VitalBE

Value of inhaled treatment with aztreonam lysine in bronchiectasis

Participant Pathway

PARTICIPANT IDENTIFICATION

Potential participants may be identified through any or all of the following:

- Secondary Care via specialist respiratory clinics or pulmonary rehabilitation classes
- Local Bronchiectasis databases where participants given consent to be contacted for future research projects, e.g. EMBARC registry
- Scottish Health Research Register (SHARE)
- Primary Care Networks. These participants will be sent out an invitation letter and bPIS from the GP practice. GP practices will also be asked to display trial posters and bPIS in their waiting rooms.
- Participant identification Centres (PICs)

INCLUSION CRITERIA

- ≥ 18 years of age
- Able to give informed consent
- Clinical diagnosis of Bronchiectasis:
- CT scan of the chest demonstrating bronchiectasis in 1 or more lobes
- A history of at least 3 exacerbations in the previous 12 months
- Bronchiectasis severity index score >4
- *Pseudomonas aeruginosa* or other Gram-negative respiratory pathogen detected in sputum or bronchoalveolar lavage on at least 1 occasion in the previous 12 months
- A sputum sample that is culture or PCR positive for *P. aeruginosa* or other Gram-negative respiratory pathogens sent at the screening visit and within 35 days of randomization. Pre-specified eligible organisms include *Eschericia coli, Haemophilus influenzae, Moraxella catarrhalis, Klebsiella pneumoniae, Proteus mirabilis, Serratia marcescens, Achromobacter, Enterobacter and Stenotrophomonas maltophilia*

EXCLUSION CRITERIA

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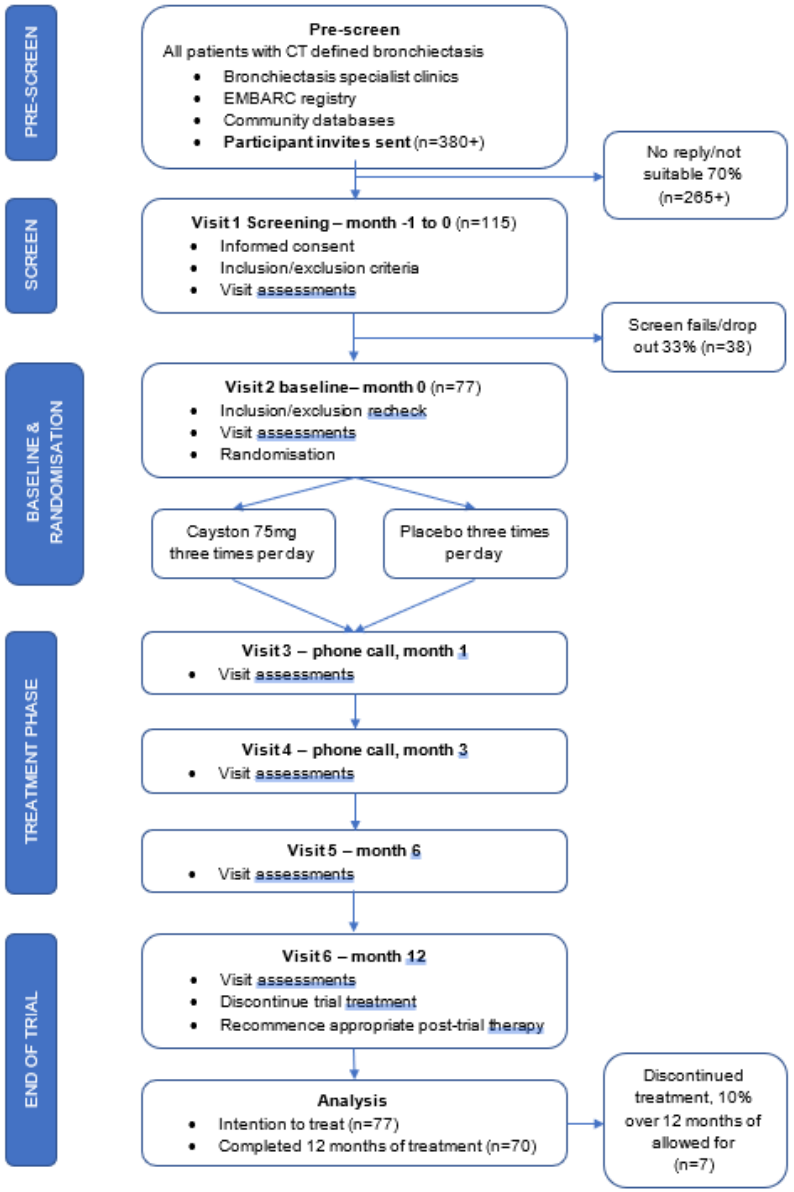
- Participant has cystic fibrosis
- Immunodeficiency requiring replacement immunoglobulin
- Active tuberculosis or nontuberculous mycobacterial infection (defined as currently under treatment or requiring treatment in the opinion of the investigator).
- Recent significant haemoptysis (a volume requiring clinical intervention, within the previous 4 weeks)
- Treatment with inhaled, systemic or nebulized anti-Pseudomonal antibiotics in the 28 days prior to randomization
- Oral macrolides which have been taken for less than 3 months prior to the start of the trial
- Treatment of an exacerbation and receiving antibiotic treatment within 4 weeks prior to randomization
- Primary diagnosis of COPD associated with >20 pack years smoking history
- History of poorly controlled asthma or a history of bronchospasm with inhaled antibiotics
- Pregnant or lactating females
- Participants with FEV_1 <30% predicted value at screening
- Previous history of hypersensitivity to aztreonam, l-lysine, sodium chloride or lactose monohydrate
- Previous history of bronchospasm reported with any inhaled anti-bacterial *
- Glomerular filtration rate (eGFR) below 30ml/min/1.73m^2 or requiring dialysis. This will be determined at screening
- Use of any investigational drugs within five times of the elimination half-life after the last trial dose or within 30 days, whichever is longer
- Unstable co-morbidities (cardiovascular disease, active malignancy) which in the opinion of the investigator would make participation in the trial not in the participant's best interest
- Long term oxygen therapy
- Women of child-bearing age or male partners of women of child-bearing age and not practicing a method of acceptable birth control


PRE-SCREEN
Pre-screen
All patients with CT defined bronchiectasis
Bronchiectasis specialist clinics
EMBARC registry
Community databases
Participant invites sent (n=380+)
No reply/not suitable 70% (n=265+)
SCREEN
Visit 1 Screening – month -1 to 0 (n=115)
Informed consent
Inclusion/exclusion criteria
Visit assessments
Screen fails/drop out 33% (n=38)
BASELINE & RANDOMISATION
Visit 2 baseline– month 0 (n=77)
Inclusion/exclusion recheck
Visit assessments
Randomisation
Cayston 75mg three times per day
Placebo three times per day
TREATMENT PHASE
Visit 3 – phone call, month 1
Visit assessments
Visit 4 – phone call, month 3
Visit assessments
Visit 5 – month 6
Visit assessments
END OF TRIAL
Visit 6 – month 12
Visit assessments
Discontinue trial treatment
Recommence appropriate post-trial therapy
Analysis
Intention to treat (n=77)
Completed 12 months of treatment (n=70)
Discontinued treatment, 10% over 12 months of allowed for (n=7)

Pre-screen

All patients with CT defined bronchiectasis

- Bronchiectasis specialist clinics
- EMBARC registry
- Community databases
- Participant invites sent (n=380+)

Of the invites sent it is anticipated no reply/not suitable 70% (n=265+)

All participants given bPIS either at a clinic or sent by post to be recorded on the Screening log.

Positive responses sent full PIS and screening visit arranged

Screening

Visit 1 – Screening Visit (n=115)

- Informed consent
- Inclusion/exclusion criteria
- Visit assessments

All participants who are consented to be recorded on Enrolment and Randomisation log.

A screen fail /drop out rate of 33% is anticipated (n=38)

Screen fails may be invited for rescreening.

Baseline & Randomisation

Visit 2 – Baseline (n = 77)

- Inclusion/exclusion criteria recheck
- Visit assessments
- Randomisation

Participants randomised to either Cayston 75 mg three times per day or Placebo 3 times per day

TREATMENT PHASE

Visit 3 – phone call, Month 1 (4 weeks)

- Visit assessments

Visit 4 – phone call, Month 3 (12 weeks)

- Visit assessments

Visit 5 – in person, Month 6 (24 weeks)

- Visit assessments

END OF TRIAL

Visit 6 – in person, Month 12 (48 weeks)

- Visit assessments
- Discontinue trial treatment
- Recommence appropriate post-trial therapy

Analysis

- Intention to treat (n=77)
- Completed 12 months of treatment (n=70)