Parent-determined oral montelukast therapy for preschool wheeze with stratification for arachidonate 5-lipoxygenase (*ALOX5*) promoter genotype: a multicentre, randomised, placebo-controlled trial

Chinedu Nwokoro, 1* Hitesh Pandya, 2 Stephen Turner, 3 Sandra Eldridge, 1 Christopher J Griffiths, 1 Tom Vulliamy, 1 David Price, 3 Marek Sanak, 4 John W Holloway, 5 Rossa Brugha, 1 Lee Koh, 1 Iain Dickson, 1 Clare Rutterford 1 and Jonathan Grigg 1

- ¹Asthma UK Centre for Applied Research, Blizard Institute, Queen Mary University of London, London, UK
- ²Department of Infection, Immunity and Inflammation, University of Leicester, Leicester, UK
- ³Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK ⁴Department of Medicine, Jagiellonian University Medical School, Krakow, Poland
- ⁵Human Development and Health, University of Southampton, Southampton General Hospital, Southampton, UK

Declared competing interests of authors: Jonathan Grigg received personal fees for Advisory Board membership for new asthma treatments in children from GlaxoSmithKline, Boehringer Ingelheim and Novartis Pharmaceuticals while the study was being done. David Price has received fees paid to Research in Real Life Ltd (RIRL) for Board membership from Aerocrine, Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Mundipharma International Ltd, Napp, Novartis Pharmaceuticals and Teva; for consultancy fees from Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Meda, Mundipharma International Ltd, Napp, Novartis Pharmaceuticals, Nycomed, Pfizer and Teva; for grants (received or pending) from Aerocrine, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Meda, Merck Sharp & Dohme Ltd, Mundipharma International Ltd, Novartis Pharmaceuticals, Nycomed, Orion, Pfizer, Takeda, Teva and Zentiva; for lecture and speaking engagements from Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Kyorin, Meda, Merck Sharp & Dohme Ltd, Mundipharma International Ltd, Novartis Pharmaceuticals, Pfizer, SkyePharma, Takeda and Teva; for manuscript preparation from Mundipharma International Ltd and Teva; for travel, accommodation and meeting expenses from Aerocrine, Boehringer Ingelheim, Mundipharma International Ltd, Napp, Novartis Pharmaceuticals and Teva; for patient enrolment or completion of research from Almirall, Chiesi, Teva and Zentiva; for contract research from Aerocrine, AKL Research and Development Ltd, Almirall, Boehringer Ingelheim, Chiesi, Meda, Mundipharma International Ltd, Napp, Novartis Pharmaceuticals, Orion, Takeda

^{*}Corresponding author

and Zentiva; has an AKL Research and Development Ltd patent pending; and has shares in AKL Research and Development Ltd, which produces phytopharmaceuticals and owns 80% of RIRL and its subsidiary social enterprise, Optimum Patient Care.

Published November 2015

DOI: 10.3310/eme02060

Plain English summary

Oral montelukast therapy for preschool wheeze

Efficacy and Mechanism Evaluation 2015; Vol. 2: No. 6

DOI: 10.3310/eme02060

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

Plain English summary

Background

Young children who wheeze can become very ill and may require large amounts of care from their families, doctors and nurses. No treatment has been shown to work very well for these children. Montelukast is an established medicine that is safe and easy to give to children.

What did we want to find out?

We wanted to see if montelukast might help in this group of children. We wanted to see whether or not children with slightly different genes might do better with montelukast than others.

What did we do?

We ran a research study comparing montelukast with a dummy medicine (referred to as placebo). We gave parents a box of medicine but did not tell them whether it was montelukast or placebo. We asked them to start giving it to their child as soon as a cold or wheezing episode began and to continue it for 10 days. We measured the number of times children needed to see a doctor or nurse in an unplanned way over the following year.

What did we find?

Montelukast did not seem to help young wheezing children any more than placebo did. It might have worked better in children with slightly different genes but we could not be certain from this study.

What does this mean?

Montelukast does not seem to be helpful for all young children who wheeze. We need to do another study to see if it really does work better in the group of children with slightly different genes.

Efficacy and Mechanism Evaluation

ISSN 2050-4365 (Print)

ISSN 2050-4373 (Online)

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

Editorial contact: nihredit@southampton.ac.uk

The full EME archive is freely available to view online at www.journalslibrary.nihr.ac.uk/eme. 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 Efficacy and Mechanism Evaluation journal

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

EME programme

The Efficacy and Mechanism Evaluation (EME) programme was set up in 2008 as part of the National Institute for Health Research (NIHR) and the Medical Research Council (MRC) coordinated strategy for clinical trials. The EME programme is broadly aimed at supporting 'science driven' studies with an expectation of substantial health gain and aims to support excellent clinical science with an ultimate view to improving health or patient care.

Its remit includes evaluations of new treatments, including therapeutics (small molecule and biologic), psychological interventions, public health, diagnostics and medical devices. Treatments or interventions intended to prevent disease are also included.

The EME programme supports laboratory based or similar studies that are embedded within the main study if relevant to the remit of the EME programme. Studies that use validated surrogate markers as indicators of health outcome are also considered.

For more information about the EME programme please visit the website: http://www.nets.nihr.ac.uk/programmes/eme

This report

The research reported in this issue of the journal was funded by the EME programme as project number 08/43/03. The contractual start date was in November 2009. The final 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 EME editors and production house have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research. 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, the MRC, NETSCC, the EME 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 EME programme or the Department of Health.

© Queen's Printer and Controller of HMSO 2015. This work was produced by Nwokoro 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).

Efficacy and Mechanism Evaluation Editor-in-Chief

Professor Raj Thakker May Professor of Medicine, Nuffield Department of Medicine, University of Oxford, UK

NIHR Journals Library Editor-in-Chief

Professor Tom Walley Director, NIHR Evaluation, Trials and Studies and Director of the HTA 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 Peter Davidson Director of NETSCC, HTA, 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 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

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