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A trial looking at the use of bronchodilator and steroid inhalers for preventing flare ups of bronchiectasis

Submission date 13/03/2020	**Recruitment status** Stopped	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data [_] Record updated in last year
Registration date 06/05/2020	**Overall study status** Stopped	
Last Edited 15/08/2025	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Bronchiectasis is a long-term lung disease which is unrelated to smoking. People with bronchiectasis have ongoing phlegm production and repeated chest infections. A feature of bronchiectasis is a worsening in symptoms (known as an exacerbation) where patients have an increased cough, phlegm discolouration, excess phlegm production, breathlessness and/or tiredness. One of the main aims of bronchiectasis treatment is to reduce the number of exacerbations that patients experience. There has been little research carried out looking at the treatment of bronchiectasis even though there are over 300,000 patients with bronchiectasis in the UK.
To date, no treatments have been approved specifically for bronchiectasis. Instead, bronchiectasis treatments are based on treatments given for other lung conditions such as asthma or COPD (chronic obstructive pulmonary disorder) and there are differences in care. The main treatments used for bronchiectasis at the moment are drugs that make breathing easier by widening the airways (known as bronchodilators), inhaled steroids and long-term antibiotics. The main aim when treating bronchiectasis is to reduce exacerbations experienced by patients. Of these treatments only antibiotics have good proof of reducing exacerbations in bronchiectasis, however, proof for the other treatments is very limited. The aim of this study is to look at the use of bronchodilators and inhaled steroids in reducing exacerbations of bronchiectasis.

Who can participate?
Adult patients with bronchiectasis

What does the study involve?
The drugs being tested will be inhalers, there are three inhalers:
1. A dual bronchodilator inhaler
2. A dual bronchodilator combined with a corticosteroid inhaler
3. A placebo inhaler (a ‘dummy’ treatment)
Participants will stop taking any inhaler(s) they are already on, with the exception of their quick-acting inhaler (such as salbutamol). They will be randomly assigned to either one of the two treatment inhalers or the placebo inhaler (‘dummy’ treatment). They will have four times the

chance of being on either one of the treatment inhalers as on the placebo inhaler. Participants and the trial doctor will not know which inhaler participants are allocated, all of the inhalers look identical. Participants will use the trial inhaler once a day for 12 months and will have four additional hospital visits over the 12 months. During these visits, participants will discuss their medical history, have some breathing tests and complete some questionnaires. They will have a telephone call every month to check that they have received their replacement inhaler through the post and will be asked to complete a diary each week for 12 months to record any bronchiectasis exacerbations they experience.

What are the possible benefits and risks of participating?
Participants cannot be assured that they will benefit directly from the taking part in the study, but the information gained may help to improve treatment for people with bronchiectasis in the future. The safety and side effects of these inhalers in other lung conditions are well known. It is possible that participants may experience side effects but these will be closely monitored, and if necessary the study doctor will be able to change their medication and put treatment in place to ease any symptoms. Participants allocated to the dummy treatment may find that they experience more exacerbations than on their current treatment.

Where is the study run from?
Newcastle University (UK)

When is the study starting and how long is it expected to run for?
October 2019 to July 2024

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2019-004466-17

Integrated Research Application System (IRAS)
275595

National Institute for Health and Care Research (NIHR)
127460

Study information

Scientific Title
A pragmatic, multicentre, placebo-controlled, three-arm, double-blinded, randomised controlled trial, incorporating an internal pilot, to determine the role of bronchodilators in preventing exacerbations of bronchiectasis

Acronym
Dual Bronchodilators in Bronchiectasis Study (DIBS)

Study objectives
DIBS is a pragmatic multi-centre, placebo-controlled three-arm double-blind randomised controlled trial, incorporating an internal pilot. The aim of the trial is to determine whether treatment with either dual bronchodilators as a standalone therapy or in combination with inhaled corticosteroid (ICS) reduce the number of exacerbations experienced by bronchiectasis patients in a 12-month period.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 01/03/2021, North East - Newcastle & North Tyneside 2 Research Ethics Committee (NHS BT Blood Donor Centre, Holland Drive, Newcastle upon Tyne, Tyne and Wear, NE2 4NQ; +44 (0)207 104 8086; newcastlenorthtyneside2.rec@hra.nhs.uk), ref: 21/NE/0020

Study design
Pragmatic multi-centre placebo-controlled three-arm double-blind randomised controlled trial

Primary study design

Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Bronchiectasis

Interventions
Participants will be randomised to one of the three trial groups in a 2:2:1 ratio to receive either dual therapy (LAMA/LABA), triple therapy (ICS/LAMA/LABA) or placebo:
1. Anoro Ellipta dry powder inhaler (LAMA/LABA - 55 micrograms umeclidinium and 22 micrograms vilanterol)
2. Trelegy Ellipta dry powder inhaler (ICS/LAMA/LABA - 92 micrograms fluticasone furoate, 55 micrograms umeclidinium and 22 micrograms vilanterol)
3. Placebo (matched placebo dry powder inhaler)

Participants will use the trial inhaler once a day for 12 months and will have four additional hospital visits over the 12 months. They will have a telephone call every month to check that they have received their replacement inhaler through the post and will be asked to complete an exacerbation diary each week for 12 months to record any bronchiectasis exacerbations.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Anoro Ellipta dry powder inhaler, Trelegy Ellipta dry powder inhaler

Primary outcome(s)
Current primary outcome measure as of 17/05/2023:
Primary outcome measure:
Number of bronchiectasis exacerbations requiring treatment with antibiotics during 12 month treatment period as measured using participant reports and completed weekly exacerbation diary

Primary economic outcome measure:
1. Cost per QALY at 12 months: costs based on the cost of the interventions, use of health services via a Health Care Utilisation questionnaire administered at 1, 6 and 12 months post-randomisation and adverse events
2. QALYs measured via the EQ-5D-5L at baseline, 1, 6 and 12 months post-randomisation
3. Transport and time for participants to utilise health care appointments will be assessed via the Time and Travel Questionnaire administered at 12 months post-randomisation

Previous primary outcome measure:
Primary outcome measure:
Number of bronchiectasis exacerbations requiring treatment with antibiotics during 12 month treatment period as measured using participant reports and completed weekly exacerbation diary

Primary economic outcome measure:
1. Cost per QALY at 12 months: costs based on the cost of the interventions, use of health services via a Participant Cost questionnaire administered at 1, 6 and 12 months post-randomisation and adverse events
2. QALYs measured via the EQ-5D-5L at baseline, 1, 6 and 12 months post-randomisation

Key secondary outcome(s))

Current secondary outcome measures as of 17/05/2023:
1. Number of hospital admissions for bronchiectasis exacerbations during 12 month treatment period, as measured using participant reports and completed weekly exacerbation diary and verified where possible by hospital discharge summary/HES data. Hospitalisation due to bronchiectasis exacerbation data collected up to 24 months after visit 1: screening/baseline, will be used to extend modelling beyond 12 months as a sensitivity analysis.
2. Time to first exacerbation of bronchiectasis as measured using participant reports/completed weekly exacerbation diary
3. Number of emergency hospital admissions (all-cause) as ascertained at 1, 6 and 12 months visits and from primary care records
4. Number of serious adverse events as a result of drug reactions or reactions to the cessation of treatment as reported by the participant to the research team or at 1, 6 and 12 months visits
5. Health status measured using SGRQ (St Georges Respiratory questionnaire) and bronchiectasis-specific quality of life measured using QOL-B (quality of life - bronchiectasis) at baseline, 1, 6 and 12 months visits
6. Health-related quality of life measured using EQ-5D-5L at baseline, 1, 3, 6 and 12 months visits
7. Breathlessness measured using BDI (baseline dyspnoea index) at baseline
8. Breathlessness measured using TDI (transition dyspnea index) at 1, 6 and 12 months visits
9. Post bronchodilator lung function (LABA within 8 hours, short-acting beta2 agonist within 2 hours) as measured by spirometry performed to ATS/ERS standards at baseline, 1, 6 and 12-month visits:
9.1. Forced expiratory volume in 1 second (FEV1)
9.2. Forced vital capacity (FVC)
10. All-cause, respiratory and cardiac mortality as ascertained from Office of National Statistics data records of trial participants (collected up to 24 months after visit 1: screening/baseline)
11. Incremental cost per exacerbation avoided; costs based on the cost of the interventions (micro-costed), use of health services collected via a Health Care Utilisation Questionnaire administered at baseline, 1, 6 and 12 months post-randomisation and adverse events collected via case report forms
12. Costs to the NHS and patients and lifetime cost-effectiveness based on extrapolation modelling; the main source of data to populate the model will come from the trial and will be supplemented by HES (Hospital Episode Statistics)/ONS (Office of National Statistics) data (collected up to 24 months after visit 1: screening/baseline) relevant literature and expert opinion and extrapolated over a patient lifetime
13. Rates of radiologically confirmed pneumonia, compared to participant's normal baseline; the number of pneumonia events and the total number of participants suffering pneumonia. This will be measured by asking participants during follow-up visits

Exploratory measures:
1. To investigate the relationship between key outcomes with baseline and median eosinophil levels and baseline BSI using:
1.1. Eosinophil measurement at baseline and the median of the last 3 measurements available
1.2. SGRQ and QOL-B as completed by participants at 1, 6 and 12-month follow-up visits
1.3. BSI measured at baseline

1.4. The number of protocol-defined bronchiectasis exacerbations requiring treatment with antibiotics during 12 month treatment period as measured using participant reports/participant completed weekly exacerbation diary
2. Subgroup of analysis of suspected aetiology comparing idiopathic and post-infectious to all other aetiologies for the key outcomes of exacerbations and quality of life using:
2.1 Disease history at baseline
2.2. The number of protocol-defined exacerbations requiring treatment with antibiotics during the 12-month treatment period as measured using participant reports/participant-completed weekly exacerbation diaries
2.3. SGRQ and QOL-B as completed by participants at 1, 6 and 12-month follow-up visits

Previous secondary outcome measures
1. Number of hospital admissions for bronchiectasis exacerbations during 12 month treatment period, as measured using participant reports and completed weekly exacerbation diary and verified where possible by hospital discharge summary/HES data
2. Time to first exacerbation of bronchiectasis as measured using participant reports/completed weekly exacerbation diary
3. Number of emergency hospital admissions (all-cause) as ascertained from primary care records at 1, 6 and 12 months visits and where needed
4. Number of adverse events/drug reactions and cessation of treatment as reported by the participant to the research team or at 1, 6 and 12 months visits
5. Health status measured using SGRQ (St Georges Respiratory questionnaire) and bronchiectasis specific quality of life measured using QOL-B (quality of life - bronchiectasis) at baseline, 1, 6 and 12 months visits
6. Health-related quality of life measured using EQ-5D-5L at baseline, 1, 3, 6 and 12 months visits
7. Breathlessness measured using BDI (baseline dyspnoea index) at baseline
8. Breathlessness measured using TDI (transition dyspnea index) at 1, 6 and 12 months visits
9. Post bronchodilator lung function (LABA within 8 hours, short-acting beta2 agonist within 2 hours) as measured by spirometry performed to ATS/ERS standards at baseline, 1, 6 and 12 month visits:
9.1. Forced expiratory volume in 1 second (FEV1)
9.2. Forced vital capacity (FVC)
10. All-cause, respiratory and cardiac mortality measured using Office of National Statistics data at 12 months
11. Incremental cost per exacerbation avoided measured using Patient Cost Questionnaire at baseline, 1, 6 and 12 months
12. Costs to the NHS and patients and lifetime cost-effectiveness based on extrapolation modelling at 12 months
13. Rates of radiologically confirmed pneumonia, compared to participant's normal baseline measured by asking participants at 1, 6 and 12 months

Exploratory measures:
Eosinophil count measured as the number of cells per microliter of blood and categorised as low - normal (0-150/mm3) and normal - high (>150/mm3) at baseline as both a single measure at that point and a median eosinophil level (median of last three available recordings when not on oral steroids)

Completion date
31/07/2024

Reason abandoned (if study stopped)

Participant recruitment issue

Eligibility

Key inclusion criteria
Current inclusion criteria as of 05/09/2022:
1. Adult patients with CT-scan-confirmed bronchiectasis and bronchiectasis is the predominant primary respiratory disease in the view of the investigator (CT images/CT reports must be available to complete radiological scoring for BSI)
2. History of 2 or more exacerbations in any 12-month period in the preceding 2 years requiring antibiotics and/or steroids
3. Evidence of airflow limitation with an FEV1/FVC ratio less than 0.7 and/or daily mucus expectoration
4. Have either:
4.1. Less than 20 pack-year history of smoking OR
4.2. Greater than 20 pack-year history of smoking with an FEV1 >79% predicted (to exclude COPD)
5. For patients taking ICS, LAMA or LABA treatment prior to recruitment, willing to have these treatments changed or stopped
6. Stable bronchiectasis with no exacerbations for 4 weeks prior to baseline
7. Stable dose of oral steroid for 4 weeks prior to baseline (only applicable for patients taking oral steroid as part of standard care)

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Previous inclusion criteria:
1. Adult patients with CT scan confirmed bronchiectasis and bronchiectasis is the predominant primary respiratory disease in the view of the investigator (CT images / CT reports must be available to complete radiological scoring for BSI)
2. History of 3 or more exacerbations in the preceding 12 months requiring antibiotics and/or steroids
3. Evidence of airflow limitation with an FEV1/FVC ratio less than 0.7 and/or daily mucus expectoration
4. Have less than 20 pack-year history of smoking
5. Willing to have baseline treatment altered / ICS etc. stopped if already taking
6. Stable for 4 weeks prior to baseline
7. Stable dose of oral steroid for 4 weeks prior to baseline (only applicable for patients taking oral steroid as part of standard care)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment

Key exclusion criteria

Current exclusion criteria as of 05/09/2022:
1. Cystic fibrosis-related bronchiectasis
2. Where bronchiectasis is not the main disease or there are contraindications to ICS withdrawal
3. Predominant COPD or asthma. (Patients who have a historical diagnosis of asthma and/or COPD but where the investigator has sufficient evidence to refute these diagnoses can still be included. This is to be documented in the source and the CRF.)
4. Indication to remain on ICS (e.g. asthma, COPD, allergic bronchopulmonary aspergillosis, inflammatory bowel disease) or known intolerance to any of the trial drugs or their ingredients
5. Patients with galactose intolerance, total lactase deficiency or glucose-galactose malabsorption
6. Inability to perform spirometry or quality of life questionnaires
7. Patients who are:
7.1. Pregnant
7.2. Breastfeeding
7.3. Of childbearing potential with a positive urine pregnancy test prior to starting trial IMP
7.4. Male or female of childbearing potential unwilling to use contraception throughout the trial (postmenopausal women must be amenorrhoeic for at least 12 months to be considered of non-childbearing potential).
8. Anyone with cognitive impairment who may not be able to consent
9. Those who do not speak English or cannot comply with trial procedures
10. Any potential participant who the investigator believes will not be able to complete the study visits and procedures
11. A history of allergy or hypersensitivity to any corticosteroid, anticholinergic/muscarinic receptor antagonist, β2-agonist, lactose/milk protein or magnesium stearate or a medical condition such as narrow-angle glaucoma, prostatic hypertrophy or bladder neck obstruction that, in the opinion of the investigator contraindicates study participation
12. Use of acute antibiotics or systemic steroids within 4 weeks of baseline
13. Malignancy diagnosed within 5 years of the first trial medication administration where the investigator feels the trial may be affected by recurrence or progression of the malignancy (e.g. patients with stable breast cancer, current prostate cancer or 'expected curative' cancer surgery may not be excluded at the investigator's discretion)
14. Administration of an investigational agent within 30 days of first dose of trial medication

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Previous exclusion criteria:
1. Cystic fibrosis related bronchiectasis
2. Where bronchiectasis is not the main disease or there are contraindications to ICS withdrawal
3. Predominant COPD or asthma (Patients who have a historical diagnosis of asthma and/or COPD but where the investigator has sufficient evidence to refute these diagnoses can still be included. This is to be documented in the source and the CRF)
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(postmenopausal women must be amenorrhoeic for at least 12 months to be considered of non-childbearing potential).
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11. Use of acute antibiotics or systemic steroids within 4 weeks of baseline

Date of first enrolment
01/06/2021

Date of final enrolment
31/07/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Liverpool University Hospitals NHS Foundation Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre

Central Manchester University Hospitals NHS Foundation Trust
Trust Headquarters, Cobbett House
Manchester Royal Infirmary
Oxford Road
Manchester
United Kingdom
M13 9WL

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

Study participating centre
Northumbria Healthcare NHS Foundation Trust
North Tyneside General Hospital
Rake Lane
North Shields
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NE29 8NH

Study participating centre
Royal Papworth Hospital NHS Foundation Trust
Papworth Road
Cambridge Biomedical Campus
Cambridge
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CB2 0AY

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Study participating centre

South Tyneside and Sunderland NHS Foundation Trust
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
Kirklands Hospital
Fallside Road
Bothwell
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G71 8BB

Study participating centre
Medway NHS Foundation Trust
Medway Maritime Hospital
Windmill Road
Gillingham
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ME7 5NY

Study participating centre
The Princess Alexandra Hospital
Hamstel Road
Harlow
United Kingdom
CM20 1QX

Study participating centre
Royal Albert Edward Infirmary
Wigan Lane
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WN1 2NN

Sponsor information

Organisation

Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from dibs@newcastle.ac.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		02/06/2025	15/08/2025	Yes	No
Protocol article		10/08/2023	14/08/2023	Yes	No
HRA research summary			28/06/2023	No	No