

A shorter duration of antibiotic treatment versus a longer duration of antibiotic treatment for patients with a flare-up of their chronic lung condition requiring intravenous antibiotics

Submission date 02/09/2023	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 16/11/2023	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 13/12/2023	Condition category Respiratory	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Bronchiectasis affects around 300,000 people in the UK, according to British Lung Foundation research. Hospital admissions due to bronchiectasis cost the NHS around £40 M per year. International guidelines recommend that patients receive intravenous antibiotics for 14 days if they are particularly unwell, have an infection with resistant organisms, or if oral antibiotics are ineffective. The duration is based on expert advice but there have not been any randomised placebo controlled trials telling us what length of course is best. Treating for too long may keep people in hospital too long or increase their risk of antibiotic side effects, treating for too short a period may increase the risk of another infection soon after completion of antibiotics.

A study in Edinburgh of 90 patients showed that patients and clinicians would enter a trial of shorter courses of intravenous antibiotic treatment. Patients receiving 7 days of intravenous antibiotics took longer to next flare up compared to those getting current recommendation of 14 days, challenging the current thinking that “more is better”. A multi-centre trial is now needed to confirm this and change the national and international guidelines recommending 14 days of treatment. This study could add to the goal of reducing inappropriate antibiotic use and reduce the chance of developing antibiotic resistance.

The Research question being addressed by this study proposal is: for bronchiectasis-related pulmonary exacerbations, is 7- or 14-days’ duration of intravenous antibiotic treatment better in delaying the next exacerbation?

Who can participate?

We will select 400 patients with bronchiectasis throughout the UK who need intravenous antibiotic treatment.

What does the study involve?

Half of the participants, at random, will receive 7 days of open labelled intravenous antibiotics and the other half will receive 14 days of open labelled intravenous antibiotics. Both groups will receive standard care in addition and be followed up for one year.

What are the possible benefits and risks of participating?

One of the reasons for running this study is to establish any benefits for patients receiving a shorter course of antibiotics and participation in this study may help to improve bronchiectasis health care in the future. We have shown in a smaller study that patients who received a shorter duration of antibiotics took longer until their next flare-up of their bronchiectasis. Reduction of antibiotics leads to less hospital acquired infections and healthcare resource use.

We anticipate that if you are assigned to the 7-day treatment arm it may delay the time to next needing an antibiotic for a flare-up. Your treatment will be less burdensome as you will receive only 7 days as opposed to 14 days of treatment. Receiving a shorter duration of antibiotic treatment than the standard course may reduce the risk of developing antibiotic resistance and experiencing fewer or shorter-lived side effects.

The benefits to you taking part in this study if you are allocated to the 14 day treatment arm are the same as if you received standard care.

There are no additional potential medical risks associated with the study.

All participants will be asked to complete study questionnaires which is a potential burden on the participant's time. To minimise this burden, we will give patients the option of completing these electronically or on paper.

The monthly telephone calls are also a potential burden on the patient's time. We will make every effort to minimise inconvenience; for example, we will offer calls at a time of their choosing and we will also make it clear that they can cancel and reschedule calls at short notice. Some patients may feel reassured by extra follow up visits and increased number of clinical reviews.

Provision of sputum and posting sample to the clinical research team may pose a burden to the participants. We will minimise this burden by providing appropriate packaging and instructions in advance, and answering any questions the patient may have.

Where is the study run from?

University of Edinburgh and NHS Lothian (UK)

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

August 2023 to August 2025

Who is funding the study?

National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?

Professor Adam Hill, adam.hill@nhs.scot

Contact information

Type(s)

Scientific, Principal Investigator

Contact name

Dr Adam Hill

Contact details

51 Little France Crescent
Edinburgh
United Kingdom
EH164SA

+44 131 242 1921
adam.hill@nhs.scot

Type(s)
Public

Contact name
Dr Public Contact

Contact details
Asthma & Lung UK
-
United Kingdom
-
-
research@asthmaandlung.org.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1007537

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
AC23072, IRAS 1007537, CPMS 58813

Study information

Scientific Title
Seven versus fourteen days antibiotics for patients with bronchiectasis requiring intravenous antibiotics - SBIVA study

Acronym
SBIVA Study

Study objectives
Primary objective:
To compare which duration of intravenous antibiotic treatment is superior for a bronchiectasis exacerbation, 7 days or 14 days. Superior is defined by a longer time elapsed until the next verified bronchiectasis exacerbation requiring antibiotic treatment (up to 1 year).

Secondary objectives:
To determine whether treatment with 7 days of intravenous antibiotics is superior to treatment with 14 days of intravenous antibiotics in terms of:
1. Health-related quality of life at day 14

2. Clinical response at day 14, defined as a 4 or more-unit improvement in either the St. George's Respiratory Questionnaire or the CAT questionnaire, and/or by change in sputum colour from baseline:

2.1. Purulent to muco-purulent, mucoid, or no sputum, or

2.2. Muco-purulent to mucoid or no sputum

3. Adverse events up to day 60

4. Drug-resistant pathogens at day 14 and at time of next exacerbation needing antibiotic therapy

5. Health economic benefits

6. Adherence with allocated intravenous antibiotic intervention

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 15/11/2023, Scotland A Research Ethics Committee (2nd Floor Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; +44 7814609032; sesres@nhslothian.scot.nhs.uk), ref: 23/SS/0101

Study design

Interventional randomized parallel group controlled trial

Primary study design

Interventional

Secondary study design

Randomised parallel trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Bronchiectasis

Interventions

Study treatment: Half the study population, at random, will receive 7 days of open labelled intravenous antibiotics and the other half will receive 14 days of open labelled intravenous antibiotics.

We have chosen to use a broad-spectrum antibiotic (meropenem 2g intravenously three times daily) as it covers both gram-positive and gram-negative bacteria, including *Pseudomonas aeruginosa* (the most frequent pathogen identified in those that need intravenous antibiotics), as well as anaerobes. In addition, it is the antibiotic of choice for participants with a penicillin allergy. Eligibility does not rest on having a meropenem sensitive organism from current or previous sputum microbiology results.

The aim is to use meropenem for both arms of the study, however the use of a protocol approved alternative anti-pseudomonal antibiotic (at Investigator discretion) will be permitted. For example due to local antibiotic use policy, if there are supply issues, or patient allergies etc. The protocol approved alternatives are piperacillin-tazobactam, ceftazidime, ciprofloxacin, aztreonam, gentamicin and colistimethate sodium.

The intravenous antibiotics will be delivered as per local institutional standard of care and will be determined by the clinical care team (either out-patient, home or as an in-patient). We will align to local practice for alternative doses and regimens.

Follow up: Participants will be asked to complete a diary during their study treatment to document adherence to their allocation, and participants in both arms will be reviewed 14 days after starting their IV antibiotic (may be carried out remotely). Participants will receive monthly follow up telephone calls from their research team for 1 year after starting trial treatment to collect exacerbation information, adverse events (up to day 60), and quality of life and health economic assessment.

Randomisation procedure: After written informed consent has been obtained and eligibility confirmed, a member of the research team will perform the randomisation using a web-based randomisation service managed by the Edinburgh Clinical Trials Unit (ECTU). Participants will be randomised on a 1:1 basis to receive intravenous antibiotics for either 7 days or 14 days. The randomisation system will stratify for bronchiectasis severity and also for planned location of treatment, either in hospital as an inpatient or self-administering intravenous antibiotics at home.

Intervention Type

Drug

Pharmaceutical study type(s)

Dose response, Pharmacoeconomic, Therapy

Phase

Phase IV

Drug/device/biological/vaccine name(s)

Meropenem [meropenem trihydrate], Tazocin [Piperacillin, Tazobactam] , Ceftazidime [ceftazidime], Ciprofloxacin [ciprofloxacin], Azactam [Aztreonam], Gentamicin [Gentamicin], Colomycin [colistimethate sodium]

Primary outcome measure

Time elapsed between starting intravenous antibiotic therapy, until needing another antibiotic course for a protocol-defined exacerbation of bronchiectasis (up to 1 year post randomisation). The following internationally agreed consensus definition of a bronchiectasis exacerbation for clinical trials will be used:

Deterioration in three or more of the following key symptoms for at least 48 h:

1. Cough
2. Sputum volume and/or consistency
3. Sputum purulence
4. Breathlessness and/or exercise tolerance

5. Fatigue and/or malaise
6. Haemoptysis
7. A clinician determines antibiotic treatment is required (either oral or intravenous)

Exacerbations will be confirmed within 7 days by a clinical member of the research team contacting the participant and reviewing their symptoms. The team member verifying the exacerbation may be an appropriately qualified doctor, nurse or allied health care professional who has been delegated this task by the PI on the site delegation log. Participants will be asked to contact their local research team as soon as possible at the onset of an exacerbation, or on a Monday if an exacerbation starts on a weekend. Participants will be given a study card to remind them of this along with contact details for their local research team. They will also be reminded at each monthly follow-up call. If the verifying person deems the exacerbation does not meet the agreed criteria, the participant will continue in the study until they feel they have another exacerbation. At this point they will then be checked again as described above. This will continue until the participant meets the primary outcome measure (up to one year). All further exacerbations will be recorded but not verified. These conversations will be documented in the patient medical records and exacerbation data entered into the eCRF.

Secondary outcome measures

The following secondary outcomes will be assessed comparing 7 versus 14 days intravenous antibiotics:

1. St. George's Respiratory Questionnaire score at baseline and day 14
2. Bronchiectasis Health Questionnaire at baseline and day 14
3. CAT Questionnaire at baseline and day 14
4. Sputum colour at baseline, day 14 and at next exacerbation
5. Adverse events recorded at day 14, month 1 and day 60
6. Sputum pathogen and drug resistance patterns following treatment from samples collected at baseline, day 14 and at the time of next verified exacerbation (up to 1 year post randomisation)
7. Health Economic analysis measured using EQ-5D-5L and Health Care Resource Use questionnaires at baseline, day 14 and at each monthly telephone follow-up (up to 1 year post randomisation) and Cost per Quality Adjusted Life Year (QALY) from a UK National Health Service and Personal Social Services perspective, as simulated via decision analytic modelling over 1, 3, and 5-year time horizons
8. Adherence with allocated intravenous antibiotic intervention having greater than or equal to four sevenths of days of treatment, assessed by diary card and routine prescribing data at day 14 visit

Overall study start date

31/08/2023

Completion date

31/08/2025

Eligibility

Key inclusion criteria

1. Adults (age 16 or over)
2. Provision of informed consent (from participant or when lacking capacity due to bronchiectasis severity, by their legal representative)
3. A clinical diagnosis of bronchiectasis made by a respiratory specialist supported by CT scan or

equivalent clinical confirmation of bronchiectasis

4. Exacerbation where intravenous antibiotics are deemed clinically appropriate

5. Ability to adhere to the study assessments/protocol in the opinion of the Investigator

Participant type(s)

Patient

Age group

Adult

Lower age limit

16 Years

Sex

Both

Target number of participants

400

Key exclusion criteria

1. Patients who are asymptomatic at start of IV antibiotics
2. Known Homozygous Cystic fibrosis
3. Known active tuberculosis
4. Breast feeding, pregnancy, or plan to become pregnant within study
5. End of life care with anticipated life span less than 6 months
6. Current enrolment in a CTIMP where co-enrolment has not been approved
7. Previous recruitment to the SBIVA trial
8. Allergy to Meropenem and protocol permitted alternatives
9. Where trial enrolment is not in the best interest of the patient in the opinion of the Investigator

Date of first enrolment

31/07/2023

Date of final enrolment

31/07/2023

Locations

Countries of recruitment

Scotland

United Kingdom

Study participating centre

Royal Infirmary of Edinburgh

51 Little France Crescent

Old Dalkeith Road

Edinburgh

United Kingdom
EH16 4SA

Sponsor information

Organisation

University of Edinburgh

Sponsor details

Level 2, Nine Edinburgh Bioquarter
9 Little France Road
Edinburgh
Scotland
United Kingdom
EH16 4UX
+44 131 651 9983
researchgovernance@ed.ac.uk

Sponsor type

University/education

Website

<http://www.ed.ac.uk/home>

ROR

<https://ror.org/01nrxf90>

Organisation

NHS Lothian

Sponsor details

The Queens Medical Research Institute
47 Little France Crescent
Edinburgh
Scotland
United Kingdom
EH16 4TJ
-
accord@nhslothian.scot.nhs.uk

Sponsor type

Hospital/treatment centre

Website

<http://www.nhslothian.scot.nhs.uk/Pages/default.aspx>

ROR

<https://ror.org/03q82t418>

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

Peer reviewed scientific journals

Internal report

Conference presentation

Publication on website

Submission to regulatory authorities

Access to raw data and right to publish freely by all investigators in study or by Independent

Steering Committee on behalf of all investigators

The data will be anonymised and made available for further research. Requests can be made to access the data by contacting the ECTU Data Sharing Committee

Intention to publish date

31/01/2028

Individual participant data (IPD) sharing plan

The datasets generated during and analysed during the current study will be available upon request made in writing via email to ECTUdatashare@ed.ac.uk in the first instance and will be reviewed in accordance with ECTU_SOP_OP_15 Data Access Request and Application Management.

IPD sharing plan summary
Available on request