

Early switch to oral antibiotics in patients with low risk neutropenic sepsis

Submission date 30/06/2015	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 01/07/2015	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 30/06/2025	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Neutropenic sepsis is a potentially life-threatening complication of chemotherapy caused by a condition known as neutropenia, in which the number of white blood cells (called neutrophils) in the blood is low. Neutrophils help the body to fight infection. People receiving chemotherapy for cancer treatment can be at risk of neutropenic sepsis because these treatments can temporarily lower the number of neutrophils in the blood. There is universal agreement that prompt antibiotic treatment is required, but less agreement about how best to manage patients thereafter. This study aims to find out whether changing from intravenous antibiotics (administered into a vein) to oral antibiotics on the first day of treatment is clinically and cost-effective in comparison with longer duration intravenous antibiotics in patients at low risk of complications.

Who can participate?

Patients undergoing chemotherapy who are admitted to hospital with low risk neutropenic sepsis.

What does the study involve?

Once you have consented you will undergo the required study tests and provide a blood sample, have your medical history and medications checked, and complete a short questionnaire. You will then be allocated to one of two groups. One group will switch from intravenous to oral antibiotics 12-24 hours after commencing intravenous treatment, for a total of five days antibiotic treatment. The other group will receive standard care intravenous antibiotics for at least 48 hours then either continue or switch to oral antibiotics at the doctor's discretion. After leaving hospital you will take any remaining antibiotic tablets and complete a progress diary, and a nurse will phone you to check on your progress and go through two short questionnaires.

What are the possible benefits and risks of participating?

The results of this study will inform the future medical care of patients who develop neutropenic sepsis while undergoing chemotherapy. The potential benefits of participating include fewer complications with intravenous lines, earlier discharge from hospital, higher quality of life and

more cost-effective treatment. The potential risks of participating include antibiotic treatment failure, side effects of antibiotic treatment, and mild discomfort when providing one additional blood sample.

Where is the study run from?

Belfast City Hospital, The Freeman Hospital, Leicester Royal Infirmary and Velindre Hospital (UK).

When is the study starting and how long is it expected to run for?

The study is due to start recruiting at four pilot sites in November 2015. If successful the main study will recruit for an additional 30 months in 12 sites across the UK.

Who is funding the study?

NIHR Health Technology Assessment Programme - HTA (UK).

Who is the main contact?

Dr Victoria Coyle
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Study website

<http://www.nictu.hscni.net/easi-switch/>

Contact information

Type(s)

Scientific

Contact name

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Type(s)

Public

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Additional identifiers**EudraCT/CTIS number**

2015-002830-35

IRAS number**ClinicalTrials.gov number****Secondary identifying numbers**

HTA 13/140/05; 15040RM-SS

Study information**Scientific Title**

Early switch to oral antibiotic therapy in patients with low risk neutropenic sepsis: a randomised, controlled, non-inferiority trial with allocation concealment

Acronym

EASI-SWITCH

Study objectives

Early switch to oral antibiotic therapy, 12-24 hours after intravenous antibiotic treatment commences in low risk cancer patients with neutropenic sepsis, is non-inferior to standard care.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Office for Research Ethics Committees Northern Ireland (ORECNI), 06/10/2015, ref: 15/NI/0161

Study design

Multi-centre interventional randomised controlled non-inferiority trial with allocation concealment

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

See study outputs table

Health condition(s) or problem(s) studied

Patients with low risk neutropenic sepsis

Interventions

Intervention arm:

Switch to oral ciprofloxacin & co-amoxiclav, 12-24 hours after starting intravenous therapy with standard dose piperacillin/tazobactam or meropenem for at least 5 days total antibiotic treatment.

Standard care arm:

Intravenous therapy with standard dose piperacillin/tazobactam or meropenem for at least 48 hours (later discontinuation +/- oral antibiotic switch at physician discretion).

Intervention Type

Drug

Phase

Phase IV

Drug/device/biological/vaccine name(s)

Ciprofloxacin, co-amoxiclav

Primary outcome measure

Treatment failure defined as one or more of the following criteria are met by day 14:

1. Persistence or recurrence of fever (temperature $>38^{\circ}\text{C}$) after 72hrs of starting intravenous antibiotic treatment
2. Physician-directed escalation from protocol antibiotic treatment
3. Re-admission to hospital (related to infection or antibiotic treatment)
4. Critical care admission
5. Death

Secondary outcome measures

1. Change in health-related quality of life EQ-5D-5L at baseline and 14 days
2. Cost-effectiveness of early switch compared to standard care at 14 days
3. Time to resolution of fever from initial IV antibiotic administration

4. Adverse events related to antibiotics
5. Duration of hospital admission
6. Readmission to hospital within 28 days
7. Death within 28 days
8. Adjustment to the subsequent scheduled cycle of chemotherapy within 28 days
9. Patient preferences for antibiotic treatment

Exploratory objective:

Identification of potential biomarkers for risk stratification in neutropenic sepsis

Overall study start date

01/08/2015

Completion date

24/12/2019

Eligibility

Key inclusion criteria

Current inclusion criteria as of 05/04/2019:

1. Age over 16 years
2. Receiving SACT for a diagnosis of cancer
3. Started on empirical intravenous piperacillin/tazobactam or meropenem, for suspected NS, for less than 24 hours. Patients who have been started on additional antimicrobial drugs (eg. gentamicin or teicoplanin) are eligible provided the physician in charge of their care is willing to stop this additional antimicrobial at the time of enrolment.
4. Absolute neutrophil count $\leq 1.0 \times 10^9/L$ with either a temperature of at least $38^{\circ}C$ or other signs or symptoms consistent with clinically significant sepsis e.g. hypothermia. Self-measurement at home or earlier hospital assessment of temperature are acceptable provided this is documented in medical notes and is within 24 hours prior to IV antibiotic administration.
5. Expected duration of neutropenia < 7 days
6. Low risk of complications using a validated risk score (MASCC score ≥ 21)
7. Able to maintain adequate oral intake and take oral medication
8. Adequate hepatic (AST &/or ALT $< 5 \times ULN$) and renal function (serum creatinine $< 3 \times ULN$) within the 24 hours prior to randomisation
9. Physician in charge of care willing to follow either the intervention or standard care protocol per randomisation, at enrolment, including not treating with colony stimulating factor (CSF). Prophylactic CSF is not an exclusion criterion if prescribed routinely as an integral component of a specific SACT regimen.

Previous inclusion criteria:

1. Age over 16 years
2. Receiving SACT for a diagnosis of cancer
3. Fever (temperature $> 38^{\circ}C$)
4. Neutropenia (absolute neutrophil count $\leq 0.5 \times 10^9/L$) within the 24 hours prior to randomisation
5. Received intravenous antibiotics (piperacillin/tazobactam or meropenem) for less than 24 hours
6. Expected duration of neutropenia < 7 days
7. Low risk of complications using a validated risk score (MASCC score ≥ 21)
8. Able to maintain adequate oral intake and take oral medication

9. Adequate hepatic (AST and/or ALT $<2.5 \times \text{ULN}$, or $<5 \times \text{ULN}$ if hepatic metastases) and renal function (serum creatinine $<3 \times \text{ULN}$) within 24 hours prior to randomisation
10. Physician in charge of care willing to follow either the intervention or standard care protocol per randomisation, at enrolment, including not treating with colony stimulating factor (CSF)

Participant type(s)

Patient

Age group

Mixed

Lower age limit

16 Years

Sex

Both

Target number of participants

230

Total final enrolment

129

Key exclusion criteria

Current exclusion criteria as of 05/04/2019:

1. Underlying diagnosis of acute leukaemia or haematopoietic stem cell transplant
2. Hypotension (systolic pressure $<90 \text{ mmHg}$ or reduction of $>40 \text{ mmHg}$ from known baseline on >1 measurement) within the 24 hours prior to randomisation
3. Prior allergy, serious adverse reaction, or contra-indication to any study drug
4. Enrolled in this trial with prior episode of neutropenic sepsis
5. Previously documented as being colonised with an organism resistant to a study drug regimen e.g. MRSA
6. Localising signs of severe infection (pneumonia, soft tissue infection, central-venous access device infection, presence of purulent collection)
7. Patients unable to provide informed consent
8. Pregnant women, women who have not yet reached the menopause (no menses for ≥ 12 months without an alternative medical cause) who test positive for pregnancy, are unwilling to take a pregnancy test prior to trial entry or are unwilling to undertake adequate precautions to prevent pregnancy for the duration of the trial
9. Breastfeeding women

Previous exclusion criteria:

1. Underlying diagnosis of acute leukaemia or haematopoietic stem cell transplant
2. Hypotension (systolic pressure $<90 \text{ mmHg}$) within the 24 hours prior to randomisation
3. Prior allergy, serious adverse reaction, or contra-indication to any study drug
4. Treatment with fluoroquinolone or penicillin antibiotics in the preceding 14 days
5. Enrolled in this trial with prior episode of neutropenic sepsis
6. Previously documented as being colonised with an organism resistant to a study drug regimen e.g. MRSA
7. Localising signs of severe infection (pneumonia, soft tissue infection, central-venous access device infection, presence of purulent collection)

8. Patients unable to provide informed consent
9. Pregnant women, women who have not yet reached the menopause (no menses for ≥ 12 months without an alternative medical cause) who test positive for pregnancy, are unwilling to take a pregnancy test prior to trial entry or are unwilling to undertake adequate precautions to prevent pregnancy for the duration of the trial
10. Breastfeeding women

Date of first enrolment

01/11/2015

Date of final enrolment

27/11/2019

Locations

Countries of recruitment

England

Northern Ireland

United Kingdom

Wales

Study participating centre

Cancer Centre, Belfast City Hospital

Belfast

United Kingdom

BT9 7AB

Study participating centre

Velindre Cancer Centre, Velindre Hospital

Cardiff

United Kingdom

CF14 2TL

Study participating centre

The Freeman Hospital

Newcastle

United Kingdom

NE7 7DN

Study participating centre

Department of Cancer Studies, Leicester Royal Infirmary
Leicester
United Kingdom
LE1 5WW

Sponsor information

Organisation

Belfast Health and Social Care Trust (UK)

Sponsor details

Research Governance
2nd Floor KEB Building
Grosvenor Road
Belfast
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United Kingdom
BT12 6BA

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/02tdmfk69>

Funder(s)

Funder type

Government

Funder Name

Health Technology Assessment Programme

Alternative Name(s)

NIHR Health Technology Assessment Programme, HTA

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Final data analysis will take place in the third quarter of 2020 (June to Sept). The trial report and dissemination should take place in Sept 2020.

The final study report will be provided by the Trial Statistician; it is anticipated that the study findings will be published in national and international peer review journals which will be led by the CI. Publications will be discussed at the TMG and will be considered on a case by case basis. This will secure a searchable compendium of these publications and make the results readily accessible to the public and health care professionals. In addition study findings may be presented at both national and international meetings and also to appropriate patient groups.

Due to limited resources, it will not be possible to provide each patient with a personal copy of the results of the trial. However, upon request, patients involved in the trial will be provided with a lay summary of the principal study findings. The most significant results will be communicated to the public through press releases. An ongoing update of the trial will also be provided on the NICTU website.

Intention to publish date

01/09/2020

Individual participant data (IPD) sharing plan

Requests for data sharing will be reviewed on an individual basis by the CI and TMG. The CI is Dr Victoria Coyle v.coyle@qub.ac.uk and Dr Ronan Mc Mullan is co-CI. ronan.mcmullan@belfasttrust.hscni.net. Please contact the TMG through the study email address: EASI-SWITCH@NICTU.HSCNI.NET

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version v8.0		05/04/2019	No	No
Protocol article	protocol	27/05/2020	29/05/2020	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet		27/05/2020	18/08/2023	No	Yes
Results article		31/03/2024	30/06/2025	Yes	No