex Medical Limited

Lunch and Learn Clinician and Corporate Briefing

Mr Nigel Lange, Interim CEO

Dr David N. Cade, CMO

mCRC Presenter: A/Prof Nick Pavlakis

HCC Presenter: Prof Bruno Sangro

Sydney, 2nd March 2017

Agenda

• Welcome	Dr David Cade
• Clinical Studies Recap & Reporting Timetable	Dr David Cade
• Session 1: Perspectives on Metastatic Colorectal Cancer	A/Prof Nick Pavlakis
• Commercial Implications (mCRC)	Mr Nigel Lange
• Session 2: Perspectives on Hepatocellular Carcinoma	Prof Bruno Sangro
• Commercial Implications (HCC)	Mr Nigel Lange
• Q&A Panel	All Speakers
• Concluding Remarks	Mr Nigel Lange

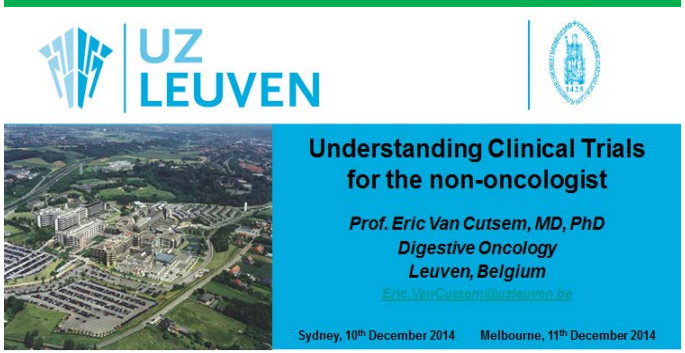
SIRTeX

Welcome

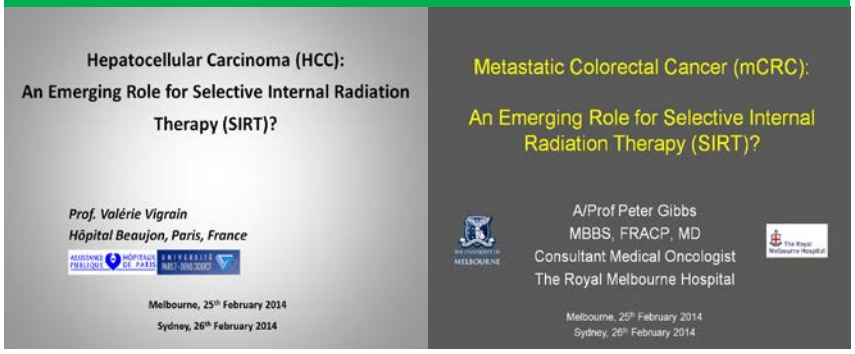
Fourth Investor ‘Lunch & Learn’ event hosted by Sirtex

July 2012

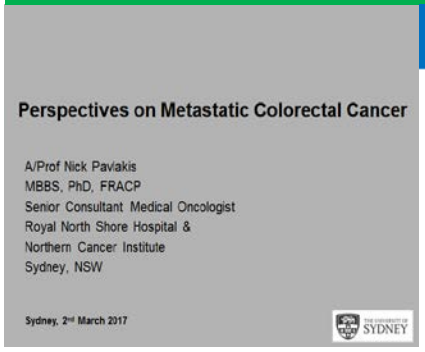
December 2014

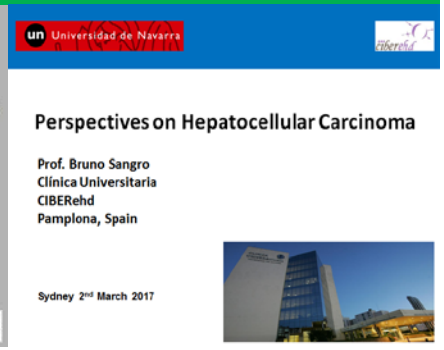


February 2014



Today





Purpose

1. **Educate investors/analysts ahead of major clinical studies**

   Two independent Key Opinion Leaders discuss the role of SIR-Spheres® microspheres in two key indications

   - Metastatic colorectal cancer (mCRC)
   - Hepatocellular carcinoma (HCC)

2. **Articulate the scientific, clinical, medical and commercial considerations**

   Please save questions until Q&A Panel

Two highly regarded Key Opinion Leaders

A/Prof Nick Pavlakis MBBS, PhD, FRACP

Medical Oncologist (Cancer Specialist)

Senior Staff Medical Oncologist, Department of Medical Oncology, RNSH

Clinical Services Director & Trial Unit Head, Northern Cancer Institute

Associate Professor in the Faculty of Medicine, University of Sydney

Translational researcher, key interests: Lung & gastrointestinal cancers

Prof Bruno Sangro MD, PhD

Hepatologist (Liver Specialist)

Director of the Liver Unit at Clinica Universitaria de Navarra, Spain

Professor of Medicine at the University of Navarra School of Medicine

Leads the radioembolisation program at Clinica Universitaria de Navarra

Senior Researcher, Centre for Biomedical Research (CIBERehd)

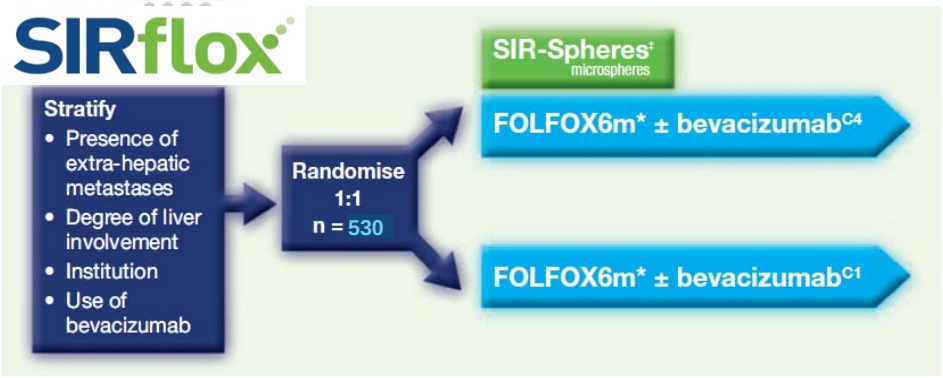
Clinical Studies Recap

Clinical Studies Recap

Metastatic colorectal cancer (mCRC)

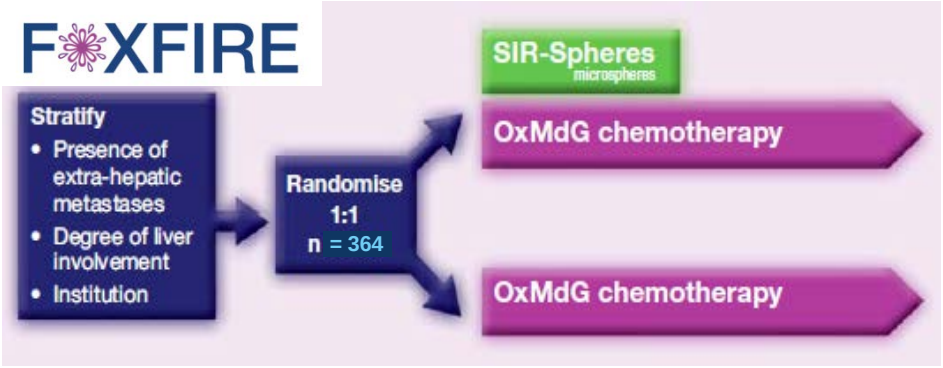
There are three similarly designed studies in metastatic colorectal cancer (mCRC)

SIRflox



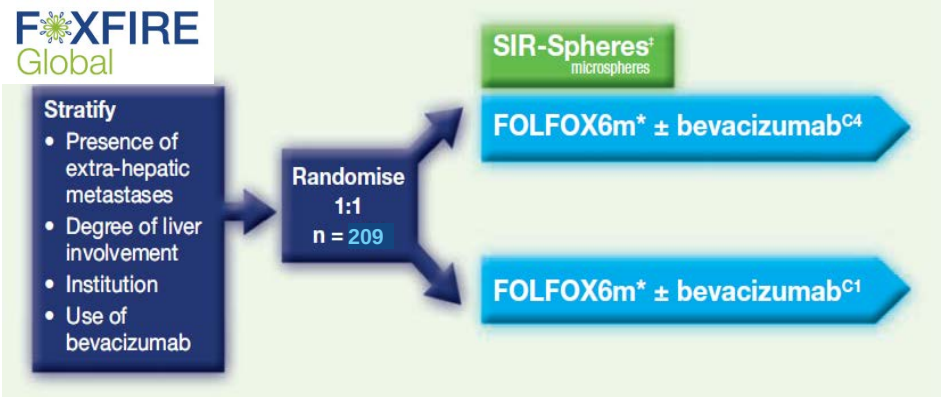
- 530 first-line patients, global
- SIRT + SOC[(1)] chemo/biologic therapy *vs* SOC alone
- Primary endpoint: PFS[(2)], reported at ASCO 2015
- OS[(3)] data not reported*

FOXFIRE



- 364 first-line patients, United Kingdom
- SIRT + SOC chemo/biologic therapy *vs* SOC alone
- Completed recruitment: October 2014
- Primary endpoint: OS*

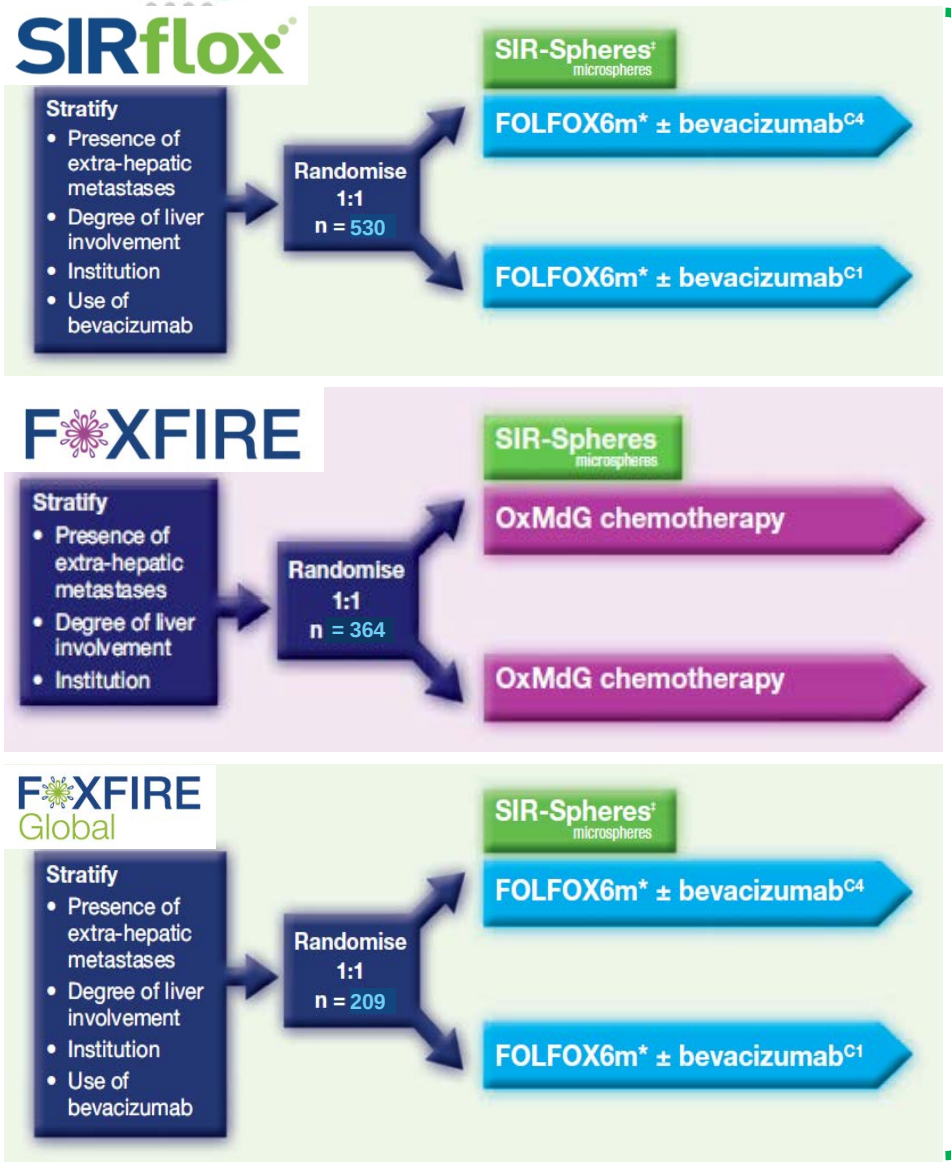
FOXFIRE Global



- 209 first-line patients, global
- SIRT + SOC chemo/biologic therapy *vs* SOC alone
- Completed recruitment: January 2015
- Primary Endpoint: OS*

*Notes: (1) SOC = standard of care; (2) PFS = progression-free survival; (3) OS = overall survival; * OS will be reported on the combined data set from the three studies*

The three studies will be combined in a pre-planned analysis of impact on Overall Survival



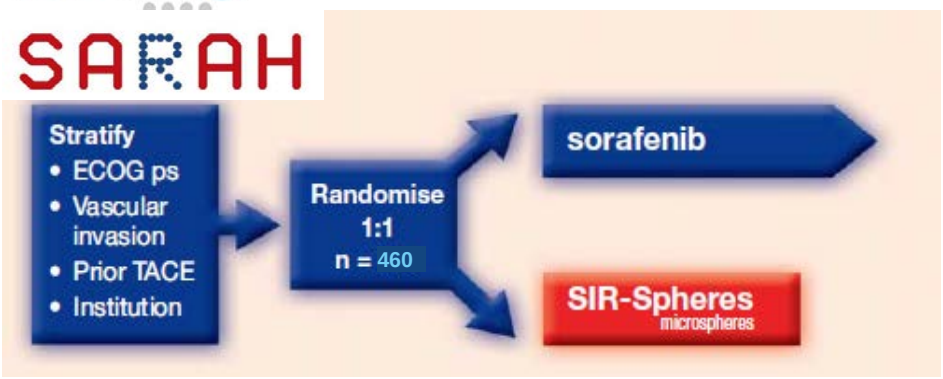
- 1,103 patient data set
- Primary endpoint: OS(1) from the pooled data set
- Seeking superiority of SIRT + SOC(2) chemo/biologic therapy *vs* SOC alone
- Key pre-defined patient sub-groups:
  - Liver-only (~60%) and liver-dominant (~40%)
  - Degree of liver involvement (≤25% *v* >25%)
  - Use of biologic agent (bevacizumab in SIRFLOX and FOXFIRE Global; bevacizumab or cetuximab in FOXFIRE)

Notes: (1) OS = overall survival; (2) SOC = standard of care

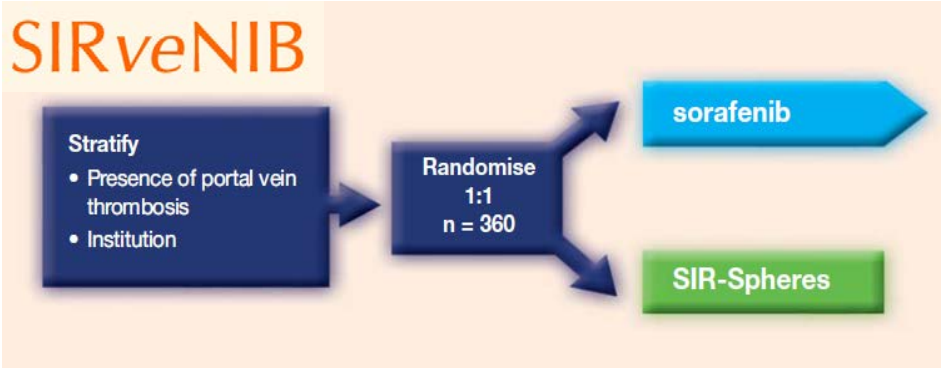
Clinical Studies Recap

Hepatocellular carcinoma (HCC)

There are three studies in hepatocellular carcinoma (HCC)



- 460 patients, France
- SIRT *vs* sorafenib(1)
- Completed recruitment: March 2015
- Primary endpoint: OS(2)

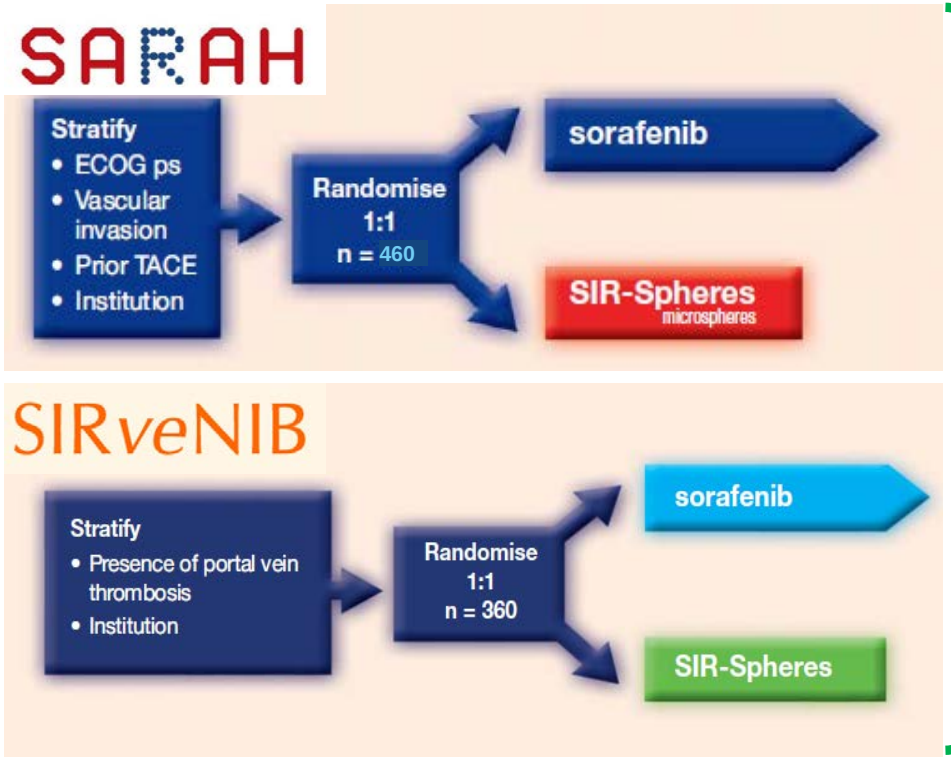


- 360 patients, Singapore & SE Asia
- SIRT *vs* sorafenib
- Completed recruitment: June 2016
- Primary endpoint: OS

- 420 patients, Europe
- SIRT + sorafenib *vs* sorafenib alone
- Completed recruitment: March 2016
- Primary Endpoint: OS

Notes: (1) sorafenib = Nexavar®, Bayer Healthcare; (2) OS = overall survival

VESPRO[(1)] is a pre-planned prospective meta-analysis of Overall Survival



- 820 patient data set
- Scientifically valid method to more fully assessing outcomes of similarly designed clinical studies
- Facilitates more robust conclusions on Overall Survival
- Facilitates more robust conclusions on several important sub-groups:
  - Patients who received prior TACE
  - Patients with tumour invasion into their portal vein
- Design incorporates a non-inferiority analysis in the event that efficacy is similar between the treatments
- Allows clinicians to make informed choices on toxicity and cost

References: (1) Gebski V et al. *JMIR Res Protoc.* 2017 6(2):e17.

Clinical Studies Reporting Timetable

Clinical Studies reporting timetable

SARAH

- **HCC – SARAH***
  - **EASL/ILC meeting**** — **19th – 23rd April 2017**
  - Abstract release (unless embargoed) — **5th April 2017**
  - Oral abstract presentation — **22nd April 2017**

SIRflox FOXFIRE FOXFIRE Global

- **mCRC – SIRFLOX/FOXFIRE/FOXFIRE Global***
  - **ASCO Annual Meeting*** — **2nd – 6th June 2017**
  - Abstract selection decision — **3rd April 2017**
  - Abstract release (unless embargoed) — **17th May 2017**
  - Presentation of abstract — **TBC**

** Study investigators may also elect to disclose certain data outside of conference dates, at which time Sirtex will make an ASX announcement*
*** All dates provided represent local time zones (EU, USA)*

Clinical Studies reporting timetable

SIR*ve*NIB

- **HCC – SIR*ve*NIB***
  - **ASCO Annual Meeting**** — **2nd – 6th June 2017**
  - Abstract selection decision — **3rd April 2017**
  - Abstract release (unless rejected/withdrawn/embargoed) — **17th May 2017**
  - Presentation of abstract — **TBC**

- **VESPRO – Combined prospective meta-analysis of SARAH + SIR*ve*NIB**
  - Results expected **2H CY17**

SORAMIC

- **HCC - SORAMIC**
  - Results expected **1H CY18**

** Study investigators may also elect to disclose certain data outside of conference dates, at which time Sirtex will make an ASX announcement*
*** All dates provided represent local time zones (EU, USA)*

Thank you

SIRTeX

Perspectives on Metastatic Colorectal Cancer

A/Prof Nick Pavlakis
MBBS, PhD, FRACP
Senior Consultant Medical Oncologist
Royal North Shore Hospital &
Northern Cancer Institute
Sydney, NSW

Sydney, 2nd March 2017

THE UNIVERSITY OF SYDNEY

Overview of today's talk

1. Introduction
2. Colorectal cancer
3. Quick review of SIRFLOX data
4. The SIRFLOX–FOXFIRE–FOXFIRE Global study

1. Introduction
2. Colorectal cancer
3. Quick review of SIRFLOX data
4. The SIRFLOX–FOXFIRE–FOXFIRE Global study

Who am I?

- Senior Staff Medical Oncologist, Department of Medical Oncology, RNSH (Ex-head)
- Clinical Services Director and Trial Unit Head, Northern Cancer Institute
- **Medical oncologist** (cancer specialist) & Clinical (translational) researcher

- We mostly deploy…
  - Chemotherapies
  - Biologic therapies
  - Immunotherapies
  - Hormonal therapies
- To achieve…
  - Cure
  - Palliation (extend life)
  - Down-staging ➡ surgery ➡ cure

- Keen research interests
  - Lung & gastrointestinal cancer (e.g. colorectal cancer)

What do Oncologists do?

- Cancer patients should be evaluated by a Multi-Disciplinary Team (MDT)…best practice since mid 2000s

- Each discipline offers a different treatment
  - **Surgical oncologist**
    - Main role is just after diagnosis…can they remove the cancer?
  - **Medical oncologist**
    - Adjuvant treatment after surgery (‘mop up’ any remaining cancer)
    - Lead the treatment of patients with advanced cancer
    - Care for the patient long-term (we are their shepherd)
  - **Radiation oncologist**
    - Use external radiation beams or radiation implants
  - **Interventional radiologist**
    - Perform minimally invasive treatments (e.g. SIRT)
  - **Palliative care physician**
    - Treat cancer symptoms and provide end of life care

SIRT has been used at Royal North Shore Hospital since 2001

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Treatment of Fluorouracil-Refractory Patients With Liver Metastases From Colorectal Cancer by Using Yttrium-90 Resin Microspheres Plus Concomitant Systemic Irinotecan Chemotherapy

Guy A. van Hazel, Nick Pavlakis, David Goldstein, Ian N. Olver, Michael J. Tapner, David Price, Geoffrey D. Bower, Gregory M. Briggs, Monica A. Rossleigh, D. James Taylor, and Jacob George

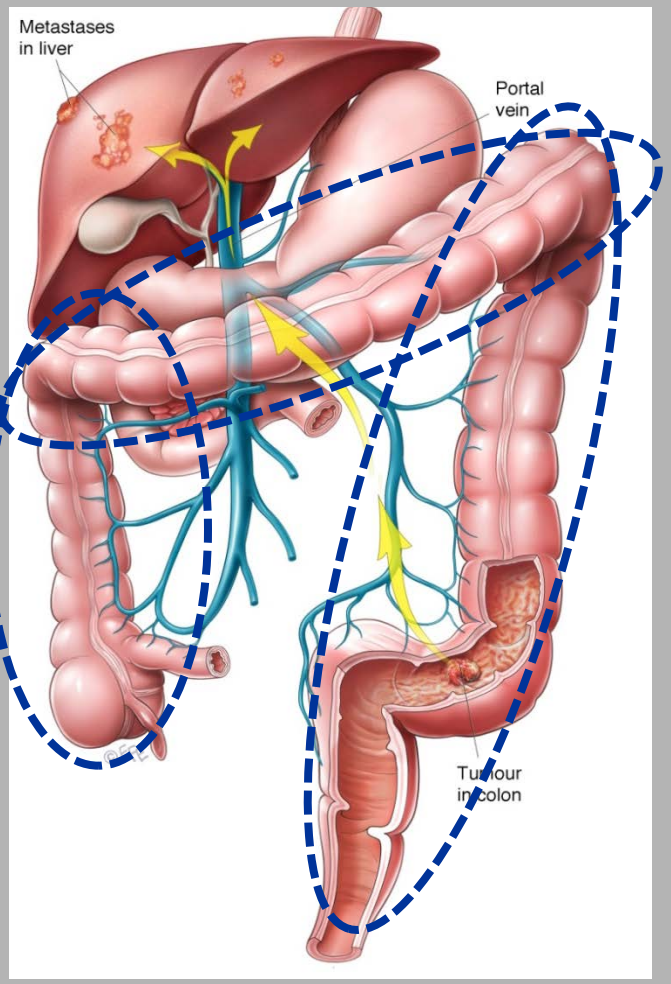
Patients

After ethics committee approval, patients were enrolled on this phase I, dose-escalation study at four Australian centers between September 2001 and October 2004. All patients were informed fully of the nature of the study and

- Involved in early trials of SIRT in mCRC
- Our MDT deploys SIRT in very novel ways
  - As a salvage therapy, OR
  - In combination with early-line chemotherapy, OR
  - As down-staging to surgery
- Very skilled Interventional Radiologists, Nuclear Medicine, Medical Physics, Surgeons

1. Introduction
2. Colorectal cancer
3. Quick review of SIRFLOX data
4. The SIRFLOX–FOXFIRE–FOXFIRE Global study

Colorectal (bowel) cancer is a disease of the large intestine (colon)



- Usually starts as a benign polyp
- Screening tests strongly recommended if >50 years old!
  - Faecal occult blood test from GP
  - Colonoscopy
  - No blood test available yet for screening
- Polyp may eventually becomes cancerous
- If left longer, may spread from the bowel
- Liver is usually the first ‘port of call’
- Also may spread to lungs, lymph glands
- Liver metastases are often the main life-limiting problem

Incidence & Cause

Colorectal cancer is the 3rd most common cancer in most first world countries[(1)]

- Worldwide incidence = 1,360,000 cases per year[(1)]

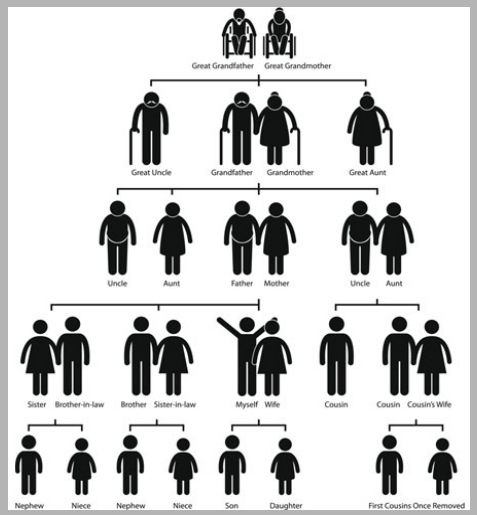
134,000

345,000

- Two main causes

Diet & Lifestyle

- Obesity
- Red & processed meat
- Alcohol
- Smoking
- Lack of exercise



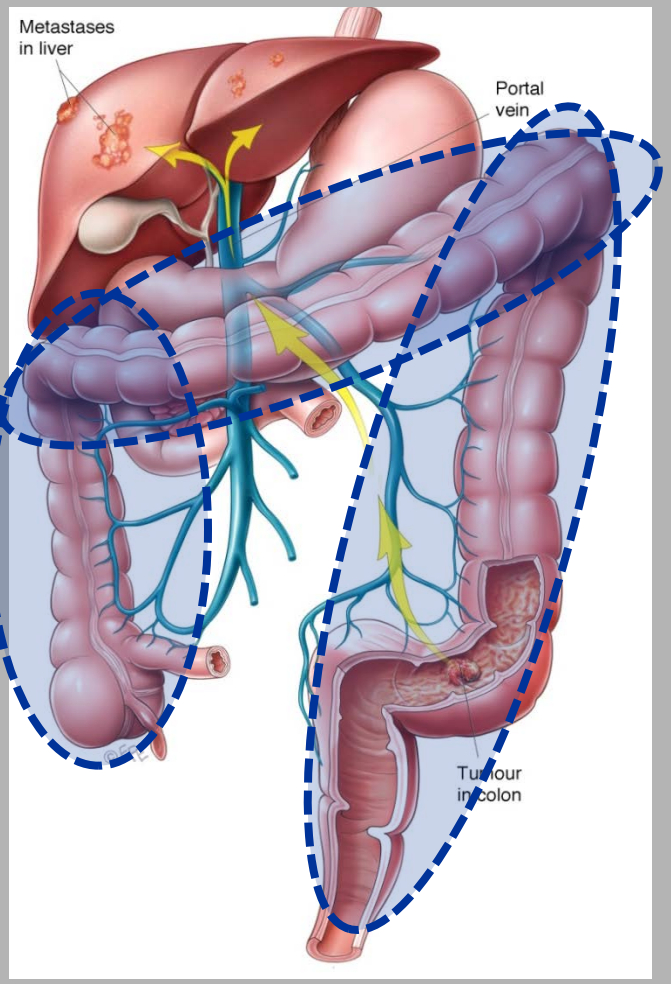
Family History

- Genetic role

Reference: (1) WHO Globocan Statistics 2012. In men prostate and lung, and in women breast and lung are the 1st and 2nd most common cancers, respectively.

Treatment

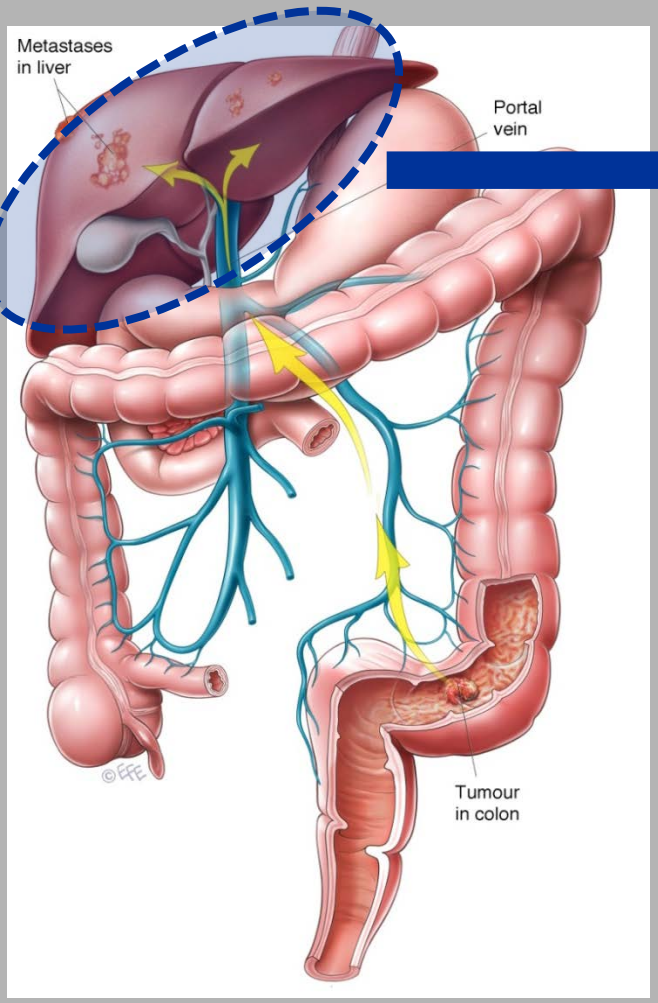
Colorectal cancer (CRC) that is confined to the bowel can often be cured



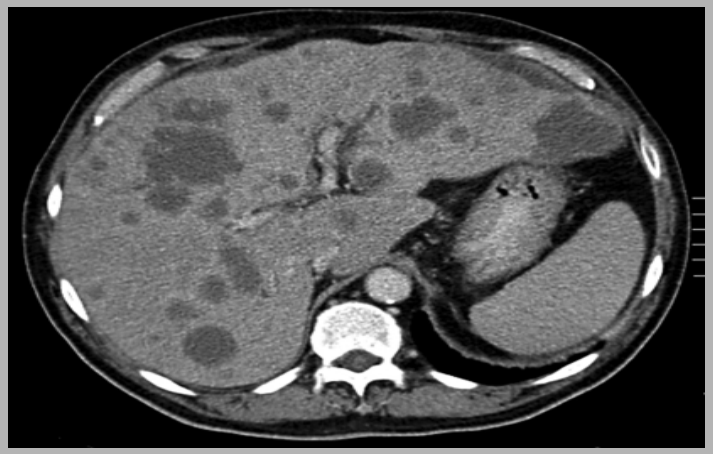
Intent of treatment ➡ achieve cure

- **Surgery alone**
  If cancer is confined within the bowel lining
- **Surgery + chemotherapy**
  If cancer has perforated through the bowel wall or if there is microscopic seeding of adjacent lymph nodes

Colorectal cancer that has metastasized (mCRC) is usually difficult to cure…



CT scan: not suitable for surgery

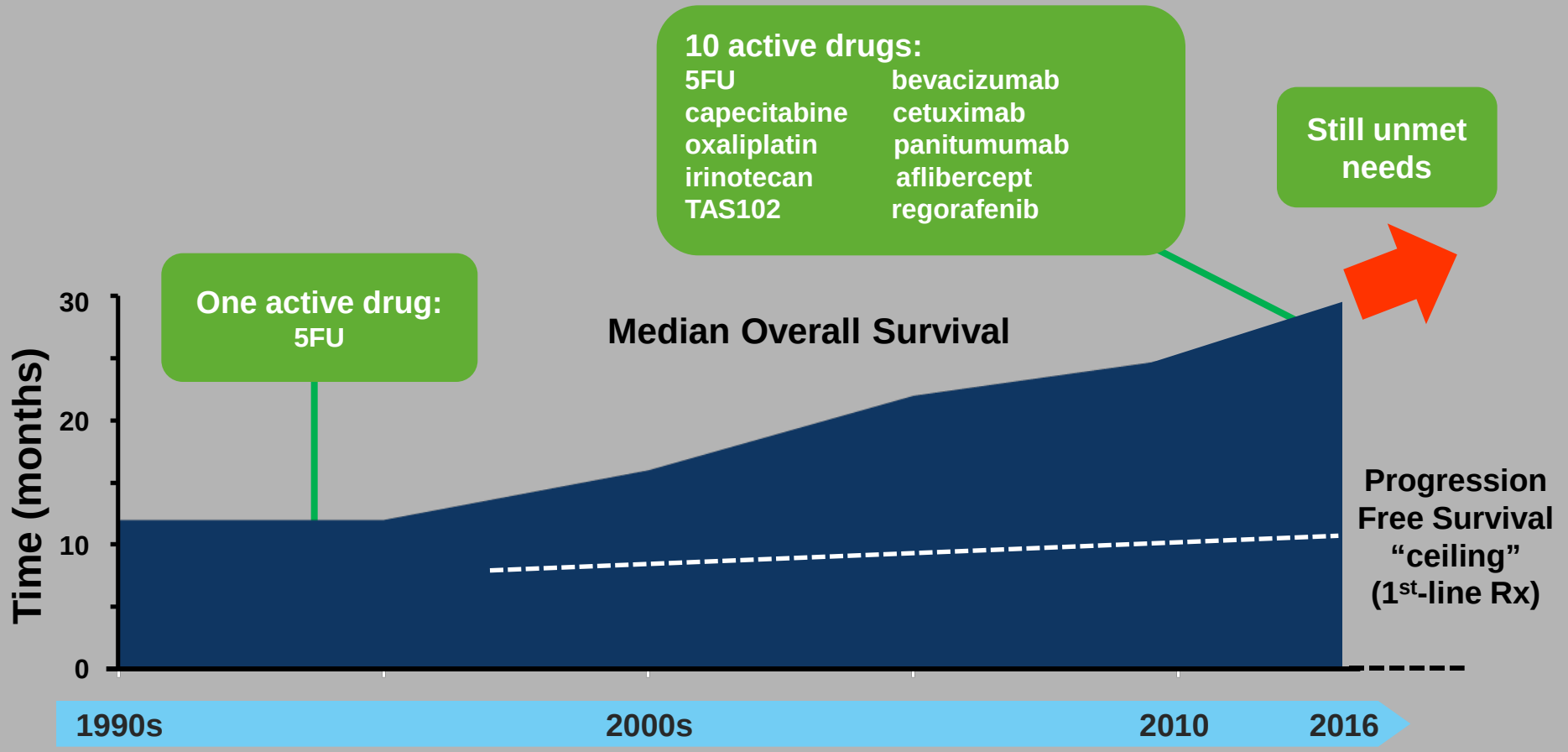


Intent of treatment ➡ palliative

(control symptoms and extend survival)

- 1st-line chemo + biologic therapy, *then*
- 2nd-line chemo + biologic therapy, *then*
- 3rd-line chemo + biologic therapy, *then*
- Salvage therapy or offer clinical trial

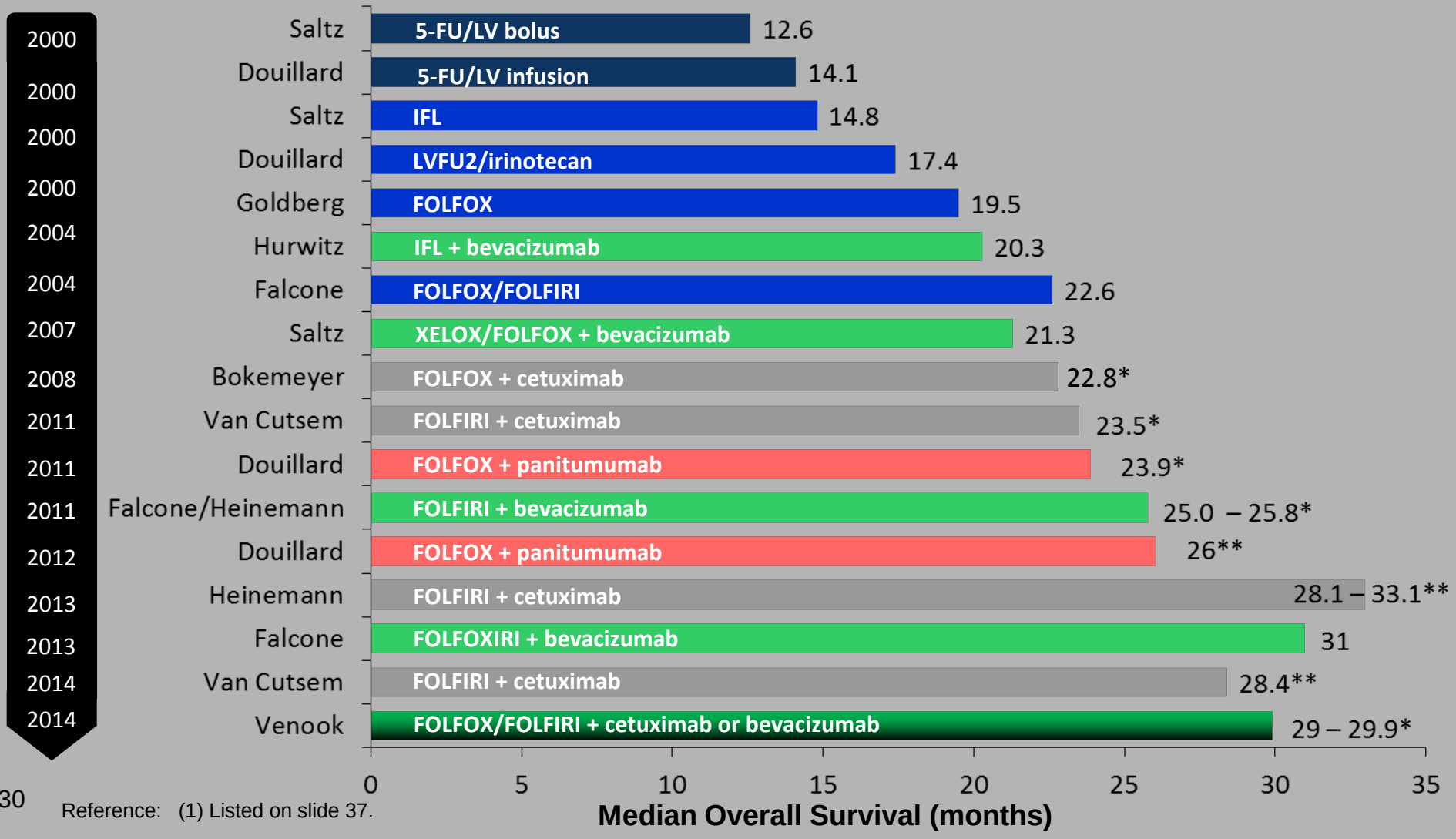
Survival in mCRC has progressively improved over the past two decades



Increasing number of treatment options

Yet, despite meaningful advances in palliative therapy, 5-year survival for mCRC remains <10%

Chemo + biologic therapy for 1st-line mCRC(1)



Reference: (1) Listed on slide 37.

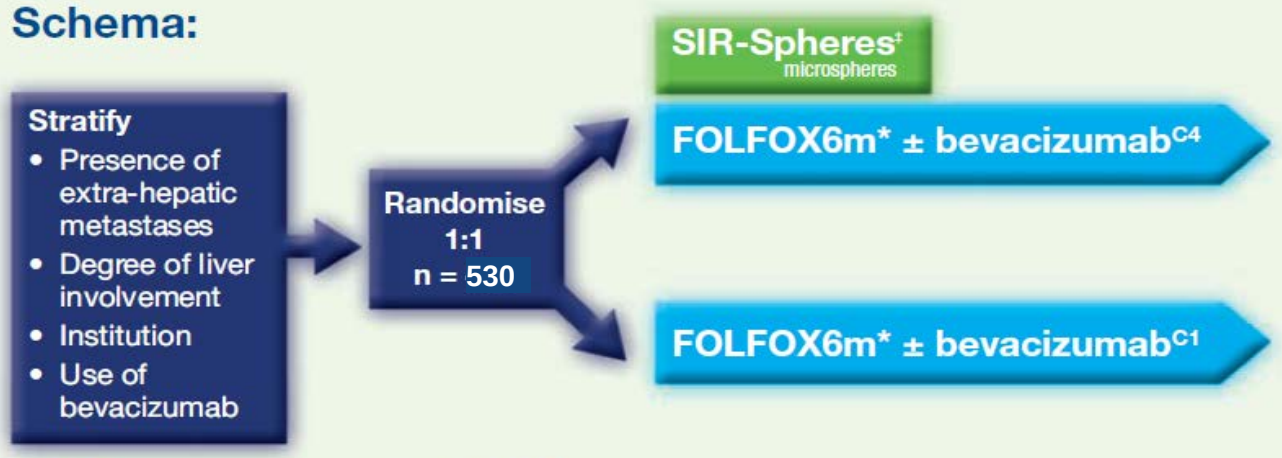
1. Introduction
2. Colorectal cancer
3. Quick review of SIRFLOX data
4. The SIRFLOX–FOXFIRE–FOXFIRE Global study

SIRFLOX compared 1st-line chemotherapy *versus* 1st-line chemotherapy + SIRT

Eligible Patients:

- Unresectable liver-only or liver-predominant colorectal cancer metastases
- No prior chemotherapy for advanced disease
- Fit for combination therapy and selective internal radiation therapy (SIRT)

Schema:



‡ SIR-Spheres microspheres implanted day 3–4 of Cycle 1

* oxaliplatin administered at 60 mg/m² for Cycles 1–3 in the SIR-Spheres microspheres + FOLFOX arm [1]

C4/C1 at the investigator's discretion, bevacizumab may commence at Cycle 4 in the test arm and at Cycle 1 (or per institutional protocol) in the control arm

Prof Gibbs presented the initial SIRFLOX results as an Oral Abstract Presentation at ASCO in June 2015(1)

SIRFLOX: Randomized phase III trial comparing first-line mFOLFOX6 (+bevacizumab) *versus* mFOLFOX6 (+bevacizumab) + selective internal radiation therapy (SIRT) in patients with metastatic colorectal cancer

Peter Gibbs (1), Volker Heinemann, Navesh K. Sharma, Michael P. N. Findlay, Jens Ricke, Val Gebski, Mark Van Buskirk, Guy A. Van Hazel, on behalf of the SIRFLOX Study Group

(1) The Royal Melbourne Hospital, Melbourne, Australia

Reference: (1) Gibbs *et al*. ASCO 2015.

And final SIRFLOX results were reported in the *Journal of Clinical Oncology* in February 2016[(1)]

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

SIRFLOX: Randomized Phase III Trial Comparing First-Line mFOLFOX6 (Plus or Minus Bevacizumab) Versus mFOLFOX6 (Plus or Minus Bevacizumab) Plus Selective Internal Radiation Therapy in Patients With Metastatic Colorectal Cancer

Guy A. van Hazel, Volker Heinemann, Navesh K. Sharma, Michael P.N. Findlay, Jens Ricke, Marc Peeters, David Perez, Bridget A. Robinson, Andrew H. Strickland, Tom Ferguson, Javier Rodriguez, Hendrik Kröning, Ido Wolf, Vinod Ganju, Euan Walpole, Eveline Boucher, Thomas Tichler, Einat Shacham-Shmueli, Alex Powell, Paul Eliadis, Richard Isaacs, David Price, Fred Moeslein, Julien Taieb, Geoff Bower, Val Gebski, Mark Van Buskirk, David N. Cade, Kenneth Thurston, and Peter Gibbs

Author affiliations appear at the end of this article.

Published online ahead of print at www.jco.org on February 22, 2016.

Written on behalf of the SIRFLOX Study Group. The principal investigators are listed in the online-only Appendix.

Processed as a Rapid Communication manuscript.

Supported by Sirtex Technology.

The protocol has been published (Gibbs et al. BMC Cancer 2014;14:897) and the results presented in part at the 2015 ASCO Annual Meeting, May 19-June 2, 2015, Chicago, IL.

Authors' disclosures of potential conflicts of interest are found in the article online at www.jco.org. Author contributions are found at the end of this article.

Clinical trial information: NCT00724503.

Corresponding author: Guy A. van Hazel, MBBS, 22/146 Mounts Bay Rd, Perth WA 6000, Australia; e-mail: gvh@perthoncology.com.au.

0732-183X/16/3499-1/$20.00

DOI: 10.1200/JCO.2015.66.1181

A B S T R A C T

Purpose

SIRFLOX was a randomized, multicenter trial designed to assess the efficacy and safety of adding selective internal radiation therapy (SIRT) using yttrium-90 resin microspheres to standard fluorouracil, leucovorin, and oxaliplatin (FOLFOX)–based chemotherapy in patients with previously untreated metastatic colorectal cancer.

Patients and Methods

Chemotherapy-naïve patients with liver metastases plus or minus limited extrahepatic metastases were randomly assigned to receive either modified FOLFOX (mFOLFOX6; control) or mFOLFOX6 plus SIRT (SIRT) plus or minus bevacizumab. The primary end point was progression-free survival (PFS) at any site as assessed by independent centralized radiology review blinded to study arm.

Results

Between October 2006 and April 2013, 530 patients were randomly assigned to treatment (control, 263; SIRT, 267). Median PFS at any site was 10.2 *v* 10.7 months in control versus SIRT (hazard ratio, 0.93; 95% CI, 0.77 to 1.12; $P = .43$). Median PFS in the liver by competing risk analysis was 12.6 *v* 20.5 months in control versus SIRT (hazard ratio, 0.69; 95% CI, 0.55 to 0.90; $P = .002$). Objective response rates (ORRs) at any site were similar (68.1% *v* 76.4% in control *v* SIRT; $P = .113$). ORR in the liver was improved with the addition of SIRT (68.8% *v* 78.7% in control *v* SIRT; $P = .042$). Grade ≥ 3 adverse events, including recognized SIRT-related effects, were reported in 73.4% and 85.4% of patients in control versus SIRT.

Conclusion

The addition of SIRT to FOLFOX-based first-line chemotherapy in patients with liver-dominant or liver-only metastatic colorectal cancer did not improve PFS at any site but significantly delayed disease progression in the liver. The safety profile was as expected and was consistent with previous studies.

J Clin Oncol 34. © 2016 by American Society of Clinical Oncology

Reference: (1) Gibbs *et al*. J Clin Oncol. 2016.

SIRFLOX study endpoints were sensible when the study was designed

Primary endpoint

- Progression-Free Survival (PFS) at any site

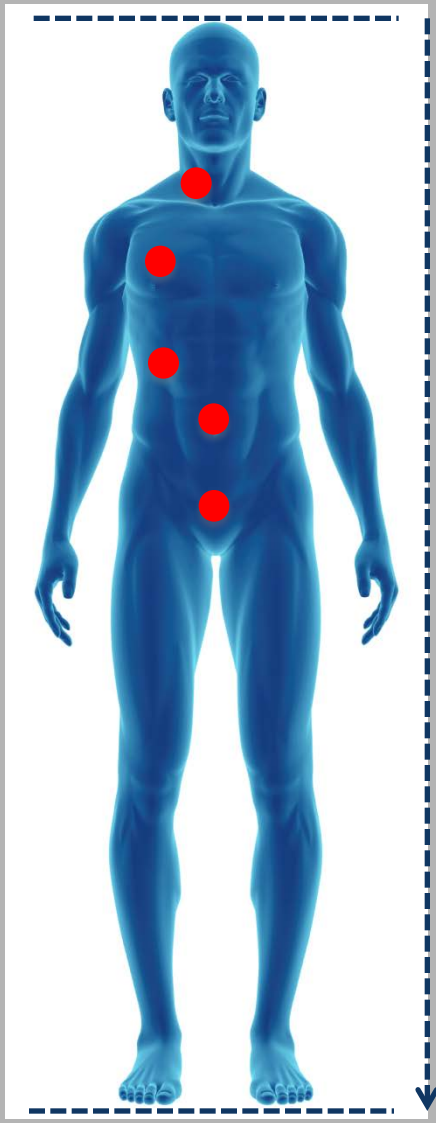
Secondary endpoints

- Progression-Free Survival (PFS) in the liver
- Tumour response rate in the liver
- Tumour response rate at any site
- Liver resection rate
- Toxicity & safety
- Health-related quality of life
- Overall survival, in a pre-planned combined analysis with FOXFIRE and FOXFIRE Global studies

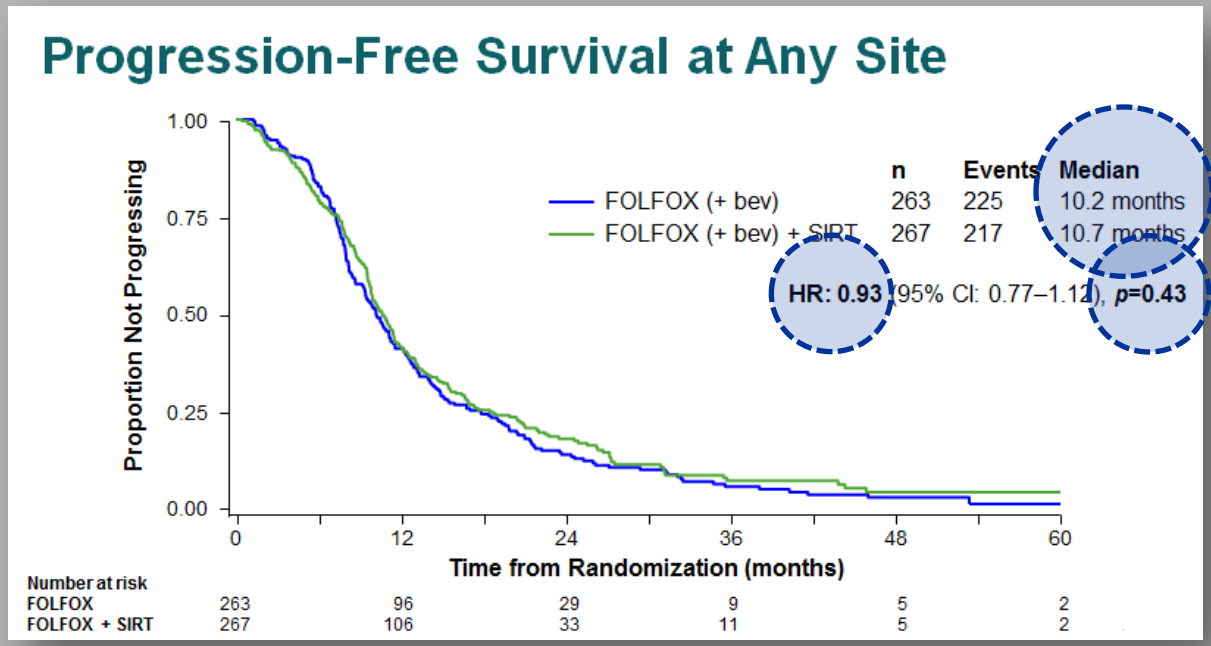
SIRFLOX's primary endpoint was Progression-Free Survival

Simply put

How long does a patient live, without tumours growing or developing at <u>any site in the body</u> i.e. "from top to toe"?



What was the significance of this result?

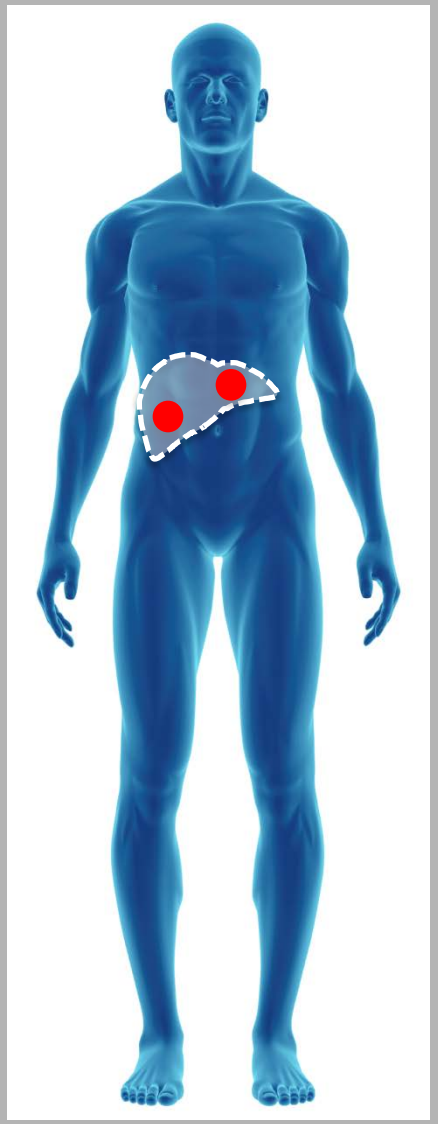


Our interpretation of this result

- P > 0.05 — Not statistically significant
- HR = 0.93 — A 7% risk reduction is not large, we want to see 20% +
- 10.2 vs 10.7 months PFS — Half a month's PFS extension is not large, we want 3 months +

Didn't meet primary endpoint

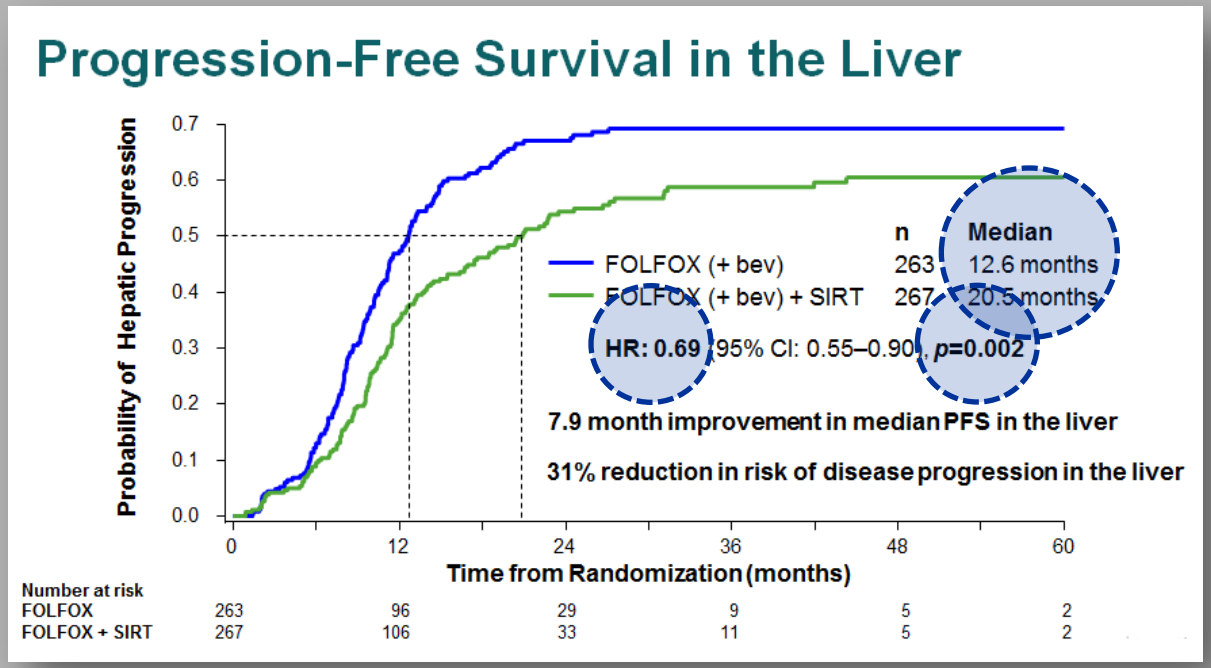
SIRFLOX's main secondary endpoint was Progression-Free Survival in the Liver



Simply put

How long does a patient live, without the tumours in the liver growing?

What was the significance of this result?



Our interpretation of this result

- P = 0.002 — Statistically significant
- HR = 0.69 — A 31% reduced risk of tumour progression in the liver, good
- 12.6 vs 20.5 months PFSL — Just under 8 months…durable tumour control in the liver

SIRT appears to deliver durable tumour control in the liver

What does this mean?

Does tumour control in the liver lead to improved survival?

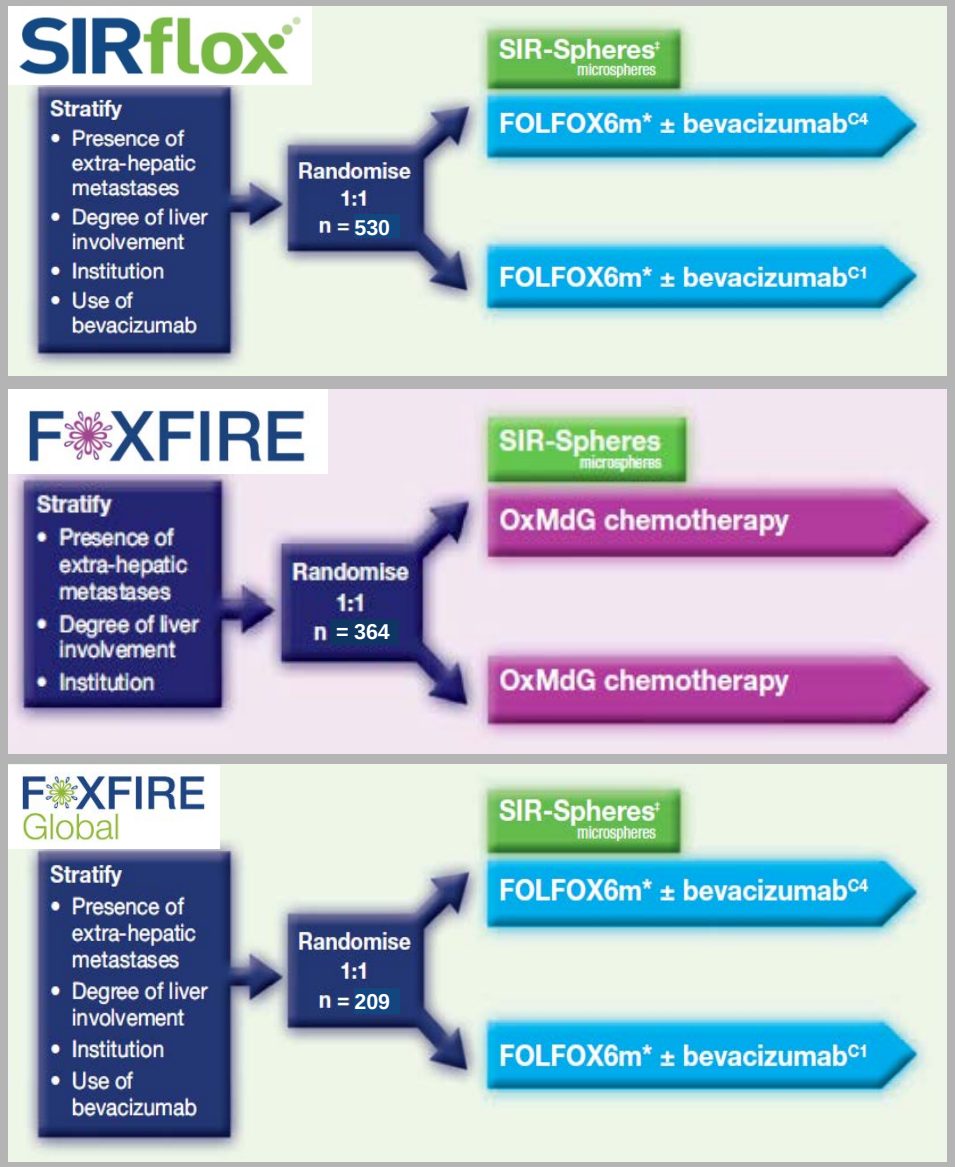
Well, definitive Overall Survival results are expected to be presented at ASCO in June 2017…

Study Name	Study Design	Geographic Region (1)	Recruitment Completed	Patients Recruited	OS Data Expected
SIRFLOX	RCT (2)	ANZ, EME, US	April 2013	530	2017
FOXFIRE	RCT (2)	UK	November 2014	364	
FOXFIRE Global	RCT (2)	ANZ, AP, EME, US	January 2015	209	
			Total accrual	1,103	

1. ANZ: Australia, New Zealand; AP: Asia Pacific; EME: Europe & Middle East; UK: United Kingdom; US: United States
2. FOLFOX-based (+ biologic) *vs.* FOLFOX-based (+ biologic) + SIRT

1. Introduction
2. Colorectal cancer
3. Quick review of SIRFLOX data
4. The SIRFLOX–FOXFIRE–FOXFIRE Global study

SIRFLOX + FOXFIRE + FOXFIRE Global will be combined in a pre-planned analysis of Overall Survival



Overall Survival

1,103 patients

SIRFLOX + FOXFIRE + FOXFIRE Global endpoints

Primary endpoint

- Overall Survival (OS)

Secondary endpoints

- Progression-Free Survival (PFS) at any site
- Progression-Free Survival (PFS) in the liver
- Safety & toxicity
- Healthcare costs / health economics
- Quality of life
- Tumour response rate
- Liver resection rate
- % of patients receiving 2nd-line therapy

How may we interpret the primary endpoint, Overall Survival?

Overall Survival results could fall into one of three main outcome scenarios

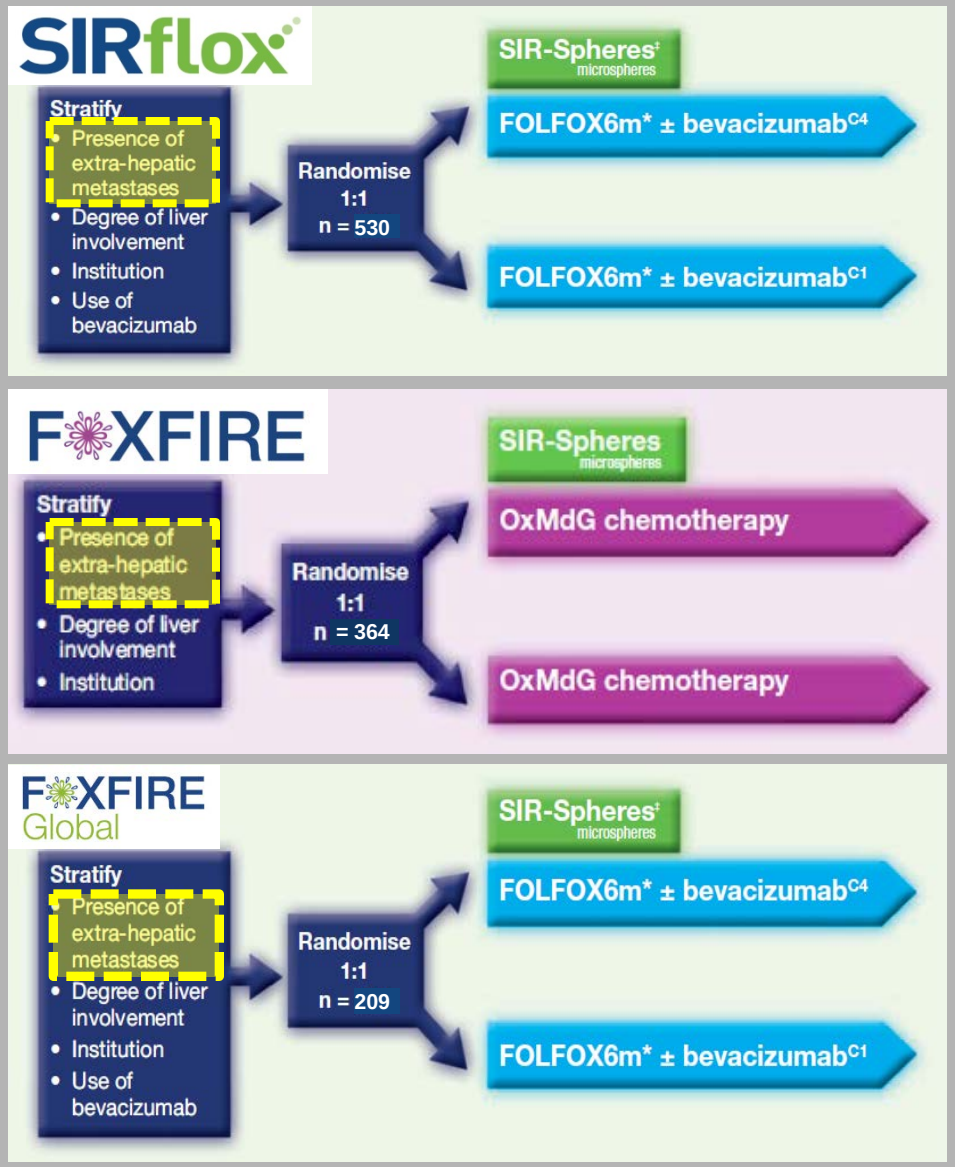
Overall Survival Result	P Value	Hazard Ratio (HR)	Interpretation
'Superior'	**<0.05**	**<0.80**	• **Statistically significant** (p<0.05): primary endpoint is 'met' • **Clinically significant** (HR<0.08): Adding SIRT to chemotherapy reduces the risk of death by at least 20% c.f. chemoTx
'No difference'	**>0.05**	**>0.90**	• **Not statistically significant** (p>0.05): 'did not meet' primary endpoint • **Possible trend towards a survival benefit** (HR>0.90): Adding SIRT to chemoTx reduces risk of death by 10% or less, c.f. chemoTx
'Possibly inferior'	**>0.05**	**≥1.00**	• **Not statistically significant** (p>0.05): 'did not meet' primary endpoint • **Possibly worse survival** (HR≥1.00): Adding SIRT to chemoTx has the same, or worsens the risk of death, c.f. chemoTx

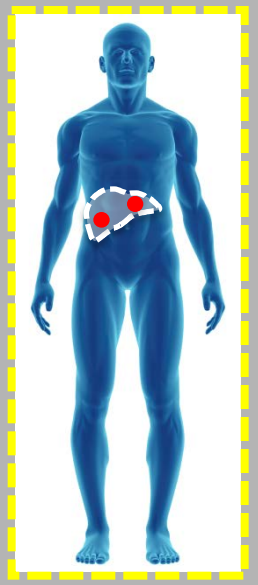
The Overall Survival result will guide the future use of SIRT in mCRC

Overall Survival Result	Future Clinical Use in mCRC
'Superior'	• **1st-line use warranted** because this extends survival – With 1st-line induction chemotherapy, OR – With 1st-line maintenance chemotherapy • Case for inclusion in **Consensus Practice Guidelines** is strong • Case for further **reimbursement** is strong
'No difference'	• **1st-line use unlikely** • Remains a late-line **'salvage' therapy or option for "chemo break"** • **Sub-groups** may be important – Patients with liver-only disease (660 out of the 1,103) is the most important sub-group
'Possibly inferior'	• Remains a late-line **'salvage' therapy** • **Sub-groups** may still be important – Patients with liver-only disease (660 out of the 1,103) is the most important sub-group

Which sub-group is the most important?

Patients with liver-only disease (LOD) are likely to gain the most survival benefit from SIRT





60% of the 1,103 patients had LOD at the time they entered the study

An Overall Survival result in patients with LOD may also guide the future use of SIRT

Overall Survival Result in LOD Subset	Future Clinical Use for Patients with LOD
'Superior'	• 1st-line use warranted because this extends survival in patients with LOD • Case for inclusion in Consensus Practice Guidelines is strong • Case for further reimbursement is strong
'No difference'	• Any 1st-line use unlikely in patients with LOD • Remains a late-line 'salvage' therapy
'Possibly inferior'	• Remains a late-line 'salvage' therapy

Thank you

References, slide 15

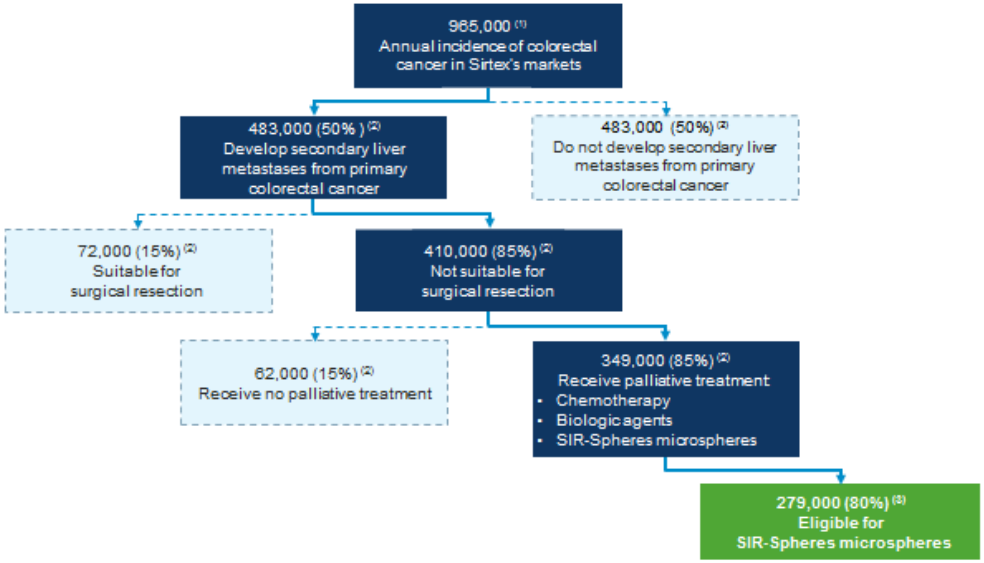
1. Saltz *et al*. *N Engl J Med*. 2000
2. Douilliard *et al*. *Lancet.* 2000
3. Goldberg *et al*. *J Clin Oncol.* 2004
4. Hurwitz *et al*. *N Engl J Med.* 2004
5. Saltz *et al*. *J Clin Oncol.* 2008
6. Falcone *et al*. *J Clin Oncol.* 2007
7. Bokemeyer *et al*. *Ann Oncol.* 2011
8. Van Cutsem *et al*. *J Clin Oncol*. 2011
9. Douilliard *et al*. *Ann Oncol.* 2014
10. Heinemann *et al*. *Lancet Oncol.* 2014
11. Falcone *et al*. ASCO 2013. Abstract 3505\
12. Douillard *et al*. *New Engl J Med.* 2013
13. Van Cutsem *et al*. Ann Oncology ESMO GI 2014 A
14. Venook *et al*. ASCO 2014. Abstract LBA3; Plenary presentation

mCRC: Commercial implications

Mr Nigel Lange
Interim CEO

mCRC: Commercial implications

- The annual addressable market opportunity in mCRC has been previously presented as **279,000** patients
- This market model is reasonable, until such time as the SIRFLOX/FOXFIRE/ FOXFIRE Global studies report findings



(1) Sirtex markets = APAC: Australia, China, Hong Kong, India, Japan, Malaysia, New Zealand, Philippines, Singapore, South Korea, Taiwan, Thailand. EMEA: Austria, Belgium, Egypt, Estonia, Finland, France, Germany, Greece, Israel, Italy, Poland, Portugal, South Africa, Spain, Sweden, Switzerland, The Netherlands, Turkey, United Kingdom. Americas: Argentina, Brazil, Canada, Mexico, USA
(2) Hind D, Tappenden P, Tumur I et. al. Technology assessment report commissioned by the HTA Programme on behalf of The National Institute for Clinical Excellence. 10 January 2005.
(3) Sirtex data and analysis.

Note the market models Sirtex provides should be considered as a guide and are based on incidence data and basic assumptions on use: they do not account for individual access to treatment via govt. or private insurance, age, extent of disease, or prevalence of disease in any one market. They provide an estimate of the addressable patient population only.

FOXFIRE *et al*: Outcome scenarios

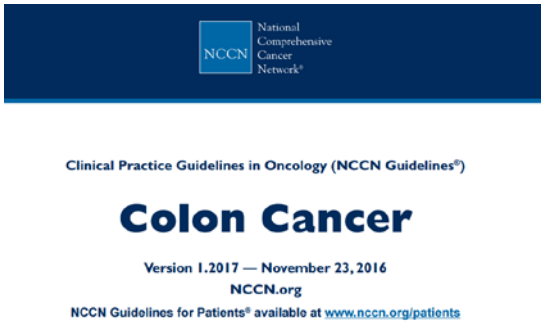
- **SIR-Spheres microspheres + Standard of Care (SOC) chemo/biologic therapy is Superior to SOC chemo/biologic therapy alone**

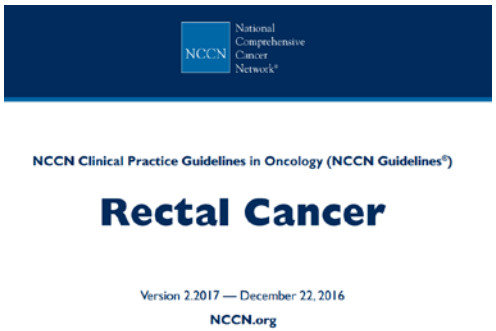
- **SIR-Spheres microspheres + SOC chemo/biologic therapy is No Different to SOC chemo/biologic therapy alone**

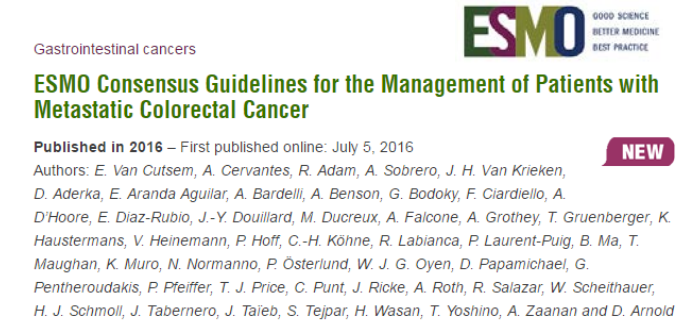
- **SIR-Spheres microspheres + SOC chemo/biologic therapy is possibly Inferior to SOC chemo/biologic therapy alone**

FOXFIRE *et al*: Priorities on superiority

- **Sales and Marketing**
  - Commence promotional activities globally on the result (all markets approved for mCRC)
  - Publication of study data in leading peer-reviewed journal <12 months
- **Update clinical practice guidelines**
  - NCCN, ESMO, other
  - May include country specific guidelines (Australia, Germany S-3, etc.)







FOXFIRE *et al*: Priorities on superiority

- **Regulatory**
  - No immediate regulatory filings required
  - Update current US PMA to reflect evidence with modern chemotherapy (FOLFOX) and biologic (bevacizumab/Avastin®) therapy
  - CE mark (Europe) remains unchanged
- **Reimbursement and Market Access**
  - Commence discussions with government and private payers
  - Update recommendations

FOXFIRE *et al*: Priorities on superiority

590,000 (1)
Annual incidence of colorectal cancer in Sirtex's **current** markets

295,000 (50%) (2)
Develop secondary liver metastases from primary colorectal cancer

251,000 (85%) (2)
Not suitable for surgical resection

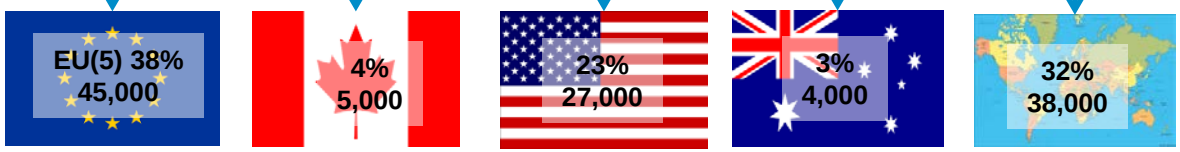
213,000 (85%) (3)
Receive 1st line chemotherapy

149,000 (70%) (4)
Liver +/- extra-hepatic metastases

64,000 (30%) (4)
Extensive non-liver metastases

119,000 (80%) (5)
Eligible for SIR-Spheres microspheres

Excluding



- **119,000** patients (pts) per annum eligible for SIR-Spheres
- **67%** of pts (81,000) within Sirtex's current key markets
- A significant opportunity

(1) Sirtex markets = APAC: Australia, Hong Kong, India, Malaysia, New Zealand, Philippines, Singapore, South Korea, Taiwan, Thailand. EMEA: Austria, Belgium, Egypt, Estonia, Finland, France, Germany, Greece, Israel, Italy, Poland, Portugal, South Africa, Spain, Sweden, Switzerland, The Netherlands, Turkey, United Kingdom. Americas: Argentina, Brazil, Canada, USA
(2) Hind D, Tappenden P, Tumur I et. al. Technology assessment report commissioned by the HTA Programme on behalf of The National Institute for Clinical Excellence. 10 January 2005.
(3) NICE Technology Appraisal TA 93: Irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer. Aug 2005.
(4) Kumar R *et al*. Colorectal cancer survival: An analysis of patients with metastatic disease synchronous and metachronous with the primary tumor. *Clin Colorectal Cancer* 2014; 13(2):87-93.
(5) 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 54 when examining data

FOXFIRE *et al*: No difference / equivocal

- **Regulatory**
  - No immediate regulatory filings required
- **Sub-group data (liver only, liver plus extra-hepatic disease)**
  - If no difference is observed in the primary endpoint, but there is a trend in Overall Survival favouring the SIR-Spheres microspheres group, then sub-group analyses become important
  - Two sub-groups of interest are the liver-only and liver plus extra-hepatic disease
- **Sales and Marketing**
  - Similar approach as superiority, focusing on sub-groups
- **Update clinical practice guidelines**
  - Similar approach as superiority, focusing on sub-groups

FOXFIRE *et al*: Sub-groups of interest

Excluding

590,000 (1)
Annual incidence of colorectal cancer in Sirtex's **current** markets

295,000 (50%) (2)
Develop secondary liver metastases from primary colorectal cancer

251,000 (85%) (2)
Not suitable for surgical resection

213,000 (85%) (3)
Receive 1st line chemotherapy

85,000 (40%) (4)
Liver-Only

64,000 (30%) (4)
Liver + extra-hepatic metastases

64,000 (30%) (4)
Extensive non-liver metastases

68,000 (80%) (5)
Eligible for SIR-Spheres microspheres

51,000 (80%) (5)
Eligible for SIR-Spheres microspheres

- If the liver-only sub-group shows a clinically & statistically significant survival benefit, potential addressable market is **68,000** pts p.a.
- If the liver-dominant sub-group shows a clinically & statistically significant survival benefit, potential addressable market is **51,000** pts p.a.

(1) Sirtex markets = see previous slides
(2) Hind D, Tappenden P, Tumur I et. al. Technology assessment report commissioned by the HTA Programme on behalf of The National Institute for Clinical Excellence. 10 January 2005.
(3) NICE Technology Appraisal TA 93: Irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer. Aug 2005.
(4) Kumar R *et al*. Colorectal cancer survival: An analysis of patients with metastatic disease synchronous and metachronous with the primary tumor. *Clin Colorectal Cancer* 2014; 13(2):87-93.
(5) 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 54 when examining data

FOXFIRE *et al*: Inferiority

Excluding

590,000 (1)
Annual incidence of colorectal cancer in Sirtex's **current** markets

295,000 (50%) (2)
Develop secondary liver metastases from primary colorectal cancer

251,000 (85%) (2)
Not suitable for surgical resection

75,000 (30%) (3)
Receive salvage chemotherapy

53,000 (70%) (4)
Liver +/- extra-hepatic metastases

22,000 (30%) (4)
Extensive non-liver metastases

42,000 (80%) (5)
Eligible for SIR-Spheres microspheres

- Remains as a third/fourth line 'salvage' therapy
- **68%** of pts (29,000) within Sirtex's key markets
- At risk of being pushed further down treatment cascade as new oral drugs receive regulatory approvals (Stivarga®, Lonsurf®)
- Requires determined sales and marketing focus/strategy

(1) Sirtex markets – see previous slides
(2) Hind D, Tappenden P, Tumur I et. al. Technology assessment report commissioned by the HTA Programme on behalf of The National Institute for Clinical Excellence. 10 January 2005.
(3) GlobalData. Colorectal cancer – Global drug forecast and market analysis to 2025. January 2017
(4) Kumar R *et al*. Colorectal cancer survival: An analysis of patients with metastatic disease synchronous and metachronous with the primary tumor. *Clin Colorectal Cancer* 2014; 13(2):87-93.
(5) 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 54 when examining data

Thank you

SIRTeX

Perspectives on Hepatocellular Carcinoma

Prof. Bruno Sangro
Clínica Universitaria
CIBERehd
Pamplona, Spain

Sydney 2nd March 2017

Overview of today's talk

1. **Introduction**
2. **Hepatocellular carcinoma**
3. **Overview of key SIRT data in HCC**
4. **The SARAH study – How will we interpret the results?**

1. **Introduction**

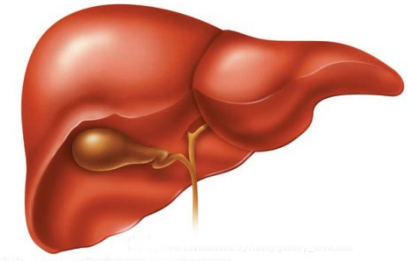
2. **Hepatocellular carcinoma**

3. **Overview of key SIRT data in HCC**

4. **The SARAH study – How will we interpret the results?**

A little about me…

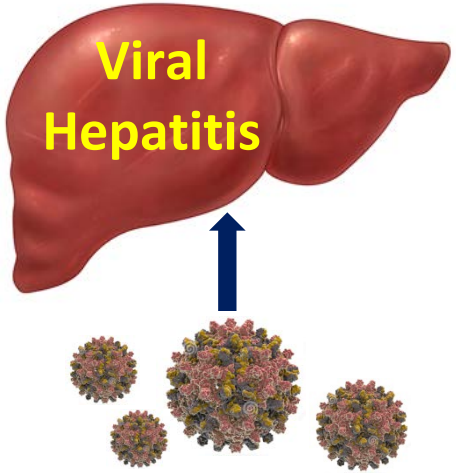
- Director of the Liver Unit, **University Clinic of Navarra**, Pamplona, Spain
- Prof of Medicine, University of Navarra School of Medicine
- Senior Researcher, Centre of Biomedical Research, Hepatic and Digestive Diseases Network (CIBERehd)
- **Hepatologist** = 'Liver Specialist'
  - Research focus is liver cancer
  - Lead the Radioembolization(1) Program at University Clinic
  - First SIRT September 2003
  - > 400 patients treated with SIRT since 2003

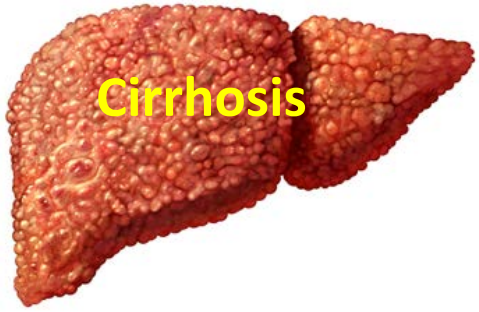


Notes: (1) Radioembolization is another term for selective internal radiation therapy (SIRT).

What do Hepatologists do?

- We treat diseases of the liver (and bile ducts, gallbladder, pancreas)
- The ‘Big Three’





- And many others to keep us occupied!

Our group has endeavoured to contribute to the scientific literature on SIRT in HCC

Published on Efficacy

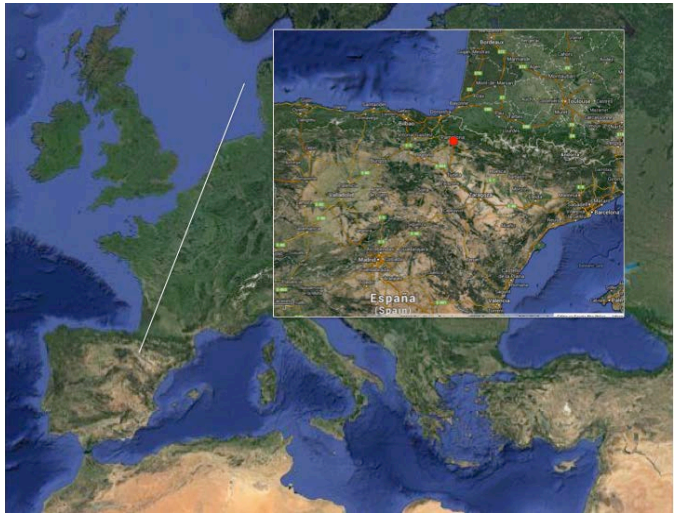
- 325 patients
- 8 European institutions

Published on Safety

- 260 patients
- Our institution

References: Sangro *et al* Hepatology, Vol. 54, No. 3, 2011; Gil-Alzugaray *et al* Hepatology, Vol 57. No.3 2013.

A little bit about University Clinic of Navarra



10,956 students

128 degrees

16 million euros for research

14% students from 86 countries

39% students participating in international exchange programs

7% international professors

A little bit about University Clinic of Navarra

- Mediterranean rim is a ‘hotspot’ for HCC
- France, Italy, Spain have led the understanding & treatment of HCC
- Private University Hospital
  - High priority focus on therapeutic innovation
  - High priority focus on research

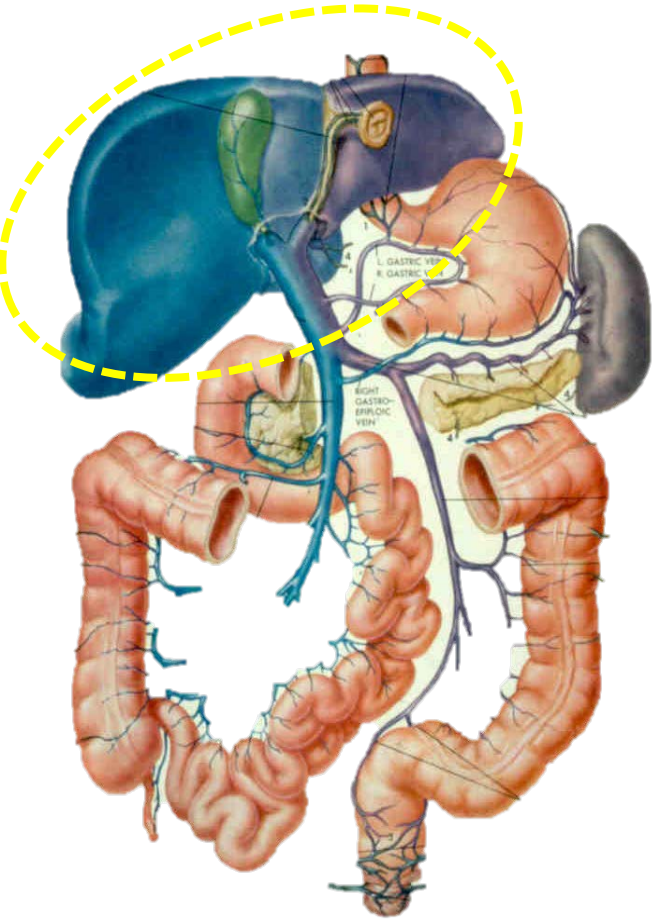
1. **Introduction**

2. **Hepatocellular carcinoma**

3. **Overview of key SIRT data in HCC**

4. **The SARAH study – How will we interpret the results?**

The liver is a football sized organ located under the ribs on the right hand side…



- ***Factory***
  - Produces proteins (blood clotting factors, hormones, albumin, cholesterol)
  - Produces bile juices
- ***Warehouse***
  - Stores glucose and vitamins
- ***Power plant***
  - Metabolizes nutrients to produce energy
- ***Decontamination unit***
  - Removes potentially toxic byproducts (internal & external)
- ***Helps fight infection***

Incidence & Cause

Hepatocellular carcinoma is the main type of primary liver cancer

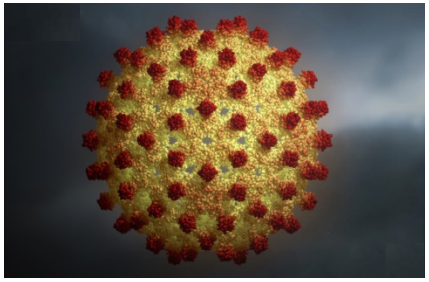
- Worldwide incidence= 780,000 cases per year[(1)] & climbing

30,000

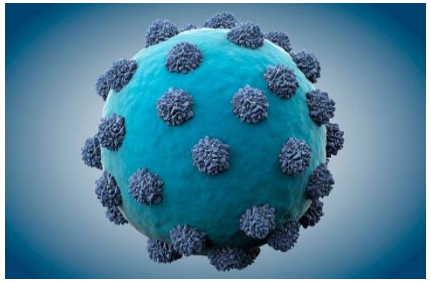
52,000

- Three main causes

Long term **alcohol** misuse



Long term viral **hepatitis B** infection

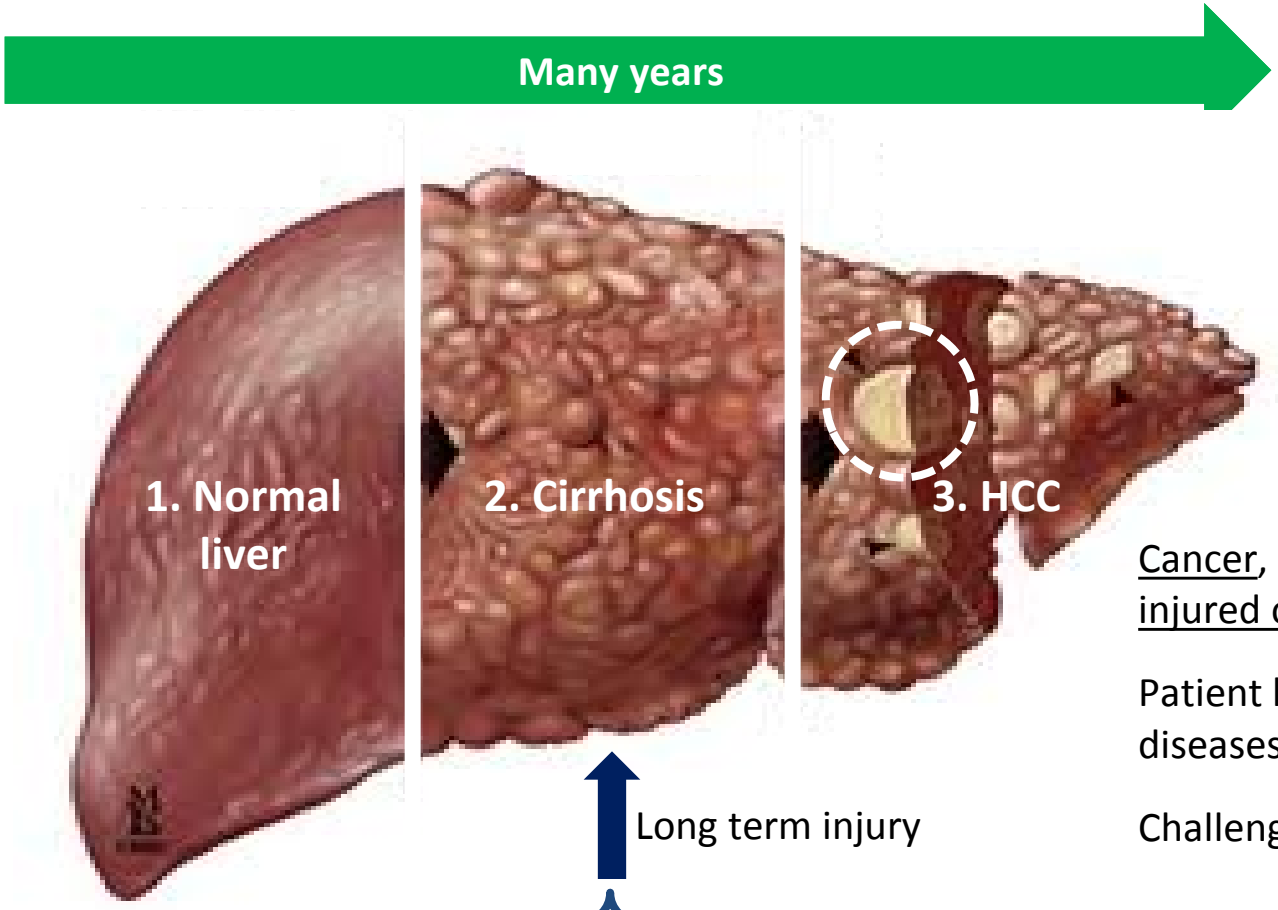


Long term viral **hepatitis C** infection

Reference: (1) World Health Organization, Globocan data.

Treatment

HCC is very difficult to treat as most patients have two diseases at once: cancer *and* an injured liver

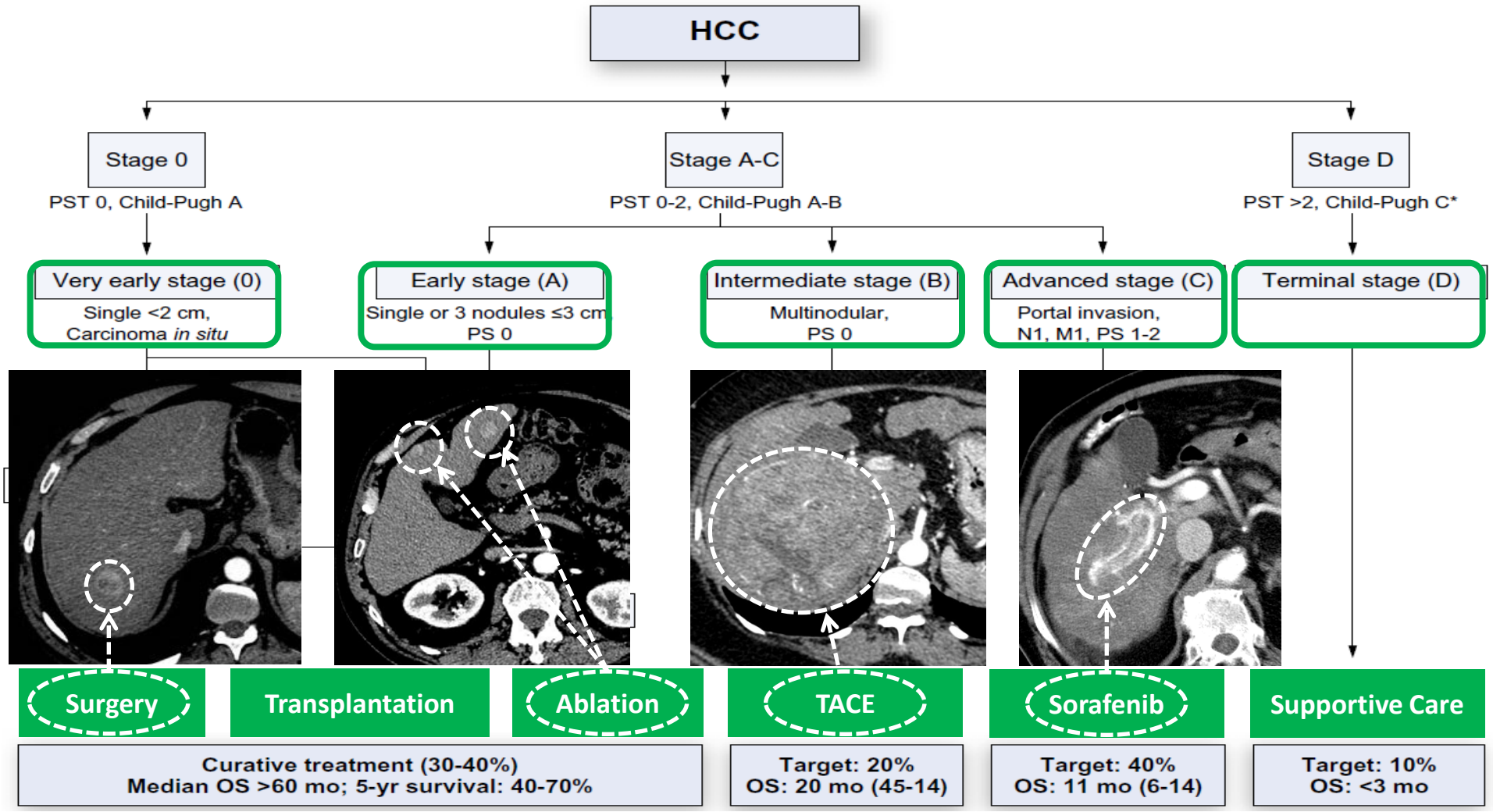


Cancer, occurring in an injured organ

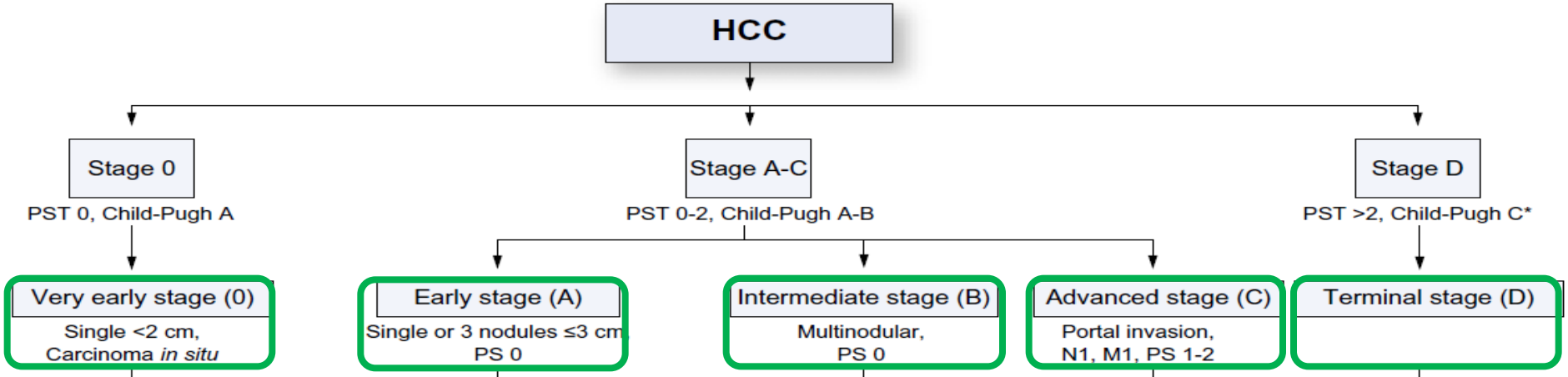
Patient has two diseases at once

Challenging to treat

For patients with HCC, the disease stage (i.e. extent) determines the treatment…and the prognosis



Early disease – effective treatments
Intermediate & advanced disease – large unmet need



What's positive?
- Surgery, transplantation, ablation offer potential cure

What's negative?
- Few patients are suitable for these options
- Transplant waiting lists

What's positive?
- TACE is reasonably effective

What's negative?
- These treatments are only palliative
- Sorafenib is the only available drug (but quite toxic)
- No new drugs since 2008

Surgery	Transplantation	Ablation	TACE	Sorafenib	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

Sorafenib has been the standard of care for advanced HCC since 2008

- No treatment available prior to 2008
- SHARP study – ASCO 2008 & New England Journal of Medicine 2008 (1)
  - Sorafenib (299 patients) — Median survival = 10.7 months
  - Placebo (303 patients) — Median survival = 7.9 months
- Sorafenib was the first effective drug for advanced HCC
- Sorafenib became new standard of care against which to compare new therapies in randomized controlled trials
  - New drugs, SIRT

Reference: (1) Llovet JM et al. N Engl J Med 2008; 359: 378–90.

Sorafenib provides a modest survival benefit in advanced HCC, but has several disadvantages

- Quite toxic
  - Hand-foot syndrome (severe rash)
  - Diarrhoea
  - Fatigue
- Have to take it continuously
- Expensive
  - US$9,000 per month
- Therefore, need new treatments…

Reference: Llovet JM et al. N Engl J Med 2008; 359: 378–90. Cheng AL et al. Lancet Oncol 2009;10:25–34.

1. Introduction

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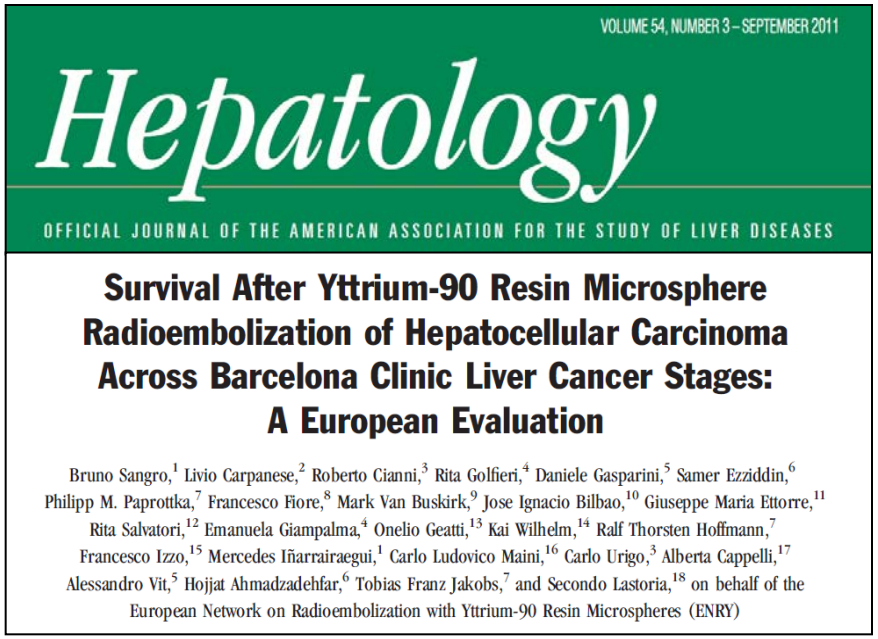
3. Overview of key SIRT data in HCC

4. The SARAH study – How will we interpret the results?

Data on the survival achieved with SIRT in advanced HCC was presented in 2011



VOLUME 54, NUMBER 3 – SEPTEMBER 2011

Hepatology

OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Survival After Yttrium-90 Resin Microsphere Radioembolization of Hepatocellular Carcinoma Across Barcelona Clinic Liver Cancer Stages: A European Evaluation

Bruno Sangro,[1] Livio Carpanese,[2] Roberto Cianni,[3] Rita Golfieri,[4] Daniele Gasparini,[5] Samer Ezziddin,[6] Philipp M. Paprottka,[7] Francesco Fiore,[8] Mark Van Buskirk,[9] Jose Ignacio Bilbao,[10] Giuseppe Maria Ettorre,[11] Rita Salvatori,[12] Emanuela Giampalma,[4] Onelio Geatti,[13] Kai Wilhelm,[14] Ralf Thorsten Hoffmann,[7] Francesco Izzo,[15] Mercedes Iñarrairaegui,[1] Carlo Ludovico Maini,[16] Carlo Urigo,[3] Alberta Cappelli,[17] Alessandro Vit,[5] Hojjat Ahmadzadehfar,[6] Tobias Franz Jakobs,[7] and Secondo Lastoria,[18] on behalf of the European Network on Radioembolization with Yttrium-90 Resin Microspheres (ENRY)

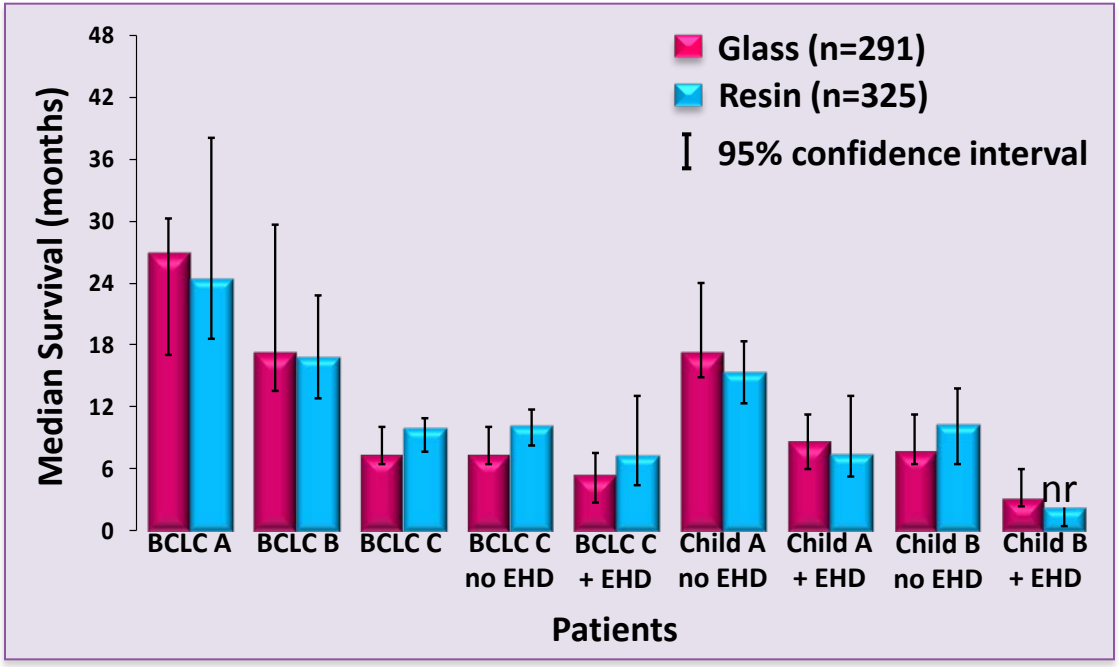
- 325 patients
- 8 European institutions
- Retrospective study of ‘real world’ use

- Median overall survival 12.8 months
- Early stage HCC 24.4 months
- Intermediate stage HCC 16.9 months
- Advanced stage HCC 10.0 months

} SARAH study patient population

Reference: Sangro *et al* Hepatology, Vol. 54, No. 3, 2011.

Additional data on the survival achieved with SIRT comes from the glass Y90 microspheres data



- Survival by HCC stage of disease is similar for resin and glass Y90 microspheres
- Apparent differences in survival are statistically insignificant

Reference: Sangro *et al* J Nucl Med Radiat Ther 2011;2:1. Salem *et al* Gastroenterology 2010; 138: 52–64.
Sangro *et al* Hepatology 2011; 54: 868–878.

1. **Introduction**

2. **Hepatocellular carcinoma**

3. **Overview of key SIRT data in HCC**

4. **The SARAH study – How will we interpret the results?**

SARAH compared SIRT *versus* sorafenib in patients with advanced HCC in France (1, 2)

Eligible Patients:

- Unresectable 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
- If cirrhotic, Child-Pugh class A or B ≤7 points
- ECOG performance status (PS) 0–1
- Fit for sorafenib and ^{90}Y

Schema:

Reference: (1) www.clinicaltrials.gov identifier NCT01482442, (2) Vilgrain *et al.* Trials 2014, 15:474.

SARAH endpoints

Primary endpoint

- Overall Survival (OS)

Secondary endpoints

- Adverse events rate (safety)
- Progression-Free Survival (PFS) at 6 months
- Tumour response rate (complete, partial, stability)
- Quality of life (general and liver specific)
- Treatment cost

How may we interpret the primary endpoint, Overall Survival?

Overall Survival results could fall into one of three main outcome scenarios

Overall Survival Result	P Value	Hazard Ratio (HR)	Interpretation
'Superior' to sorafenib	**<0.05**	**<0.80**	o **Statistically significant** (p<0.05): primary endpoint is 'met' o **Clinically significant** (HR<0.80): SIRT reduces the risk of death c.f. sorafenib by at least 20%
'No different' to sorafenib	**>0.05**	**>0.90**	o **Not statistically significant** (p>0.05): 'did not meet' primary endpoint o **Possible trend towards a survival benefit** (HR>0.90): SIRT reduces the risk of death c.f. sorafenib by 10% or less
'Possibly inferior' to sorafenib	**>0.05**	**≥1.00**	o **Not statistically significant** (p>0.05): 'did not meet' primary endpoint o **Possibly worse survival** (HR≥1.00): SIRT has the same, or worsens the risk of death, c.f. sorafenib

Statistical significance

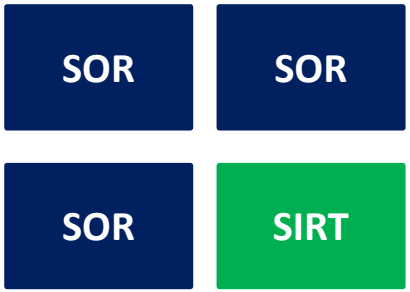
Clinical significance

The Overall Survival result will guide the future use of SIRT in the treatment of HCC

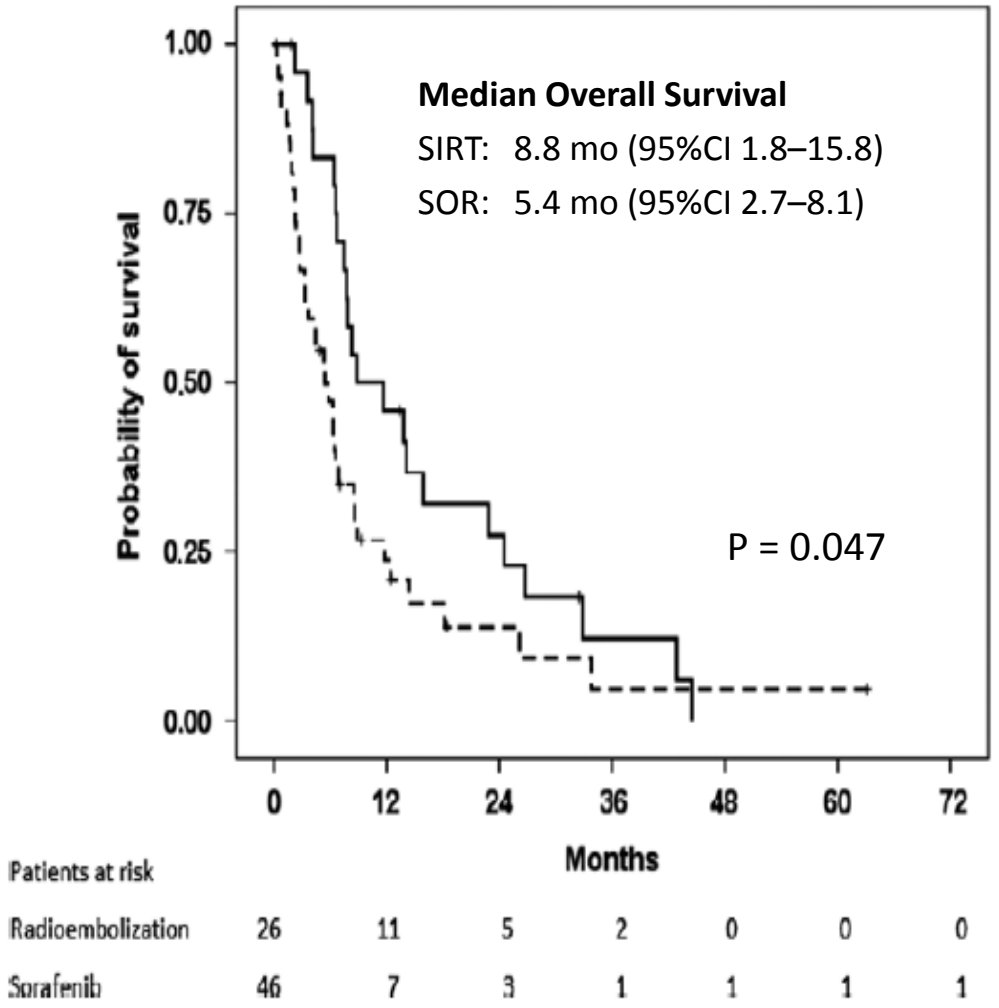
Overall Survival Result	Future Clinical Use in HCC
'Superior' to sorafenib	o SIRT potentially a new standard of care in **Advanced HCC** as it extends survival ➢ Highly feasible, as HCC is already treated mainly with liver directed therapies (Surgery, Transplantation, Ablation, TACE) o Case for inclusion in **Consensus Practice Guidelines** is strong o Case for further **reimbursement** is strong o Case for **regulatory submission** to US FDA seeking HCC indication is strong
'No different' to sorafenib	o SIRT may still be used in **Advanced HCC** ➢ SIRT is usually less toxic than sorafenib o VESPRO meta-analysis becomes important ➢ Pre-specified sub-groups
'Possibly inferior' to sorafenib	o VESPRO meta-analysis becomes important ➢ Pre-specified sub-groups

A key sub-group of interest is patients with portal vein involvement (PVI)

- Patients with HCC and PVI treated with SIRT or SOR in 4 Spanish hospitals between 2005 and 2013



- Retrospective analysis of survival
- A multivariate prognostic model was adjusted by a propensity score based on factors that may determine the probability of exposure to SIRT



Reference: (1) De la Torre M, et al. Liver Int 2016 (epub ahead of print)

Conclusions

- SARAH is a critical RCT in HCC
- SIR*ve*NIB is a very similar RCT in HCC in Asian patients
- Results may change management in advanced HCC…
- …But advanced HCC is a very difficult disease to treat
- …No successful new drugs approved since 2008
- Results will confirm / refute survival benefit of SIRT
- Even a ‘no survival difference’ result may be important if the toxicity of SIRT < sorafenib
- Results are highly awaited!

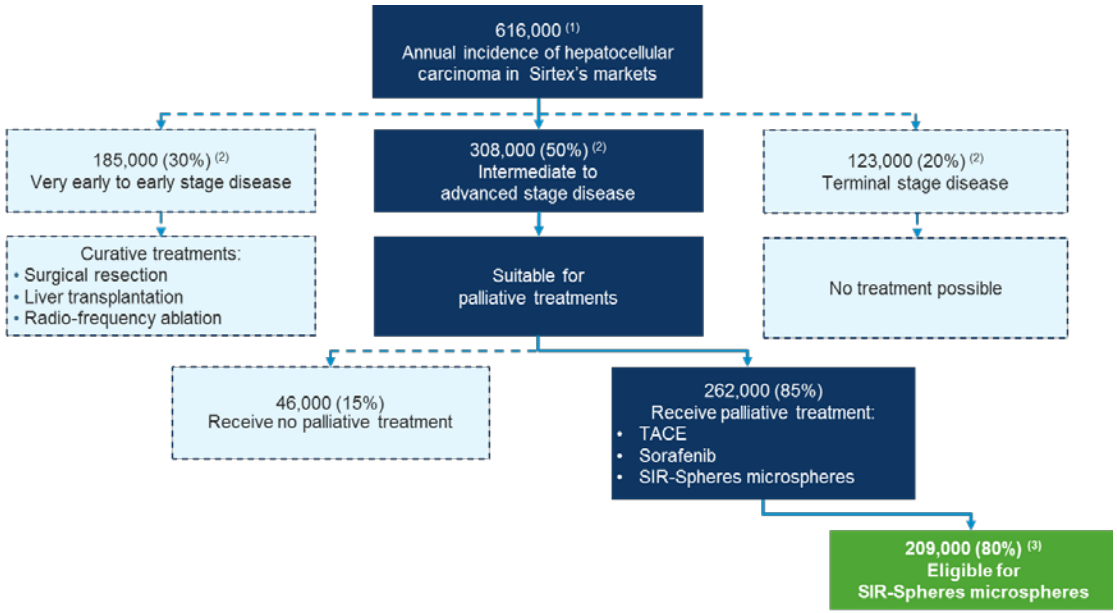
Thank you for your attention!

HCC: Commercial considerations

Mr Nigel Lange
Interim CEO

HCC: Commercial considerations

- The annual addressable market opportunity in HCC has been previously presented as **209,000** patients
- This market model is reasonable, until such time as the SARAH, SIR*ve*NIB, VESRPO and SORAMIC studies report findings



(1) Sirtex markets = APAC: Australia, China, Hong Kong, India, Japan, Malaysia, New Zealand, Philippines, Singapore, South Korea, Taiwan, Thailand. EMEA: Austria, Belgium, Egypt, Estonia, Finland, France, Germany, Greece, Israel, Italy, Poland, Portugal, South Africa, Spain, Sweden, Switzerland, The Netherlands, Turkey, United Kingdom. Americas: Argentina, Brazil, Canada, Mexico, USA.
(2) Llovet et. al. Design and endpoints of clinical trials in hepatocellular carcinoma. J Natl Cancer Inst 2008.
(3) Sirtex data and analysis.

Note the market models we will provide should be considered a guide and are based on incidence data and basic assumptions on use: they do not account for individual access to treatment via govt. or private insurance, age, extent of disease, or prevalence of disease in any one market. They provide an estimate of the addressable patient population only.

SARAH: Outcome scenarios

- SIR-Spheres microspheres is Superior to sorafenib
- SIR-Spheres microspheres is No Different to sorafenib
- SIR-Spheres microspheres is Inferior to sorafenib

SARAH: Priorities on superiority

Regulatory

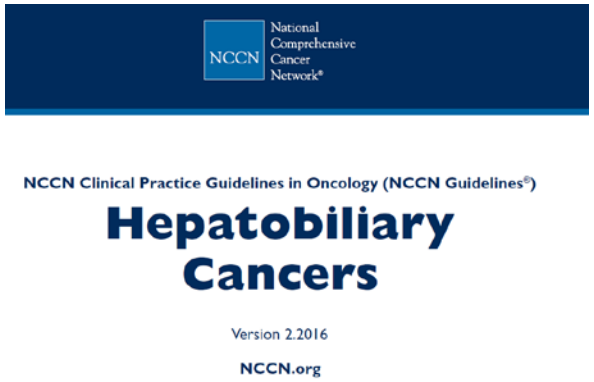
- Submit a Pre-Market Approval (PMA) Supplement to the US FDA to include an HCC claim on the current label (mCRC only) - 2H CY17, min.180 day review
- Submissible as a foreign clinical study that conforms with Declaration of Helsinki on ethical principles

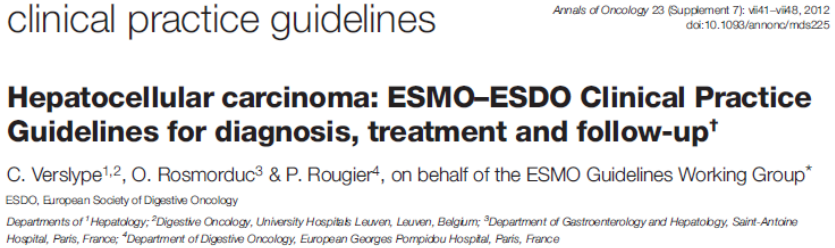
Update clinical practice guidelines

- NCCN, ESMO, BCLC, other

Guidance for Industry and FDA Staff

FDA Acceptance of Foreign Clinical Studies Not Conducted Under an IND Frequently Asked Questions



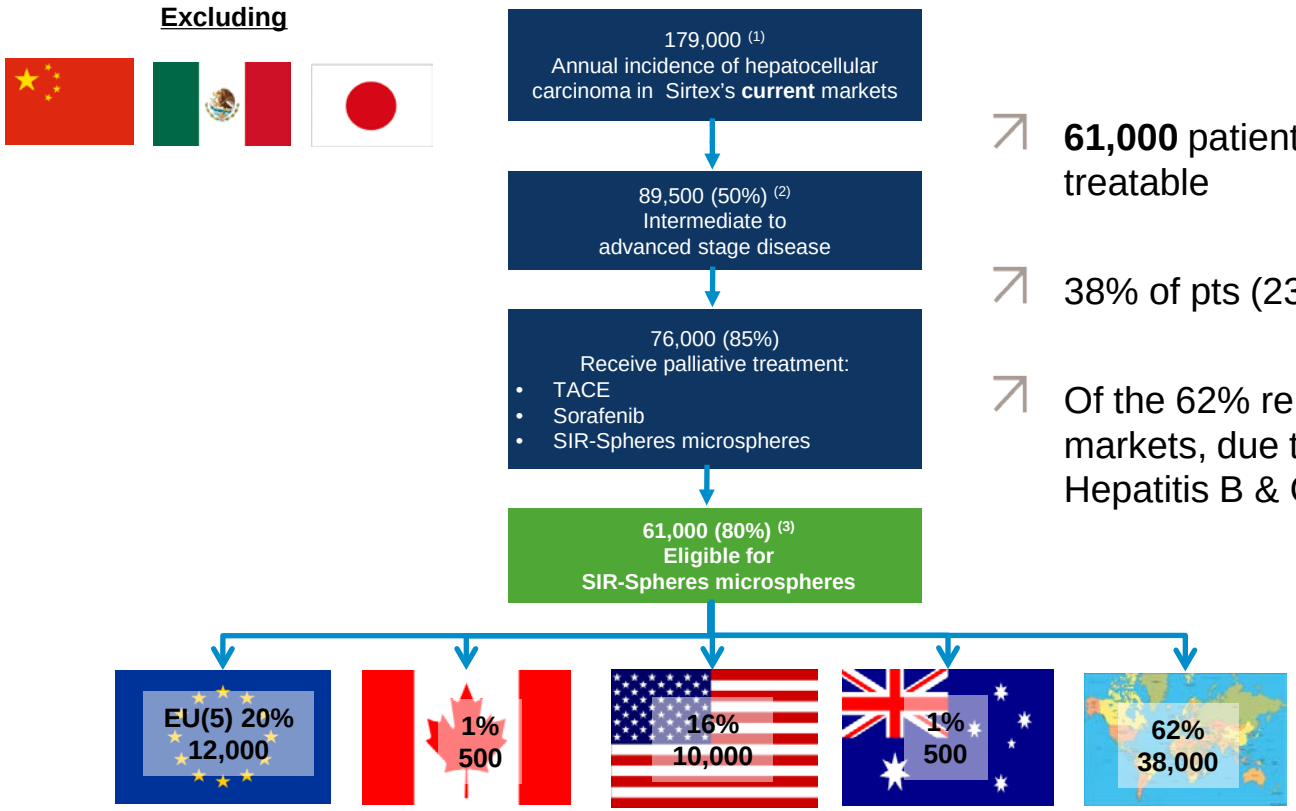


SIRTeX

SARAH: Priorities on superiority

- **Sales & Marketing**
  - Commence promotional activities across EMEA, Latin America, APAC
  - No marketing possible in the USA (until granted PMA Supplement) and Taiwan (mCRC only label)
  - Publication of study in leading peer-reviewed journal (<12 months)
- **Reimbursement and Market Access**
  - Commence discussions with private and government payers

SARAH: Market potential on superiority



- **61,000** patients (pts) per annum potentially treatable
- 38% of pts (23,000) within Sirtex's key markets
- Of the 62% remaining, majority reside in Asian markets, due to high infection rates of Hepatitis B & C

(1) Sirtex markets = APAC: Australia, Hong Kong, India, Malaysia, New Zealand, Philippines, Singapore, South Korea, Taiwan, Thailand. EMEA: Austria, Belgium, Egypt, Estonia, Finland, France, Germany, Greece, Israel, Italy, Poland, Portugal, South Africa, Spain, Sweden, Switzerland, The Netherlands, Turkey, United Kingdom. Americas: Argentina, Brazil, Canada, USA.
(2) Llovet et. al. Design and endpoints of clinical trials in hepatocellular carcinoma. J Natl Cancer Inst 2008.
(3) 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

SARAH: No difference / equivocal

- **If a similar Overall Survival benefit is observed between SIR-Spheres and sorafenib, several secondary endpoints are of interest**
  - Adverse events (i.e. safety and toxicity) – is SIR-Spheres better?
  - Quality of life - is SIR-Spheres better?
  - Health care costs – is SIR-Spheres more cost effective?
  - In the event that one or more favour SIR-Spheres, **there is still commercial value**
- **Sales & Marketing**
  - Commence promotional activities across EMEA, Canada, APAC based on similar OS benefit and potentially improved patient/payer benefits
  - No marketing possible in the USA (unless if granted PMA Supplement) and Taiwan (mCRC only label)

SARAH: Market potential on No difference / equivocal

Excluding

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

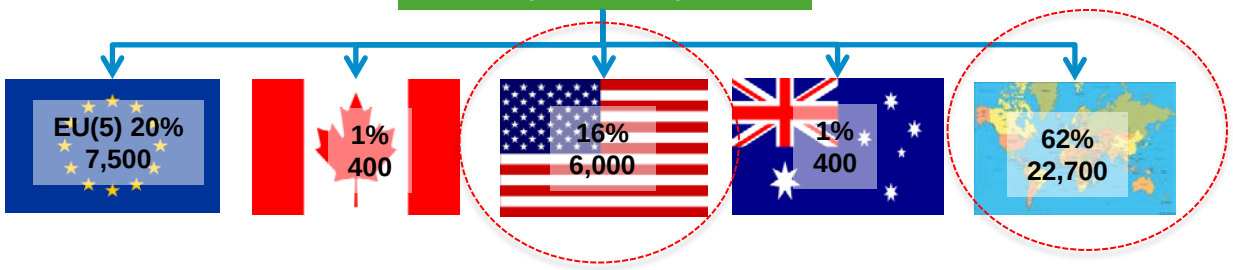
89,500 (50%) (2)
Intermediate to advanced stage disease

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



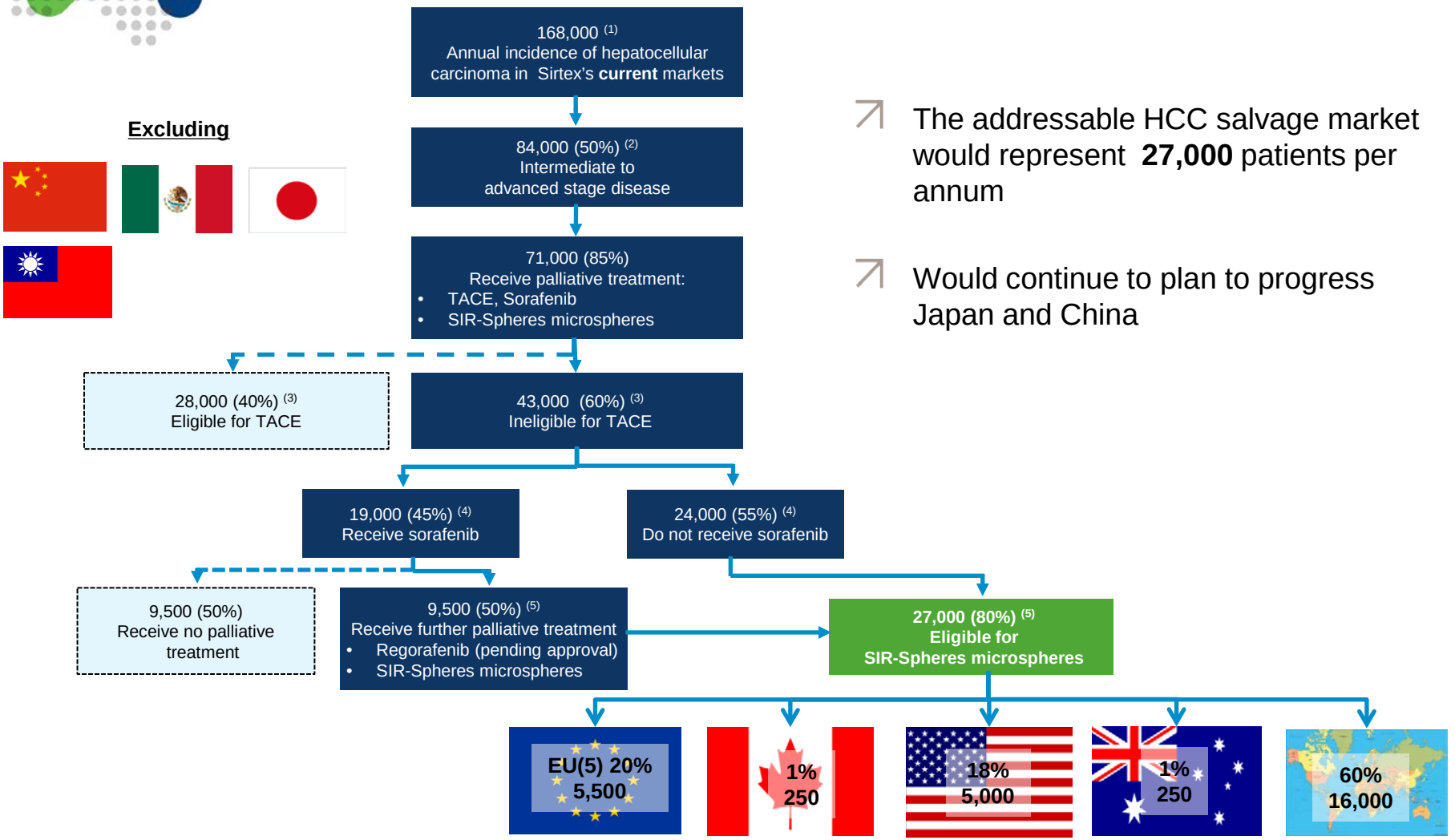
- Option for clinicians to switch sorafenib patients to SIR-Spheres
- USA depends on submissibility or otherwise of study data to FDA – VESPRO becomes important consideration
- EU(5) a near term significant opportunity due to funding restrictions on sorafenib
- Asian market potential contingent on SIR*ve*NIB and potentially VESPRO data

(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

SARAH: Inferiority

- **SIR-Spheres continues as ‘salvage’ therapy**
  - For patients who are unable to access sorafenib (cost, reimbursement)
  - For patients where the doctor preferences SIR-Spheres
  - For patients who are intolerant to sorafenib
  - For patients who progress on sorafenib and regorafenib (assuming approval)
- **SIR*ve*NIB, VESPRO & SORAMIC**
  - For Asian patients, utilisation of SIR-Spheres will be dependent on outcomes of SIR*ve*NIB study
  - VESPRO meta analysis will be useful in identifying if SIR-Spheres are Non-Inferior or if there is a benefit in sub-groups (more later)
  - SORAMIC results in 1H CY18 may show SIR-Spheres + sorafenib superior to sorafenib alone – strategies will be similar to ‘superiority’ scenario of SARAH

SARAH: Market potential on Inferiority

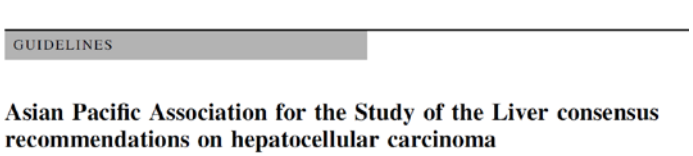


- The addressable HCC salvage market would represent **27,000** patients per annum
- Would continue to plan to progress Japan and China

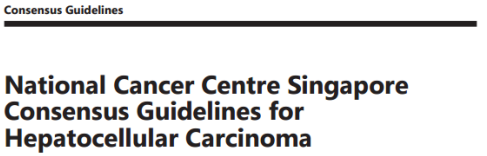
(1) Sirtex markets – see previous slides
(2) Llovet et. al. Design and endpoints of clinical trials in hepatocellular carcinoma. J Natl Cancer Inst 2008.
(3) Geschwind et. al. Use of Transarterial Chemoembolization (TACE) and Sorafenib in Patients with Unresectable Hepatocellular Carcinoma: US Regional Analysis of the GIDEON Registry. Liver Cancer 2016,
(4) GlobalData
(5) 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

SIR*ve*NIB

- Outcome scenarios identical to that of SARAH:
  - SIR-Spheres microspheres is **superior** to sorafenib
  - SIR-Spheres microspheres is **no different** to sorafenib
  - SIR-Spheres microspheres is **inferior** to sorafenib
- SIR*ve*NIB study data alone is not submissible to US FDA for a label change (PMA Supplement) in the event that SIR-Spheres is superior to sorafenib
- In general, the sales & marketing and treatment guideline strategies under these scenarios would also be similar to SARAH, albeit made in the context of the Asian region


GUIDELINES

Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma


Consensus Guidelines

National Cancer Centre Singapore Consensus Guidelines for Hepatocellular Carcinoma

- It is important to note that Asian clinicians are highly expert in use liver-directed therapies (TACE, RFA, SIRT) due to high incidence of HCC and the availability of sorafenib is limited (efficacy, cost, reimbursement)

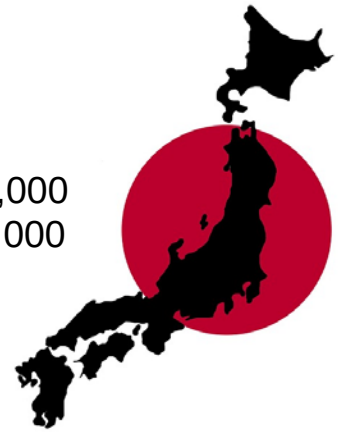
SIR*ve*NIB

- Secondary endpoints of note in the SIR*ve*NIB study, which may support SIR-Spheres use if primary endpoint not reached:
  - Safety and Toxicity
  - Health-related quality of life
  - Liver resection rate
  - Liver transplantation rate

Leverage any benefit(s) over sorafenib & lack of large RCTs (Level I Evidence) of Liver-Directed Therapies (TACE) for HCC in Asian populations

- Failure of the study does not impede our market expansion activities across Asia, nor does it impact on our plans to enter Japan and China

HCC incidence: 36,000
CRC incidence: 113,000



HCC incidence: 395,000
CRC incidence: 253,000

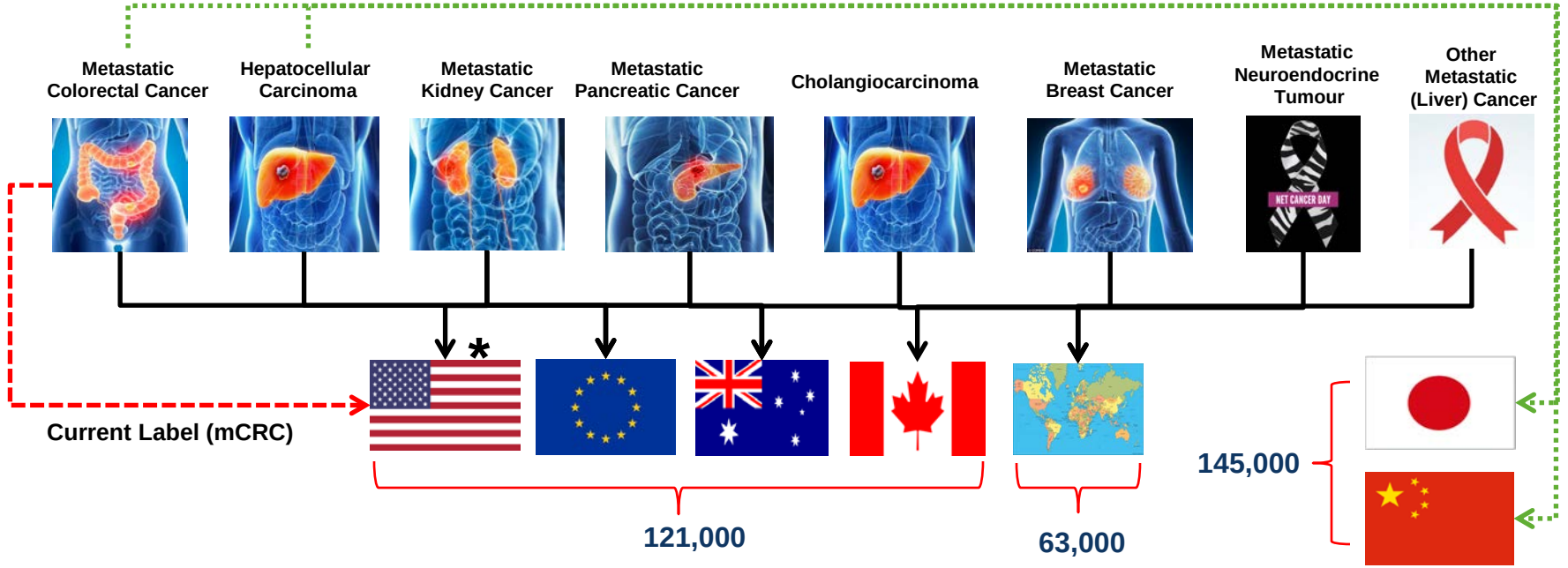
The Importance of VESPRO

- Prospective meta-analysis will allow for increased precision to estimate efficacy (survival) across 819 SARAH/SIR*ve*NIB patients
- Increased power to detect clinically important differences in sub-groups including those pre-treated with TACE, or invasion into portal vein (a contraindication for TACE)
- Articulates a methodology, in a prospective manner, to examine the pooled data for non-inferiority to sorafenib
  - May allow SIR-Spheres to compete on basis of better safety & toxicity, Quality of Life (QoL) or cost-effectiveness
- Positive data may support an additional label claim in the US based on superiority or non-inferiority or sub-group benefits

What is the opportunity in the event that all clinical studies are unsuccessful and no commercial value can be obtained?

- Salvage Only

Base Case (Salvage Only): total global opportunity



- Salvage opportunity presented as existing 'on-label' regulatory clearances, future expansion of indications (USA) and assumes mCRC/HCC for Japan/China
- **TOTAL** potential salvage opportunity in **existing** markets – **184,000 pts p.a.**

Note the market models Sirtex provides should be considered a guide and are based on incidence data and basic assumptions on use: they do not account for individual access to treatment via govt. or private insurance, age, extent of disease, or prevalence of disease in any one market. They provide an estimate of the addressable patient population only.

* Intended future label for USA would include multiple disease indications (currently only cleared for mCRC).
ROW = Sirtex markets: Malaysia, India, NZ, Philippines, Singapore, Sth Korea, Thailand, Turkey, Brazil, Argentina
Globocan http://globocan.iarc.fr/Pages/fact_sheets_population.aspx

Q&A

Concluding remarks

- Successful clinical studies have the capability to transform the business
- Significant growth opportunities exist within our base (salvage) business, in the event the clinical studies are unsuccessful
- Sirtex greatly appreciates Professor Sangro and Associate Professor Pavlakis taking time out of their busy schedules to present to investors today
- We look forward to updating investors as the clinical studies progressively report findings throughout the remainder of this CY and the 1H of CY18

Thank you

SIRTeX