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Optimising the use of azithromycin antibiotic to reduce Bronchiectasis flare-ups

Submission date 15/03/2025	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 08/05/2025	**Overall study status** Ongoing	
Last Edited 08/05/2025	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims

People living with bronchiectasis may experience worsening symptoms such as shortness of breath, cough and wheezing in addition to changes that may be expected for having bronchiectasis. The worsening of symptoms is called exacerbation or flare-up and can be debilitating and frightening, requiring additional treatment, often with azithromycin. This is an antibiotic medicine that also has anti-inflammatory properties. It is prescribed as long-term prevention to reduce the risk of flare-ups. Some people may be affected by side effects from azithromycin. Antibiotic resistance is another concern, especially when using azithromycin for prevention rather than to treat active infection. It is currently unknown whether to advise people to stop taking azithromycin once bronchiectasis has stabilised. It is also unknown if azithromycin is more effective in some people or more likely to cause side effects in others. Given these uncertainties, it is challenging to know how best to use azithromycin in managing bronchiectasis. Azithromycin is a valuable antibiotic. To maintain its benefit while avoiding unnecessary side effects it is necessary to reduce the chances of bacteria becoming resistant to it. This trial aims to establish the effects of stopping azithromycin in people whose bronchiectasis has stabilized after taking it for at least 3 months. It will compare continuing azithromycin with stopping it completely, examining the effects of these two treatments on flare-ups, symptoms, and quality of life, and identifying factors that may affect individual responses.

Who can participate?

Patients aged 16 years old and over with clinically stable bronchiectasis and prescribed prophylactic azithromycin or an equivalent long-term macrolide for at least 90 days in the past 12 months due to reduce the risk of bronchiectasis exacerbations

What does the study involve?

In this study, patients will continue taking azithromycin or switch to a placebo for 12 months. The dosage will match what they were already taking, which could be 250mg once a day three times a week, 500mg once a day three times a week, or 250mg once a day every day. The medication will be taken orally.

What are the possible benefits and risks of participating?
Participants may have no personal benefit from taking part in this trial. They will have trial-related monitoring and interactions with healthcare professionals during the trial. They may experience fewer azithromycin-related side effects. However, the results from this trial will benefit patients with bronchiectasis in the future because it will help the researchers know how best to use azithromycin long-term treatment for people with bronchiectasis. Information from the trial will also help the researchers better understand frailty in bronchiectasis from the data that are collected as participants will be followed up. The researchers also hope to gain information about the best approaches to aid recruitment into clinical trials.

Participants may experience more flare-ups of their bronchiectasis or may experience side effects from the azithromycin which will be closely monitored by the trial teams at participating sites. If they experience 3 or more flare-ups within the year, the participant will be advised to stop the trial medication and possibly re-start their standard azithromycin treatment (clinician's decision).

Although the participants would have been on azithromycin for at least 90 days before recruitment to the trial, there may be some burden linked to participants being asked to self-administer oral medication. There may be a risk that tablets may not be taken (underdose) or taken too much (overdose). This will be mitigated by regular checks of compliance over the telephone/visits. The regimen will also match that of the patient's routine prescription for the IMP that they had been taking for at least the previous 90 days to minimise any further burden on the participants.

There may be a risk with IMP delivery for participants unable to collect the IMP at baseline / 6 months visit whereby there is either a delay of the participant receiving the IMP, or not receiving the IMP at all. This could be due to delivery issues, the participant not being at home, or someone else taking the delivery, etc. This will be mitigated by trial team contact with the participant within a week of the participant's enrolment to the trial and the 6 months visit.

If trial visits cannot coincide with the participant's standard of care (SoC) appointments, there may be the burden of additional visits to the hospital. This burden will be mitigated by carrying out those visits remotely.

Where is the study run from?
Newcastle University, UK

When is the study starting and how long is it expected to run for?
March 2025 to May 2029

Who is funding the study?
NIHR Health Technology Assessment Programme (HTA)

Who is the main contact?
Prof Anthony De Soyza, anthony.de-soyza@newcastle.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Anthony De Soyza

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1010479

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
10730

Study information

Scientific Title
Bronchiectasis: Optimising Azithromycin prevention Treatment to reduce exacerbations (BOAT): A double blind pragmatic 2 arm phase IV randomised controlled trial

Acronym
BOAT

Study objectives
To evaluate the benefits and risks of complete discontinuation of azithromycin chemoprophylaxis vs continued azithromycin chemoprophylaxis treatment in people with stable Bronchiectasis at high risk of exacerbations and assess these effects in specific patient subgroups.

Further evaluation of clinical effectiveness defined by effect on exacerbations (specifically number/rate and severity of exacerbations).
Health status as measured by symptoms and quality of life.
Hospitalisation and healthcare use.
Mortality (all-cause, respiratory, cardiac).
Adverse events of special interest and serious adverse reactions.
To determine what factors or patient subgroups impact interventions assessed.
To estimate the cost-effectiveness of complete discontinuation of azithromycin chemoprophylaxis in people with Bronchiectasis at high risk of exacerbations.
To evaluate adherence to the trial medication.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 29/04/2025, North of Scotland Research Ethics Committee (Summerfield House, 2 Eday Road, Aberdeen , AB15 6RE , United Kingdom; +44 (0)1224 558458 ; gram.nosres@nhs.scot), ref: 25/NS/0027

Study design
Randomized placebo-controlled double-blind parallel-group-assignment study

Primary study design
Interventional

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Medical condition: Bronchiectasis
Medical condition in lay language: Bronchiectasis
Therapeutic areas: Diseases [C] - Respiratory Tract Diseases [C08]

Interventions
The intervention is the continuation of long-term azithromycin compared to a matched placebo. The dose is matched to the patient's pre-existing long-term macrolide dose commonly 250mg once a day azithromycin thrice weekly, azithromycin 500mg once a day thrice weekly or azithromycin 250mg once a day every day. The route of administration is enteral. Randomisation will be performed using the "Sealed envelope" online system. The duration of treatment is 12 months.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Azithromycin [Azithromycin]

Primary outcome(s)
Time to first exacerbation of bronchiectasis, as defined by a sustained increase in symptoms, usually of 72 hours, requiring antibiotic therapy measured using data collected from electronic case report forms (eCRF). The primary endpoint does not have a fixed time point of evaluation. The maximum treatment period is 12 months with further follow-up after trial allocation medication ends from 13-24 months.

Key secondary outcome(s))
The following secondary outcome measures are assessed at 3, 6, 12, 18, and 24 months unless otherwise stated:
1. Further evaluation of clinical effectiveness, defined by the effect on exacerbations

(specifically number/rate and severity of exacerbations) measured using data collected from eCRF
2. Health status as measured using the following tools for symptoms and quality of life:
2.1. EuroQol 5-Dimension 5-Level (EQ-5D-5L)
2.2. Quality of Life Bronchiectasis (QoLB)
2.3. Chronic Airways Assessment Tool (CAAT)
2.4. Visual Analog Scale (VAS)
2.5. Patient Health Questionnaire-2 (PHQ-2)
2.6. Generalized Anxiety Disorder-2 (GAD-2)
2.7. Clinical Frailty Score (CFS)
2.8. Self-Rated Health Scale (SRHS)
3. Hospitalisation and healthcare use measured using a Health Utilisation Questionnaire at 6, 12, 18, 24 months
4. Mortality (all-cause, respiratory, cardiac) measured using data collected from eCRF
5. Adverse events of special interest and serious adverse reactions measured using data collected from eCRF
6. Factors or patient subgroups that impact interventions measured using data collected from eCRF
7. To estimate the cost-effectiveness of complete discontinuation of azithromycin chemoprophylaxis in people with Bronchiectasis at high risk of exacerbations measured using a Health Utilisation Questionnaire
8. To evaluate adherence measured using pill counts at trial visits

Completion date
31/05/2029

Eligibility

Key inclusion criteria
1. Age 16 years or older (no upper age limit)
2. Be able and willing to provide informed consent.
3. Have clinically stable Bronchiectasis, i.e. no Bronchiectasis exacerbation for at least 30 days.
4. Established clinical diagnosis of Bronchiectasis and prescribed receiving prophylactic azithromycin or an equivalent long-term macrolide for at least 90 days in the past 12 months to reduce risk of Bronchiectasis exacerbations
5. Historical CT scan report confirming bronchiectasis (or equivalent e.g. bronchogram)
6. Any suspected aetiology of Bronchiectasis can be included
7. Any treatment regimen of azithromycin or an equivalent long-term macrolide (noting current guidelines allow 250mg OD thrice weekly, 250mg each day or 500mg OD thrice weekly of azithromycin)
8. Available data (more than 5 parameters from the following routinely collected data) to calculate Bronchiectasis Severity Index (BSI) (1) age, 2) sex, 3) FEV1% predicted current or historical in last 12 months), 4) number of prior exacerbations, 5) prior hospitalisations in last 24 months, 6) MRC dyspnoea score, 7) microbiology status (Pseudomonas colonies or other) , 8) BMI. CT Reiff scoring also preferred but not essential.

In addition to the main trial inclusion criteria:
Participants who are able may choose to provide informed consent for the optional sub-study. This will be a separate consent question to tick on the consent form (for the feedback questionnaire only, or feedback questionnaire and possibility of telephone call to gain further in-depth feedback).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Sex
All

Key exclusion criteria
1. Known hypersensitivity to any of the trial drugs or excipients.
2. Current breast feeding, pregnancy or planned pregnancy during the trial.
3. Any medical history or clinically relevant abnormality that makes patient ineligible for inclusion because of a safety concern relating to continuing or discontinuing azithromycin or other considerations.
4. Bronchiectasis exacerbation requiring treatment with antibiotics and/or steroids up to 30 days prior to study enrolment (can be re-screened after 30 days).
5. Azithromycin prophylaxis prescribed for non-Bronchiectasis condition or as part of treatment regimen for Non-tuberculosis mycobacteria.
6. Azithromycin prophylaxis prescribed for <90 days.
7. Participation in other trial of investigational medicinal product of bronchiectasis (unless a co-enrolment agreement has been developed and approved). Participation in observational studies is allowed.
8. Where participant / supervising clinician does not feel at equipoise for randomisation to either continuation or withdrawal of macrolide.
9. Participant has usual regimen of azithromycin of winter on therapy/ summer cessation of therapy AND patient unwilling to be randomised to trial allocation for 12 months.

Date of first enrolment
01/07/2025

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Freeman Hospital [Lead site]
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Royal Brompton & Harefield Hospital
Sydney Street
London
United Kingdom
SW3 6NP

Study participating centre
North Tyneside General Hospital
Rake Lane
North Shields
United Kingdom
NE29 8NH

Study participating centre
Royal Papworth Hospital
Papworth Road
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0AY

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre

Bradford Royal Infirmary
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Torbay Hospital
Newton Road
Torquay
United Kingdom
TQ2 7AA

Study participating centre
Greater Lancashire Hospitals
Wyder Court
Ribbleton
Preston
United Kingdom
PR2 5BW

Study participating centre
Westmorland General Hospital
Burton Rd
Kendal
United Kingdom
LA9 7RG

Study participating centre
Bristol Royal Infirmary
Marlborough Street
Bristol
United Kingdom
BS2 8HW

Study participating centre
Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9LT

Study participating centre
Liverpool Heart & Chest Hospital
Broadgreen Hospital
Thomas Drive
Liverpool
United Kingdom
L14 3PE

Study participating centre
Glenfield Hospital
Groby Road
Leicester
United Kingdom
LE3 9QP

Study participating centre
University Hospital of North Tees
Hardwick Road
Stockton-on-tees
United Kingdom
TS19 8PE

Study participating centre
Kingston Hospital
Galsworthy Road
Kingston upon Thames
United Kingdom
KT2 7QB

Study participating centre

Royal Devon & Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
South Tyneside District Hospital
Harton Lane
South Shields
United Kingdom
NE34 0PL

Study participating centre
Royal Derby Hospital (nuh)
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
University Hospital (coventry)
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
Ninewells Hospital
Ninewells Avenue
Dundee
United Kingdom
DD1 9SY

Study participating centre
Victoria Hospital - NHS Fife
Hayfield House
Hayfield Road
Kirkcaldy
United Kingdom
KY2 5AH

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Crescent
Old Dalkeith Road
Edinburgh
United Kingdom
EH16 4SA

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0SF

Study participating centre
University Hospital Llandough
Penlan Road
Llandough
Penarth
United Kingdom
CF64 2XX

Study participating centre
Prince Philip Hospital
Bryngwynmawr
Dafen
Llanelli
United Kingdom
SA14 8QF

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

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
A separate data sharing policy with appropriate safeguards (i.e. controlled access, as advised by NHS England) will be established and in keeping with the policies of the Sponsor and funder.

IPD sharing plan summary
Data sharing statement to be made available at a later date