Selective internal radiation therapies for unresectable early-, intermediate- or advanced-stage hepatocellular carcinoma: systematic review, network meta-analysis and economic evaluation

Matthew Walton,¹ Ros Wade,^{1*} Lindsay Claxton,¹ Sahar Sharif-Hurst,¹ Melissa Harden,¹ Jai Patel,² Ian Rowe,² Robert Hodgson¹ and Alison Eastwood¹

¹Centre for Reviews and Dissemination, University of York, York, UK ²Leeds Teaching Hospitals NHS Trust, Leeds, UK

Declared competing interests of authors: Jai Patel attended a product training course for using TheraSphere™ [BTG Ltd, London, UK (now Boston Scientific, Marlborough, MA, USA)] in Essen, Germany, in 2016, which was sponsored by Biocompatibles UK Ltd (Farnham, UK) [acquired by BTG Ltd], and is a member of the National Institute for Health and Care Excellence Medical Technologies Advisory Committee (June 2015 to present). Ian Rowe reports personal fees from AbbVie Inc. (North Chicago, IL, USA) and personal fees from Norgine BV (Amsterdam, the Netherlands), outside the submitted work.

Published September 2020

DOI: 10.3310/hta24480

Plain English summary

Selective internal radiotherapies for hepatocellular carcinoma Health Technology Assessment 2020; Vol. 24: No. 48

DOI: 10.3310/hta24480

NIHR Journals Library www.journalslibrary.nihr.ac.uk

^{*}Corresponding author ros.wade@york.ac.uk

Plain English summary

epatocellular carcinoma is the most common type of liver cancer. The choice of treatment depends on the extent of the cancer and liver function. Selective internal radiation therapies deliver radiation directly to liver tumours via tiny beads injected into the main blood vessel into the liver. There are three selective internal radiation therapies: TheraSphere™ [BTG Ltd, London, UK (now Boston Scientific, Marlborough, MA, USA)], SIR-Spheres® (Sirtex Medical Ltd, Woburn, MA, USA) and QuiremSpheres® (Quirem Medical BV, Deventer, the Netherlands).

Our aim was to assess the clinical effectiveness of selective internal radiation therapies for patients with hepatocellular carcinoma that is not treatable by surgery, and to assess whether or not these therapies represent good value for money.

There was no meaningful difference between SIR-Spheres and sorafenib (Nexavar®; Bayer plc, Leverkusen, Germany), which is a cancer drug for advanced hepatocellular carcinoma. Studies of other selective internal radiation therapies and studies in patients with less advanced disease were generally of poor quality, so their results may not be reliable. We could not assess whether or not selective internal radiation therapies are beneficial to patients with early- or intermediate-stage hepatocellular carcinoma, or whether or not TheraSphere and QuiremSpheres are beneficial.

Compared with sorafenib or lenvatinib (Kisplyx®; Eisai Ltd, Tokyo, Japan) (another systemic cancer drug), none of the selective internal radiation therapies were good value for money for treating patients with advanced hepatocellular carcinoma. We found that TheraSphere might be cheaper than SIR-Spheres and QuiremSpheres, but differences between TheraSphere and SIR-Spheres were small.

There was not enough evidence for patients with early or intermediate disease to say whether or not selective internal radiation therapy is good value for treating these patients. Future studies in these populations, alongside any studies comparing the selective internal radiation therapies against each other, would be helpful.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.370

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, the Cochrane Library and Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the Health Technology Assessment journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

This report

The research reported in this issue of the journal was commissioned and funded by the HTA programme on behalf of NICE as project number 17/109/19. The protocol was agreed in March 2019. The assessment report began editorial review in September 2019 and was accepted for publication in January 2020. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care.

© Queen's Printer and Controller of HMSO 2020. This work was produced by Walton et al. under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).

Editor-in-Chief of **Health Technology Assessment** and NIHR Journals Library

Professor Ken Stein Professor of Public Health, University of Exeter Medical School, UK

NIHR Journals Library Editors

Professor John Powell Chair of HTA and EME Editorial Board and Editor-in-Chief of HTA and EME journals. Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK, and Senior Clinical Researcher, Nuffield Department of Primary Care Health Sciences, University of Oxford, UK

Professor Andrée Le May Chair of NIHR Journals Library Editorial Group (HS&DR, PGfAR, PHR journals) and Editor-in-Chief of HS&DR, PGfAR, PHR journals

Professor Matthias Beck Professor of Management, Cork University Business School, Department of Management and Marketing, University College Cork, Ireland

Dr Tessa Crilly Director, Crystal Blue Consulting Ltd, UK

Dr Eugenia Cronin Senior Scientific Advisor, Wessex Institute, UK

Dr Peter Davidson Consultant Advisor, Wessex Institute, University of Southampton, UK

Ms Tara Lamont Senior Scientific Adviser (Evidence Use), Wessex Institute, University of Southampton, UK

Dr Catriona McDaid Senior Research Fellow, York Trials Unit, Department of Health Sciences, University of York, UK

Professor William McGuire Professor of Child Health, Hull York Medical School, University of York, UK

Professor Geoffrey Meads Professor of Wellbeing Research, University of Winchester, UK

Professor John Norrie Chair in Medical Statistics, University of Edinburgh, UK

Professor James Raftery Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

Dr Rob Riemsma Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

Professor Helen Roberts Professor of Child Health Research, UCL Great Ormond Street Institute of Child Health, UK

Professor Jonathan Ross Professor of Sexual Health and HIV, University Hospital Birmingham, UK

Professor Helen Snooks Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

Professor Ken Stein Professor of Public Health, University of Exeter Medical School, UK

Professor Jim Thornton Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

Professor Martin Underwood Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

Please visit the website for a list of editors: www.journalslibrary.nihr.ac.uk/about/editors

Editorial contact: journals.library@nihr.ac.uk