Clinical effectiveness and cost-effectiveness results from the randomised, Phase IIB trial in previously untreated patients with chronic lymphocytic leukaemia to compare fludarabine, cyclophosphamide and rituximab with fludarabine, cyclophosphamide, mitoxantrone and low-dose rituximab: the Attenuated dose Rituximab with ChemoTherapy In Chronic lymphocytic leukaemia (ARCTIC) trial

Dena R Howard,1 Talha Munir,2 Lucy McParland,1 Andy C Rawstron,3 Anna Chalmers,1 Walter M Gregory,1 John L O’Dwyer,4 Alison Smith,4 Roberta Longo,4 Abraham Varghese,2 Alexandra Smith1 and Peter Hillmen5*

1Clinical Trials Research Unit, Leeds Institute of Clinical Trials Research, University of Leeds, Leeds, UK
2Department of Haematology, St James’s University Hospital, Leeds, UK
3Haematological Malignancy Diagnostic Service, St James’s University Hospital, Leeds, UK
4Academic Unit of Health Economics, Leeds Institute of Health Sciences, University of Leeds, Leeds, UK
5Section of Experimental Haematology, Leeds Institute of Cancer and Pathology (LICAP), University of Leeds, Leeds, UK

*Corresponding author Peter.Hillmen@nhs.net

Declared competing interests of authors: Dr Rawstron reports personal fees from Roche, personal fees from Biogen Idec, personal fees from Gilead, personal fees from Abbvie, personal fees and non-financial support from BD Biosciences, personal fees from Celgene and personal fees from GlaxoSmithKline, outside the submitted work. Professor Gregory reports personal fees from Janssen and personal fees from Celgene, outside the submitted work. Professor Hillmen received research funding and speakers’ fees from Roche Pharmaceuticals and grants and personal fees from GlaxoSmithKline, outside the submitted work.

Published May 2017
DOI: 10.3310/hta21280
Plain English summary

Clinical effectiveness and cost-effectiveness results from ARCTIC trial
Health Technology Assessment 2017; Vol. 21: No. 28
DOI: 10.3310/hta21280

NIHR Journals Library www.journalslibrary.nihr.ac.uk
Plain English summary

What was the problem?

The first treatment that patients with chronic lymphocytic leukaemia (CLL) usually receive is a combination of the drugs fludarabine, cyclophosphamide and rituximab (Mabthera®, Roche Products Ltd) (FCR). However, research suggested that adding a fourth drug called mitoxantrone to FCR would improve response rates and that a lower dose of rituximab would work just as well as the standard dose.

What did we do?

We established the Attenuated dose Rituximab with ChemoTherapY In CLL trial to compare fludarabine, cyclophosphamide, mitoxantrone and low-dose rituximab (FCM-miniR) with the standard FCR treatment. The trial recruited 200 participants.

What did we find?

Three months after the end of treatment, participants were assessed to see how well they had responded. Part-way through the trial we looked at how half of the participants had responded and we found that participants who had received FCR had better response rates and fewer side effects than participants who had received FCM-miniR. The trial, therefore, closed early and participants who were still receiving FCM-miniR were offered the chance to have FCR instead.

Follow-up assessments are ongoing but, to date, disease progression and overall survival data are good for all participants compared with previous studies.

What does this mean?

The results of this trial show that FCR is a more effective treatment than FCM-miniR, and the addition of mitoxantrone to FCR increases side effects. FCR remains the best available therapy for CLL in patients who are considered fit for treatment with fludarabine.
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 07/01/38. The contractual start date was in January 2009. The draft report began editorial review in January 2015 and was accepted for publication in June 2015. 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 2017. This work was produced by Howard 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

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

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 Health Sciences Research, Health and Wellbeing Research Group, University of Winchester, UK

Professor John Norrie  Chair in Medical Statistics, University of Edinburgh, 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 Riemsmma  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: journals.library@nihr.ac.uk