

TRAPEZE: a randomised controlled trial of the clinical effectiveness and cost-effectiveness of chemotherapy with zoledronic acid, strontium-89, or both, in men with bony metastatic castration-refractory prostate cancer

Nicholas James,^{1,2*} Sarah Pirrie,³ Ann Pope,³ Darren Barton,³ Lazaros Andronis,⁴ Ilias Goranitis,⁴ Stuart Collins,³ Duncan McLaren,⁵ Joe O'Sullivan,⁶ Chris Parker,⁷ Emilio Porfiri,¹ John Staffurth,^{8,9} Andrew Stanley,¹⁰ James Wylie,¹¹ Sharon Beesley,¹² Alison Birtle,¹³ Janet Brown,¹⁴ Prabir Chakraborti,¹⁵ Martin Russell¹⁶ and Lucinda Billingham³

¹Department of Oncology, University Hospital Birmingham NHS Foundation Trust, Birmingham, UK

²Cancer Research Unit, University of Warwick, Coventry, UK

³Cancer Research UK Clinical Trials Unit, University of Birmingham, Birmingham, UK

⁴Health Economics Unit, University of Birmingham, Birmingham, UK

⁵Edinburgh Cancer Centre, Western General Hospital, Edinburgh, UK

⁶Department of Oncology, Belfast City Hospital, Belfast, UK

⁷Department of Oncology, Royal Marsden Hospital, Sutton, UK

⁸Institute of Cancer and Genetics, Cardiff University, Cardiff, UK

⁹Velindre Cancer Centre, Cardiff, UK

¹⁰Pharmacy Department, City Hospital, Birmingham, UK

¹¹Department of Oncology, The Christie Hospital, Manchester, UK

¹²Kent Oncology Centre, Maidstone Hospital, Kent, UK

¹³Rosemere Cancer Centre, Royal Preston Hospital, Preston, UK

¹⁴Department of Oncology, St James' University Hospital, Leeds, UK

¹⁵Department of Oncology, Royal Derby Hospital, Derby, UK

¹⁶Beatson West of Scotland Cancer Centre, Glasgow, UK

*Corresponding author

Declared competing interests of authors: Professor James reports trial support (free trial drug for the Phase II part of the trial and a grant awarded to investigation sites for recruitment of Phase III patients with trial numbers 301–700) and lecturing fees from Sanofi-aventis. He also reports free trial drug for the Phase II part of the trial followed by a trial-linked discount for sites ordering trial drug for Phase III patients and lecturing fees from Novartis Pharmaceuticals UK Ltd. In addition, there was a trial-linked discount for sites ordering trial drug from GE Healthcare. Professor James also reports trial support, consultancy work and lecture fees from Sanofi-aventis and Novartis Pharmaceuticals UK Ltd who were directly related and consultancy work and lecture fees from Bayer HealthCare, Algeta, Amgen, Janssen, Astellas Pharma and Affinity OncoGeneX Pharmaceuticals Inc. who were related to prostate cancer but not the drugs in this study. Dr Pope reports trial support (free trial drug for the Phase II part of the trial and a grant awarded to investigation sites for recruitment of Phase III patients with trial numbers 301–700) from Sanofi-aventis; trial support (free trial drug for the Phase II part of the Phase III patients) from Novartis Pharmaceuticals UK Ltd; and trial support (trial-linked discount for sites ordering trial drug) from GE Healthcare from GP Health Care, during the conduct of the study. Dr Parker reports personal fees from Bayer HealthCare, BN ImmunoTherapeutics Inc. (BNIT), Astellas Pharma, Janssen, Sanofi-aventis and Takeda UK Ltd, outside the submitted work. Dr Stanley reports that Teva Pharmaceutical Industries Ltd supported his attendance at European Society for Medical Oncology, he received personal fees from Calgene, Inc., and Amgen, Inc. supported part of his attendance at British Oncology Pharmacy Association, outside the submitted work. Dr Brown reports personal fees and non-financial support from Novartis Pharmaceuticals UK Ltd for advisory board in different cancer and writing assistance for different cancer outside the submitted work. Dr Billingham reports personal fees from Eli Lilly, and from Pfizer, both for expenses paid for contributing to educational events, outside the submitted work.

Published July 2016

DOI: 10.3310/hta20530

Plain English summary

TRAPEZE: effectiveness of chemotherapy with ZA, Sr-89, or both

Health Technology Assessment 2016; Vol. 20: No. 53

DOI: 10.3310/hta20530

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

Plain English summary

TRAPEZE evaluated the use of two bone-targeting therapies, strontium-89 (Sr-89) and zoledronic acid (ZA), in men receiving docetaxel chemotherapy for relapsing prostate cancer involving the skeleton. Bony disease can cause pain, fractures and other serious complications. Docetaxel has been shown to increase survival and improve quality of life (QoL) in this setting. Intravenous ZA has been shown to reduce skeletal complications in prostate cancer, but is not recommended for general use because of doubts over its cost-effectiveness. Sr-89 is a radioactive drug taken up by bone cancer deposits and is recommended by the National Institute for Health and Care Excellence when chemotherapy is unsuitable.

TRAPEZE showed that adding Sr-89 to docetaxel delayed deterioration by around a month, but did not result in any improvement in overall survival. Adding ZA did not delay deterioration but did reduce subsequent serious bone complications by around one-third, with a 50% reduction in the most serious events such as fracture and spinal cord compression. QoL was well maintained. Both drugs increased treatment costs but decreased post-trial therapy costs because of delayed deterioration and, for ZA, decreased surgery and radiotherapy for bone complications.

Incremental costs per quality-adjusted life-year (QALY) for branded ZA and Sr-89 were calculated at £42,047 and £16,590, respectively. Sr-89 net acquisition was £1341 with modest gains in QoL and cost per QALY gained, a measure of the effectiveness of drug treatments. For ZA, net acquisition was £1319, but this cost was reduced to £251 by using the generic drug. The cost per QALY for the generic drug fell to £8005, making ZA both cost-effective and clinically effective as a therapy.

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.058

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI 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: nhredit@southampton.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

The HTA programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

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.

For more information about the HTA programme please visit the website: <http://www.nets.nihr.ac.uk/programmes/hta>

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 06/303/205. The contractual start date was in April 2007. The draft report began editorial review in December 2013 and was accepted for publication in October 2014. 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. 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.

© Queen's Printer and Controller of HMSO 2016. This work was produced by James *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. 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).

Health Technology Assessment Editor-in-Chief

Professor Hywel Williams Director, HTA Programme, UK and Foundation Professor and Co-Director of the Centre of Evidence-Based Dermatology, University of Nottingham, UK

NIHR Journals Library Editor-in-Chief

Professor Tom Walley Director, NIHR Evaluation, Trials and Studies and Director of the EME Programme, UK

NIHR Journals Library Editors

Professor Ken Stein Chair of HTA Editorial Board and Professor of Public Health, University of Exeter Medical School, UK

Professor Andree Le May Chair of NIHR Journals Library Editorial Group (EME, HS&DR, PGfAR, PHR journals)

Dr Martin Ashton-Key Consultant in Public Health Medicine/Consultant Advisor, NETSCC, UK

Professor Matthias Beck Chair in Public Sector Management and Subject Leader (Management Group), Queen's University Management School, Queen's University Belfast, UK

Professor Aileen Clarke Professor of Public Health and Health Services Research, Warwick Medical School, University of Warwick, UK

Dr Tessa Crilly Director, Crystal Blue Consulting Ltd, UK

Dr Eugenia Cronin Senior Scientific Advisor, Wessex Institute, UK

Ms Tara Lamont Scientific Advisor, NETSCC, UK

Professor Elaine McColl Director, Newcastle Clinical Trials Unit, Institute of Health and Society, Newcastle University, UK

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

Professor Geoffrey Meads Professor of Health Sciences Research, Health and Wellbeing Research and Development Group, University of Winchester, UK

Professor John Norrie Health Services Research Unit, University of Aberdeen, UK

Professor John Powell Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), 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 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 Jim Thornton Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

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

Please visit the website for a list of members of the NIHR Journals Library Board:
www.journalslibrary.nihr.ac.uk/about/editors

Editorial contact: nihredit@southampton.ac.uk