# Early switch from intravenous to oral antibiotic therapy in patients with cancer who have low-risk neutropenic sepsis: the EASI-SWITCH RCT

Vicky Coyle,<sup>1\*</sup> Caroline Forde,<sup>1</sup> Richard Adams,<sup>2</sup> Ashley Agus,<sup>3</sup> Rosemary Barnes,<sup>4</sup> Ian Chau,<sup>5</sup> Mike Clarke,<sup>6</sup> Annmarie Doran,<sup>3</sup> Margaret Grayson,<sup>7</sup> Danny McAuley,<sup>8</sup> Cliona McDowell,<sup>3</sup> Glenn Phair,<sup>3</sup> Ruth Plummer,<sup>9</sup> Dawn Storey,<sup>10</sup> Anne Thomas,<sup>11</sup> Richard Wilson<sup>12</sup> and Ronan McMullan<sup>8</sup>

## **Disclosure of interests**

**Full disclosure of interests:** Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/RGTP7112.

Primary conflicts of interest: Vicky Coyle reports a Cancer Research UK Doctoral Fellowship research grant that part-supported this submitted work. She also reports research grants from Cancer Research UK and Astex Pharmaceuticals (UK) as well as personal fees and non-financial support from Servier Laboratories (France) for attending educational meetings, all unrelated to the submitted work. Richard Adams reports research grants from AstraZeneca PLC (UK) and Merck Sharp & Dohme Ltd (MSD, UK) as well as personal fees from Bayer Healthcare Pharmaceuticals LLC (Germany), Amgen Inc. (USA) and Servier Laboratories and non-financial support for attending meetings from Amgen Inc., Servier Laboratories and Merck Serono (Switzerland), all unrelated to the submitted work. Ashley Agus reports membership of the NIHR HTA Programme General Funding Committee. Ian Chau reports grants or

<sup>&</sup>lt;sup>1</sup>Patrick G Johnston Centre for Cancer Research, Queen's University Belfast, Belfast, UK

<sup>&</sup>lt;sup>2</sup>Centre for Trials Research - Cancer Division, Cardiff University, Cardiff, UK

<sup>&</sup>lt;sup>3</sup>Northern Ireland Clinical Trials Unit, Belfast Health and Social Care Trust, Belfast, UK

<sup>&</sup>lt;sup>4</sup>School of Medicine, Cardiff University, Cardiff, UK

<sup>&</sup>lt;sup>5</sup>Department of Medicine, Royal Marsden Hospital, Surrey, UK

<sup>&</sup>lt;sup>6</sup>Centre for Public Health, Queens University Belfast, Belfast, UK

<sup>&</sup>lt;sup>7</sup>Northern Ireland Cancer Research Consumer Forum, Belfast Health and Social Care Trust, Belfast, UK

<sup>&</sup>lt;sup>8</sup>Wellcome-Wolfson Institute for Experimental Medicine, Queens University Belfast, Belfast, UK

<sup>&</sup>lt;sup>9</sup>Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK

<sup>&</sup>lt;sup>10</sup>The Beatson West of Scotland Cancer Centre, Gartnavel General Hospital, Glasgow, UK

<sup>&</sup>lt;sup>11</sup>Leicester Cancer Research Centre, University of Leicester, Leicester, UK

<sup>&</sup>lt;sup>12</sup>Institute of Cancer Sciences, University of Glasgow, Glasgow, UK

<sup>\*</sup>Corresponding author v.coyle@qub.ac.uk

contracts from Janssen-Cilag and Eli Lilly and Company. He also reports personal fees from Eli Lilly and Company (USA), AstraZeneca PLC, MSD, Merck Serono, Bristol Meyers Squibb Inc. (USA), Bayer Healthcare Pharmaceuticals LLC, Roche AG (Switzerland), OncXerna (China), Pierre Fabre Pharmaceuticals Inc. (France), Boehringer Ingelheim (Germany), Incyte Inc. (USA), Astellas Pharma (Japan), GlaxoSmithKline Ltd (UK), SOTIO (Czech Republic), Eisai (Japan), Five Prime Therapeutics, Inc. (USA), Symphogen (Denmark) and Servier Laboratories. Mike Clarke reports membership of the NIHR CRSU Funding Board, NIHR HTA Funding Teleconference Members, NIRH HTA Prioritisation Committee B Methods Group and NIHR HTA General Committee. Daniel McAuley reports research grants from NIHR, Innovate UK, Medical Research Council (MRC), Novavax Inc. (USA), the Northern Ireland HSC R&D Division, and the Wellcome Trust as well as personal fees from Bayer Healthcare Pharmaceuticals LLC, GlaxoSmithKline Ltd (UK), Boehringer Ingelheim (Germany), Novartis AG (Switzerland) and Eli Lilly and Company (USA); he also reports non-financial support for attending meetings from Vir Biotechnology Inc. (USA) and Faron Pharmaceuticals (Finland). He also reports spousal personal fees from Insmed, Inc. and the California Institute for Regenerative Medicine. Apart from NIHR funding for this trial, all others listed are unrelated to the submitted work. He is co-director of research for the Intensive Care Society (UK) and Programme Director of the NIHR/MRC Efficacy & Mechanisms Evaluation (EME) Programme. He also reports membership of the EME Strategy Advisory Committee, the EME Funding Committee, the EME Funding Committee Sub-Group: Remit and Competitiveness and former membership of the NIHR/UKRI COVID-19 reviewing committee and the HTA General Committee and Commissioning Committees. Ronan McMullan reports research grants from the NIHR HTA Programme, NIHR EME Programme, Wellcome Trust, NI Chest, Heart & Stroke Association and Randox Laboratories Ltd (UK), as well as personal fees and non-financial support for attending meetings from Gilead Sciences Europe Ltd (UK), all unrelated to the submitted work. He is also a member of the NIHR HTA Programme Prioritisation Committee B. Ruth Plummer reports membership of the NIHR EME Funding Committee. Caroline Forde, Rosemary Barnes, Annmarie Doran, Margaret Grayson, Cliona McDowell, Glenn Phair, Dawn Storey, Anne Thomas and Richard Wilson report no competing interests.

Published March 2024 DOI: 10.3310/RGTP7112

# Plain language summary

Early switch from intravenous to oral antibiotic therapy in patients with cancer who have low-risk neutropenic sepsis: the EASI-SWITCH RCT

Health Technology Assessment 2024; Vol. 28: No. 14

DOI: 10.3310/RGTP7112

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

# **Plain language summary**

## The background

Neutropenic sepsis, or infection with a low white blood cell count, can occur following cancer treatment. Usually patients receive treatment with intravenous antibiotics (antibiotics delivered into a vein) for two or more days. Patients at low risk of complications from their infection may be able to have a shorter period of intravenous antibiotics benefitting both patients and the NHS.

#### What did we do?

The trial compared whether changing from intravenous to oral antibiotics (antibiotics taken by mouth as tablets or liquid) 12–24 hours after starting antibiotic treatment ('early switch') is as effective as usual care. Patients could take part if they had started intravenous antibiotics for low-risk neutropenic sepsis. Patients were randomly allocated to 'early switch' or to usual care.

The main outcome measured was treatment failure. Treatment failure happened if fever persisted or recurred despite antibiotics, if patients needed to change antibiotics, if they needed to be re-admitted to hospital or needed to be admitted to intensive care within 14 days or died.

### What did we find?

We had originally intended that 628 patients would take part, but after review of the design of the study the number needed to take part was revised to 230. We were not able to complete the trial as planned as unfortunately only 129 patients took part. As the trial was smaller than expected we were not able to draw conclusions as to whether 'early switch' is no less effective than usual care. Our findings suggest that 'early switch' might result in a shorter time in hospital initially; however, treatment failure was more likely to occur, meaning some patients had to return to hospital for further antibiotics. There were no differences in side effects and no serious complications from treatment or treatment failure (such as intensive care admission or death) among the 65 patients in the 'early switch' group. Patients were satisfied with 'early switch'.

## What does this all mean?

Early switch may be a treatment option for some patients with low-risk neutropenic sepsis who would prefer a shorter duration of hospital admission but accept a risk of needing hospital re-admission.

# **Health Technology Assessment**

ISSN 2046-4924 (Online)

Impact factor: 3.6

A list of Journals Library editors can be found on the NIHR Journals Library website

Launched in 1997, *Health Technology Assessment* (HTA) has an impact factor of 3.6 and is ranked 32nd (out of 105 titles) in the 'Health Care Sciences & Services' category of the Clarivate 2022 Journal Citation Reports (Science Edition). It is also indexed by MEDLINE, CINAHL (EBSCO Information Services, Ipswich, MA, USA), Embase (Elsevier, Amsterdam, the Netherlands), NCBI Bookshelf, DOAJ, Europe PMC, the Cochrane Library (John Wiley & Sons, Inc., Hoboken, NJ, USA), INAHTA, the British Nursing Index (ProQuest LLC, Ann Arbor, MI, USA), Ulrichsweb™ (ProQuest LLC, Ann Arbor, MI, USA) and the Science Citation Index Expanded™ (Clarivate™, Philadelphia, PA, USA).

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.

#### Criteria for inclusion in the Health Technology Assessment journal

Manuscripts 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

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

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.

#### This manuscript

The research reported in this issue of the journal was funded by the HTA programme as award number 13/140/05. The contractual start date was in October 2015. The draft report began editorial review in September 2021 and was accepted for publication in October 2022. 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' manuscript 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 manuscript.

This manuscript presents independent research funded by the National Institute for Health and Care 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, 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, the HTA programme or the Department of Health and Social Care.

Copyright © 2024 Coyle *et al.* This work was produced by Coyle *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This is an Open Access publication distributed under the terms of the Creative Commons Attribution CC BY 4.0 licence, which permits unrestricted use, distribution, reproduction and adaptation in any medium and for any purpose provided that it is properly attributed. See: https://creativecommons.org/licenses/by/4.0/. For attribution the title, original author(s), the publication source – NIHR Journals Library, and the DOI of the publication must be cited.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Newgen Digitalworks Pvt Ltd, Chennai, India (www.newgen.co).