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

Submission date
30/06/2015

Recruitment status
No longer recruiting

Registration date
01/07/2015

Overall study status
Completed

Last Edited
30/06/2025

Condition category
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] 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?
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Contact information

Type(s)
Scientific

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-002830-35

Protocol serial number
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

Study type(s)
Treatment

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 piperacilin/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(s)
Treatment failure defined as one or more of the following criteria are met by day 14:
1. Persistence or recurrence of fever (temperature >38oC) 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

Key secondary outcome(s))
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

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 ≤1.0x109/L with either a temperature of at least 38oC 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 <5xULN) and renal function (serum creatinine <3 x 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 >38oC)
4. Neutropenia (absolute neutrophil count ≤0.5x109/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 <2.5xULN, or <5xULN if hepatic metastases) and renal function (serum creatinine <3xULN) 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

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

16 years

Sex

All

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 <90mmHg or reduction of >40mmHg 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 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
United Kingdom

England

Northern Ireland

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
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Sponsor information

Organisation
Belfast Health and Social Care Trust (UK)

ROR
https://ror.org/02tdmfk69

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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?
Results article		31/03/2024	30/06/2025	Yes	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
Participant information sheet	Participant information sheet version v8.0	11/11/2025	11/11/2025	No	Yes
Protocol file			05/04/2019	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes