# Selective Internal Radiation Therapy Using Y-90 Resin Microspheres vs Conventional Transarterial Chemoembolization in Barcelona Clinic Liver Cancer Stage B Hepatocellular Carcinoma: A Budget Impact Analysis in England

Pollock RF<sup>1</sup>, Agirrezabal I<sup>2</sup>, Carion PL<sup>2</sup>, Roe R<sup>3</sup>, Shergill S<sup>3</sup>, Ross PJ<sup>4</sup>

<sup>1</sup>Covalence Research Ltd, Harpenden, UK <sup>2</sup> Sirtex Medical Europe GmbH, Bonn, Germany <sup>3</sup> Sirtex Medical United Kingdom Ltd, London, UK <sup>4</sup> Guy's and St Thomas' NHS Foundation Trust, London, UK

### Introduction

### **Background**

Selective internal radiation therapy (SIRT) is a well-tolerated treatment for hepatocellular carcinoma (HCC) that has been investigated extensively in patients with Barcelona Clinic Liver Cancer (BCLC) stage B HCC.<sup>1</sup>

In 2021, the National Institute for Health and Care Excellence (NICE) recommended SIRT using Y-90 resin microspheres as an option for treating unresectable advanced HCC in adults with Child—Pugh grade A liver impairment when conventional transarterial therapies are inappropriate.<sup>2</sup> SIRT is also recommended by the European Society for Medical Oncology for the treatment of subsets of patients with HCC in BCLC stage B and C, such as those with absence of extra-hepatic disease, good liver function, and unsuitable for systemic therapy.<sup>1</sup>

Conventional transarterial chemoembolization (cTACE) involves the intra-arterial injection of a chemotherapeutic emulsion followed by embolization of the blood vessel with an embolic agent to achieve a cytotoxic effect enhanced by ischemia. While cTACE has been uniformly adopted in clinical practice, its therapeutic efficacy for HCC is still a matter of debate, with the Cochrane Group reporting an "absence of evidence of TACE having a beneficial effect on survival in participants with unresectable HCC".<sup>3</sup>

### **Objective**

The objective of the present analysis was to evaluate the budgetary implications of using SIRT with Y-90 resin microspheres (SIR-Spheres) versus cTACE in treating patients with BCLC B HCC from the perspective of the Department of Health and Social Care.

# Methods

# **Economic Model**

A budget impact model was developed in Microsoft Excel to capture costs of initial treatment, adverse events (AEs), and subsequent therapy lines. The model was structured as a Markov model with states corresponding to those in a traditional partitioned survival model (progression-free survival [PFS], post-progression survival [PPS], and death). The Markovian nature of the model facilitated derivation of transition probabilities from published arm-level data on the duration of progression-free survival and overall survival (OS) without needing access to patient-level time-to-event data.

### **Clinical Data**

All patients started in the progression-free state on the initial treatment (either SIRT or cTACE) and progressed to subsequent treatment lines based on derived transition probabilities. Transition probabilities were derived from published studies in HCC. For the first-line treatments, OS and PFS were based on the SARAH randomized controlled trial (RCT) and PFS and OS were assumed to be the same after initial treatment with SIRT and cTACE.<sup>4</sup> The model captured incidence of grade 3/4 adverse events with SIRT based on the SARAH RCT. The corresponding rates with TACE were then based on an overall odds ratio from a 2016 systematic review and meta-analysis comparing SIRT with TACE.<sup>5</sup>

**Table 1: Adverse event costs** 

Adverse event	Cost basis	Cost basis detail	Cost (GBP)
Infection	HRG	WH07X	1,484
Fever	HRG	WJ07X	1,088
Fatigue	PSSRU	GP nurse visit	846
Weight loss	PSSRU	Dietician visit	894
Alopecia	HRG	JD07K	359
Skin AEs (except alopecia)	HRG	JC40Z, JC41Z, JC42X, JC43C	649
Anorexia	PSSRU	Dietician visit	894
Diarrhoea	HRG	FD10X (ICD-10 K59.1)	1,723
Nausea and vomiting	HRG	FD10X (ICD-10 R11.X)	1,723
GI bleeding	HRG	FD03X	1,335
GI ulcer	HRG	FD10X (ICD-10 K25.9)	1,723
Abdominal pain	HRG	FD05X	494
Ascites	HRG	FF53X	787
Liver dysfunction	HRG	GC01X	2,119
Radiation pneumonitis	HRG	CA63Z	2,935
Hypertension	HRG	EB04Z	423
Cardiac failure, congestive	HRG	EB03X	4,275
Pulmonary embolism	HRG	YR23B	2,408
Hyperbilirubinaemia	Guide price	Medical Oncology Service	937
Other increased liver values	Guide price	Medical Oncology Service	937
Haematological biological abnormalities	HRG	SA04X	4,275
Renal dysfunction (increased creatinine)	HRG	LB37X	698
Hyponatraemia	HRG	KC05X	538
Haemorrhage (non- gastrointestinal)	HRG	EB14X	1,569

AEs, adverse events; GBP, pounds sterling; GI, gastrointestinal; HRG, healthcare resource group; ICD, International Classification of Disease; PSSRU, Personal Social Services Research Unit

### **Costs and Resource Use**

Costs of SIRT using Y-90 resin microspheres and cTACE were calculated from the DHSC perspective using healthcare resource group (HRG) tariff codes and costs from the National Tariff 2022/23. In the case of SIRT, the list price of SIR-Spheres Y-90 resin microspheres was obtained from the manufacturer (Sirtex Medical United Kingdom Ltd) and added to the HRG tariff costs. Costs of Grade 3/4 AEs were based on HRGs, guide prices for outpatient consultations from the National Tariff, and dietician or GP visits (Table 1).

Subsequent systemic and curative treatments (atezolizumab-bevacizumab, sorafenib, regorafenib, ablation, resection, and liver transplant) were captured based on expert opinion and costed based on the British National Formulary and appropriate HRG codes. Where weight-based dosing was required for systemic treatments, mean bodyweight was assumed to be 70 kg.

The number of SIRT and cTACE procedures received was based on a 2015 RCT comparing the two interventions and validated by expert opinion, specifically one SIRT procedure versus 3.4 cTACE procedures.<sup>7</sup>

Analyses were run both for SIRT with separate hospital spells for the SIRT work-up and the SIRT procedure, and for "same stay" SIRT using the Order-Map-Treat (OMT) Program, which requires only a single hospital admission.<sup>8</sup>

All analyses were conducted over a three-year time horizon and future costs were not discounted in line with budget impact modeling good practice guidance from the International Society of Pharmacoeconomic and Outcomes Research.<sup>9</sup>

### Results

### **UK Analysis of SIRT versus cTACE**

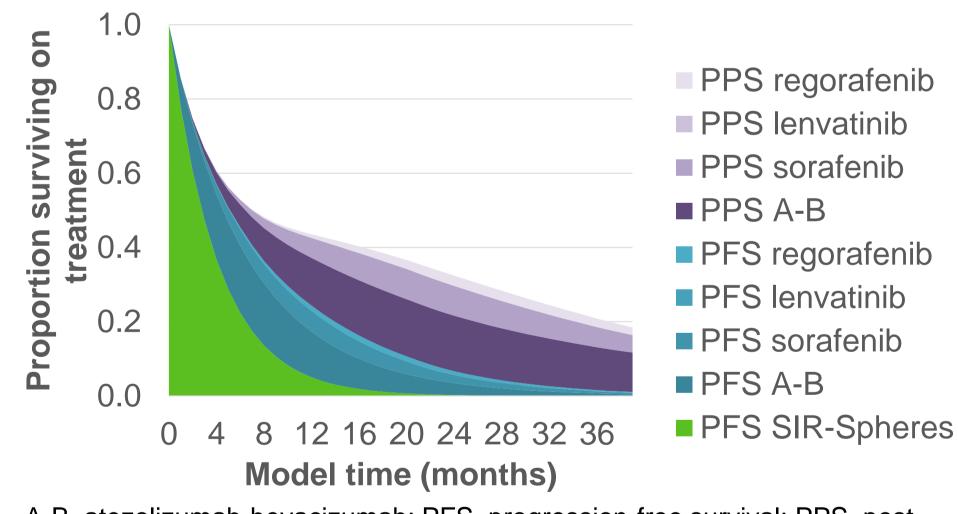
Relative to cTACE, SIRT with "same-stay" OMT resulted in cost savings of GBP 2,401 per patient over 3 years (GBP 34,892 versus GBP 37,293; Table 2), while SIRT in which the work-up was performed during a separate hospital spell was approximately cost neutral, saving GBP 57 versus cTACE (GBP 37,236 versus GBP 37,293; Table 2). The analysis was most sensitive to the number of SIRT and TACE procedures performed per-patient and assumptions around time to progression.

Table 2: Base case results in 2022 pounds sterling (GBP) broken down by cost category

	TACE	SIRT without OMT	Δ vs TACE	SIRT with OMT	Δ vs TACE
Work-up	674	2,344	+1,671	0	-674
Procedure	15,234	13,812	-1,422	13,812	-1,422
A-B	15,535	15,535	0	15,535	0
Sorafenib	3,357	3,357	0	3,357	0
Regorafenib	933	933	0	933	0
Ablation	38	38	0	38	0
Resection	106	106	0	106	0
Transplant and immunosuppression	399	399	0	399	0
Grade 3/4 AEs	1,017	712	-305	712	-305
Total	37,293	37,236	-57	34,892	-2,401

A-B, atezolizumab-bevacizumab; AEs, adverse events; OMT, Order-Map-Treat; TACE, transarterial chemoembolization; SIRT, selective internal radiation therapy.

Figure 1: Survival curves showing patient distribution across pre-progression and post-progression states by treatment line



A-B, atezolizumab-bevacizumab; PFS, progression-free survival; PPS, post-progression survival.

# Conclusions

Same-stay SIRT using SIR-Spheres Y-90 resin microspheres was found to be cost saving versus cTACE from the perspective of the DHSC in patients with HCC in BCLC B.

### References

- 1. Vogel A, Cervantes A, Chau I, et al. Hepatocellular carcinoma: ESMO Clinical Practice
- Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2018;29(Suppl 4):iv238-iv255.
  National Institute for Health and Care Excellence. Selective internal radiation therapies for treating hepatocellular carcinoma: technology appraisal guidance [TA688]. 2021. Available at: https://www.nice.org.uk/guidance/TA688.
- 3. Oliveri RS, Wetterslev J, Gluud C. Transarterial (chemo) embolisation for unresectable hepatocellular carcinoma. Cochrane Database Syst Rev. 2011; (3):Cd004787.
- 4. Vilgrain V, Pereira H, Assenat E, *et al.*; SARAH Trial Group. Efficacy and safety of selective internal radiotherapy with yttrium-90 resin microspheres compared with sorafenib in locally advanced and inoperable hepatocellular carcinoma (SARAH): an open-label randomised controlled phase 3 trial. Lancet Oncol. 2017;18(12):1624-1636.
- Facciorusso A, Serviddio G, Muscatiello N. Transarterial radioembolization vs chemoembolization for hepatocarcinoma patients: A systematic review and meta-analysis. World J Hepatol. 2016 28;8(18):770-8.
- 6. NHS England. National tariff payment system documents, annexes and supporting documents. Available from: https://www.england.nhs.uk/publication/national-tariff-payment-system-documents-annexes-and-supporting-documents/ Last accessed September 28, 2022.
- Kolligs FT, Bilbao JI, Jakobs T, et al. Pilot randomized trial of selective internal radiation therapy vs. chemoembolization in unresectable hepatocellular carcinoma. Liver Int. 2015;35(6):1715-21.
   Pollock RF, Shergill S, Carion PL, von Oppen N, Agirrezabal I, Brennan VK. Advances in
- Delivery of Selective Internal Radiation Therapy (SIRT): Economic and Logistical Effects of Same-Stay Work-Up and Procedure in the Treatment of Unresectable Liver Tumors in England. Adv Ther. 2022. Online publication ahead of print. DOI: 10.1007/s12325-022-02323-x
- Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysisprinciples of good practice: report of the ISPOR 2012 Budget Impact Analysis

Good Practice II Task Force. Value Health. 2014;17(1):5-14.

