Amisulpride for very late-onset schizophrenia-like psychosis: the ATLAS three-arm RCT

Robert Howard,1* Elizabeth Cort,1 Rosie Bradley,2 Emma Harper,3 Linda Kelly,3 Peter Bentham,4 Craig Ritchie,5 Suzanne Reeves,1 Waleed Fawzi,6 Gill Livingston,7 Andrew Sommerlad,7 Sabu Oomman,8 Ejaz Nazir,9 Ramin Nilforooshan,10 Robert Barber,11 Chris Fox,12 Ajay Macharouthu,13 Pranathi Ramachandra,14 Vivek Pattan,15 John Sykes,16 Valerie Curran,17 Cornelius Katona,7 Tom Dening,18 Martin Knapp,19 Renee Romeo20 and Richard Gray2 on behalf of the ATLAS Triallists Group

1Department of Old Age Psychiatry, King’s College London, London, UK
2Medical Research Council Population Health Research Unit, University of Oxford, Oxford, UK
3Nuffield Department of Population Health, University of Oxford, Oxford, UK
4Birmingham and Solihull Mental Health NHS Foundation Trust, Birmingham, UK
5West London Mental Health NHS Trust, Southall, UK
6East London NHS Foundation Trust, London, UK
7Division of Psychiatry, University College London, London, UK
8Cheshire and Wirral Partnership NHS Foundation Trust, Chester, UK
9South Staffordshire and Shropshire Healthcare NHS Foundation Trust, Stafford, UK
10Surrey and Borders Partnership NHS Foundation Trust, Leatherhead, UK
11Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, UK
12Norwich Medical School, University of East Anglia, Norwich, UK
13NHS Ayrshire & Arran, Ayr, UK
14Cambridgeshire and Peterborough NHS Foundation Trust, Cambridge, UK
15NHS Forth Valley, Stirling, UK
16Derbyshire Healthcare NHS Foundation Trust, Derby, UK
17Black Country Partnership NHS Foundation Trust, West Bromwich, UK
18Division of Psychiatry and Applied Psychology, University of Nottingham, Nottingham, UK
19Department of Health Policy, London School of Economics and Political Science, London, UK
20Health Service and Population Research Department, King’s College London, London, UK

*Corresponding author robert.howard@ucl.ac.uk
Declared competing interests of authors: Robert Howard reports membership of the Heath Technology Assessment (HTA) Commissioning Board. Peter Bentham reports grants from the HTA programme during the course of this study. Craig Ritchie reports grants and personal fees from Merck Sharp & Dohme Ltd (Kenilworth, NJ, USA), personal fees from Pfizer Inc. (New York City, NY, USA), Eisai Co. Ltd (Tokyo, Japan), Actinogen (Sydney, NSW, Australia), Kyowa Hakko Kirin (Tokyo, Japan), Eli Lilly and Company (Indianapolis, IN, USA), and F. Hoffmann-La Roche AG (Basel, Switzerland), grants from Biogen Inc. (Cambridge, MA, USA) and grants and non-financial support from Janssen EMEA (Beerse, Belgium) and Takeda Pharmaceutical Company Ltd (Osaka, Japan) during the conduct of the study. Craig Ritchie was also the co-coordinator and academic lead for the European Prevention of Alzheimer’s Dementia (EPAD) project, which has numerous commercial partners in keeping with the mechanisms of the European Union’s Innovative Medicine’s Initiative [i.e. Janssen, Eisai Co. Ltd, Pfizer, Eli Lilly and Company, Roche Diagnostics (Risch-Rotkreuz, Switzerland), Boehringer Ingelheim GmbH (Ingelheim am Rhein, Germany), Novartis International AG (Basel, Switzerland), AC Immune SA (Lausanne, Switzerland), IXICO (London, UK), Aridhia (Glasgow, UK), Amgen Inc. (Thousand Oaks, CA, USA), Berry Consultants (Abingdon, UK), H. Lundbeck A/S (Copenhagen, Denmark), Sanofi SA (Paris, France), IQVIA (formerly Quintiles IMS Holdings, Inc.) (Durham, NC, USA) and Takeda Pharmaceutical Company]. Andrew Sommerlad reports grants from the Wellcome Trust outside the submitted work. Ramin Nilforooshan reports personal fees from Eli Lilly and Company and non-financial support from Janssen outside the submitted work. Martin Knapp reports grants from Merck Sharp & Dohme outside the submitted work.

Published November 2018
DOI: 10.3310/hta22670

Plain English summary

The ATLAS three-arm RCT
Health Technology Assessment 2018; Vol. 22: No. 67
DOI: 10.3310/hta22670

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

Some people develop serious mental health illness resembling schizophrenia for the first time after the age of 60 years, which is called very late-onset schizophrenia-like psychosis (VLOSLP). This is characterised by false beliefs or delusions that other people are trying to harm or steal from them. VLOSLP can be extremely frightening and distressing. It can cause sufferers to break off contact with friends and family, thus becoming isolated.

Effective drug and psychological treatments are already available for schizophrenia. However, there have been no randomised clinical trials of antipsychotic treatment in older patients, who are often not prescribed antipsychotics because of a lack of effectiveness evidence and clinician anxieties about risks.

The study investigated the safety and effectiveness of treating VLOSLP patients with ≤ 24 weeks of low-dose amisulpride (an antipsychotic drug, used to treat schizophrenia) compared with an inactive placebo tablet.

The study found that amisulpride treatment was associated with significantly greater improvement in mental health symptoms than was seen with placebo. Patients receiving amisulpride showed improvements on measures of hostility, suspiciousness, hallucinations, tension, lack of co-operation and overactivity. These improvements did not lead to improvements in patients’ self-rated quality of life, but this could reflect lack of sensitivity of the quality-of-life measure in this group. More participants who were taking placebo were withdrawn from the trial by their doctors because their psychosis symptoms were not responding or got worse.

The most common and troubling side effects of antipsychotics resemble Parkinson’s disease, with slowness, muscle stiffness and shaking (older people being particularly susceptible). The study monitored these symptoms in the participants. There was a small increase in these symptoms in the amisulpride group compared with the placebo group; 11% of people taking amisulpride had clinically significant movement problems compared with 0% of people taking placebo.

The results indicate that patients with VLOSLP benefit from treatment with a low-dose antipsychotic, such as amisulpride, and that this treatment is generally well tolerated. We hope that mental health teams and general practitioners providing care to these patients are encouraged to offer them antipsychotic treatment in the light of our findings.
Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the 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

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 09/55/06. The contractual start date was in October 2011. The draft report began editorial review in November 2017 and was accepted for publication in May 2018. 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 2018. This work was produced by Howard 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).
NIHR Journals Library Editor-in-Chief

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

NIHR Journals Library Editors

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

Professor Andrée Le May  Chair of NIHR Journals Library Editorial Group (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  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 Wellbeing Research, 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 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 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