A randomised, double-blind, parallel-group trial to assess mercaptopurine versus placebo to prevent or delay recurrence of Crohn’s disease following surgical resection (TOPPIC)

Jack Satsangi,1* Nicholas A Kennedy,1,2,3 Craig Mowat,4 Ian Arnott,5 Catriona Keerie,6 Steff Lewis6 and Holly Ennis6 on behalf of the TOPPIC Collaborators Group

1Gastrointestinal Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, UK
2Department of Gastroenterology, Royal Devon and Exeter Hospital, Exeter, UK
3School of Medicine, University of Exeter, Exeter, UK
4Gastrointestinal Unit, Ninewells Hospital, Dundee, UK
5Gastrointestinal Unit, Western General Hospital, Edinburgh, UK
6Edinburgh Clinical Trials Unit, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK

*Corresponding author J.Satsangi@ed.ac.uk

Declared competing interests of authors: Jack Satsangi reports personal fees from Takeda Pharmaceutical Company Ltd, AbbVie Inc. and Dr Falk Pharma UK Ltd, and research funding from the European Commission. Nicholas A Kennedy reports grants from The Wellcome Trust; personal fees from Merck & Co., Inc., Takeda Pharmaceutical Company Ltd, Dr Falk Pharma UK Ltd, Allergan, plc, and Pharmacosmos A/S; non-financial support from Norgine BV, AbbVie Inc., Shire, plc, and Janssen Global Services, LLC; and other support from Merck & Co., Inc., AbbVie Inc. and Takeda Pharmaceutical Company Ltd outside the submitted work. Ian Arnott reports personal fees from Vifor Pharma Management Ltd, Takeda Pharmaceutical Company Ltd and Dr Falk Pharma UK Ltd. Steff Lewis reports membership of the Health Technology Assessment Efficient Study Designs Board and University of Edinburgh grant funding.

Published September 2017
DOI: 10.3310/eme04040

Plain English summary

The TOPPIC RCT
Efficacy and Mechanism Evaluation 2017; Vol. 4: No. 4
DOI: 10.3310/eme04040

NIHR Journals Library www.journalslibrary.nihr.ac.uk
Crohn’s disease (CD) is a serious disease causing a swelling and ulceration of the gut wall. Most patients are treated with medicines but, after 10 years, two out of three people with CD need an operation. CD can often come back after an operation, and almost half of those who have one will need another one.

Several medicines have been tested to see if they help stop CD coming back after an operation. Azathioprine and mercaptopurine (MP) are medicines called thiopurines that alter the way that the immune system works. Over the last 10 years, they have become widely used for CD when it is not easily treated with other medicines but is not serious enough to need an operation. They have also been tested to see if they can stop CD coming back after an operation, but previous studies were relatively small and did not look at all relevant measures, so there was a need for a large modern study to look at the role of thiopurines again.

The Trial Of Prevention of Post operative Crohn’s disease (TOPPIC) was a double-blind, randomised controlled trial done to find out whether the use of MP after an operation can prevent or delay CD coming back. Following informed consent, 240 patients were recruited into the study between 2007 and 2012 and randomly got either a daily dose of MP or matching placebo for 36 months. Data and samples were collected regularly during the study.

Mercaptopurine reduced how often CD came back after an operation only in smokers, who were also the people most at risk of recurrence.
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 09/800/04. The contractual start date was in October 2007. The final report began editorial review in February 2016 and was accepted for publication in March 2017. 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 2017. This work was produced by Satsangi 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 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)

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 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 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