A randomised placebo-controlled trial investigating efficacy and mechanisms of low-dose intradermal allergen immunotherapy in treatment of seasonal allergic rhinitis

Anna Slovick,1,2 Abdel Douiri,3 Rachel Muir,4 Andrea Guerra,1 Konstantinos Tsioulos,1 Evie Haye,1 Emily PS Lam,1 Joanna Kelly,5 Janet L Peacock,3 Sun Ying,1 Mohamed H Shamji,6 David J Cousins,1,2,7 Stephen R Durham6 and Stephen J Till1,2*

1Division of Asthma, Allergy and Lung Biology, King's College London, School of Medicine, Guy's Hospital, London, UK
2Medical Research Council (MRC)–Asthma UK Centre for Allergic Mechanisms of Asthma, London, UK
3Division of Health and Social Care Research, King’s College London, London, UK
4Clinical Research Facility, NIHR Biomedical Research Centre, Guy's Hospital, London, UK
5King’s Clinical Trials Unit, King’s College London, Institute of Psychiatry, London, UK
6Allergy and Clinical Immunology, National Heart and Lung Institute, Faculty of Medicine, Imperial College, London, UK
7Department of Infection, Immunity and Inflammation, National Institute for Health Research (NIHR) Leicester Respiratory Biomedical Research Unit, Leicester Institute for Lung Health, University of Leicester, Leicester, UK

*Corresponding author

Declared competing interests of authors: Stephen J Till reports personal fees and grants from ALK Abelló, and personal fees from Thermofisher Scientific, outside the submitted work. Mohamed H Shamji reports grants from BioTech Tools and Regeneron USA, outside the submitted work. David J Cousins reports grants from GlaxoSmithKline, Asthma UK, and the Medical Research Council, outside the submitted work. Stephen R Durham reports grants from ALK Abelló, grants and personal fees from Merck, grants from Regeneron USA, personal fees from Biomay Austria and personal fees from Circassia UK, outside the submitted work; in addition, Stephen R Durham has a patent pending. Emily Lam is a Health Technology Assessment Primary Care, Community and Preventive Interventions panel member.

Published December 2016
DOI: 10.3310/eme03100
Plain English summary

Trial of immunotherapy for treatment of seasonal allergies
Efficacy and Mechanism Evaluation 2016; Vol. 3: No. 10
DOI: 10.3310/eme03100

NIHR Journals Library www.journalslibrary.nihr.ac.uk
Several million people in the UK have hay fever, which significantly affects their quality of life. In such people, an allergy vaccine (called ‘immunotherapy’) may reduce the allergic response to grass pollen. Although current vaccines are effective, they are expensive and involve frequent visits to specialist clinics for injections or daily self-dosing with tablets or drops for several years.

Based on encouraging results from a pilot study, we undertook a clinical trial of a potentially new and very different form of grass pollen immunotherapy. The new approach involved giving very small grass pollen doses (thousands of times less than existing methods) by injections directly into the topmost skin layer (called the dermis). We recruited 93 participants, who were randomly selected to receive seven such injections every 2 weeks before the 2013 summer grass pollen season, or seven dummy injections. The severity of hay fever symptoms and usage of allergy medications was then recorded. We also performed experiments to see the effect of the new vaccine on the immune system.

The results of the study conclusively showed that the new approach had no benefit in reducing hay fever symptoms or need for medications. Unexpectedly, symptoms in the nose were actually modestly worse in those who had the grass pollen injections. Our experiments also indicated a small stimulation effect on the immune system.

These results have implications for other future research in this area, and also make an important scientific contribution to our understanding of the mechanisms that can drive allergies.
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 11/20/05. The contractual start date was in September 2012. The final report began editorial review in September 2015 and was accepted for publication in March 2016. 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 2016. This work was produced by Slovick 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 David Crossman  Bute Professor of Medicine and Dean and Head of Faculty of Medicine, University of St Andrews, and Honorary Consultant Cardiologist, NHS Fife Health Board, 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 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 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