Vital BE

Value of inhaled treatment with aztreonam lysine in bronchiectasis

Visits

All Visits

Participant Transport

Participants should be offered a taxi to bring them to the appointment and return them home. This has been proven to help recruitment and retention of trial participants.

- An account should be set up with a local taxi company for this as per local practice.
- Alternatively, participants wishing to use public transport should have their cost reimbursed or petrol paid. This should be done as per local procedure e.g. from petty cash or by completing a travel expense form.

Participant Identity

Participant identity should be checked at each visit. Some examples of identification are listed below:

- Current Passport
- Current photographic driving licence
- Current matriculation card
- Young person's or senior citizen's railcard
- Proof of Address
- National Insurance Card
- CHI Number/Medical Card

All Visits

Participant trial ID

All participants consented to the trial should be allocated a participant ID number.

Participant ID numbers are made up of four numbers:

- First two numbers to indicate the site and
- Last two indicate the participant number at that site. e.g. 01-001 is the first participant at site one.
- Use participant ID numbers in order
- ensure site ID is correct for your site.

If participant fails screening, and does not go on to randomisation, their participant ID number should not be re-used.

Worksheets

Worksheets will be provided to facilitate data collection

Their use is not mandatory

If worksheets are used to record source data, they must be filed in the medical notes.

All Visits

Trial Matrix

Type of visit	Screening V1	Baseline and randomization V2	Follow-up phone call V3	Follow-up phone call V4	Follow-Up Assessments V5	Final visit Assessments V6	Unscheduled visit Assessments
Timeline	Month -1 to 0	Up to 35 days after screening	Month 1 (4 weeks) (+/- 2 Weeks)@	Month 3 (12 weeks) (+/- 2 Weeks)@	Month 6 (24 weeks) (+/-2 Weeks)@	Month 12 (48 weeks) (+/- 2 weeks)@	As Required
Informed Consent	X						
Inclusion/Exclusion Criteria Check	X	X					
Medical History	X						
Record Concomitant Medications	X	X	X	X	X	X	X
Physical Examination	X						X
Height	X						
Weight	X						
Check Vital Signs^	X	X			X	X	X
ECG	X						
Full blood count	X						
Urea and electrolytes	X						
Liver function tests	X						
Sputum samples for C+S and antibiotic resistance testing#	X				X	X	X
Research Blood Sample *		X			X	X	X
Sputum sample for storage[b]		X			X	X	X
Standard Spirometry	X	X			X	X	X
Quality of life bronchiectasis questionnaire&		X	X&	X&	X&	X	X
SGRQ		X	X	X	X	X	
BHQ		X	X	X	X	X	X
Exacerbation recording		X	X	X	X	X	X
Viral nasal swab		X				X	X
Supervised first dose of trial medication		X					
Safety Spirometry Post trial medication		X					
Bronchiectasis severity index and components e.g MRC dyspnoea score	X						
Pregnancy Testing If Applicable	X	X			X	X	X
Record Adverse Events		X	X	X	X	X	X
Randomisation		X					
Dispense Trial Drugs**		X[a]	X[a]	X[a]	X[a]		
Courier drugs to participant			X	X			
Drug Return And Compliance Check			X	X	X	X	
Randomisation		X					
Dispense Trial Drugs**		X[a]	X[a]	X[a]	X[a]		
Courier drugs to participant			X	X			
Drug Return And Compliance Check			X	X	X	X	

Visit 1 – Screening (approx. 2 – 3 hours)

- Establish participant identity
- Informed consent
- Medical history including concomitant medication check
- Physical examination (doctor)
- Height & weight
- Vital Signs
- ECG
- Full blood count, urea & electrolytes and liver function tests (local NHS labs)
- Serum pregnancy test, if required (local NHS labs)
- Research blood samples
- Sputum sample for *P. aeruginosa* testing (local NHS labs)
- Spirometry
- Bronchietasis severity index
- Questionnaires

- ECG and all NHS lab results to be reviewed by doctor on Delegation Log
- If found to be ineligible, all procedures except blood and sputum sample collection should be completed, if participant agreeable.
- Where an ineligible participant's medical condition or concomitant medications change sufficiently so that they are deemed potentially eligible for the trial, they may be rescreened.
  - Must receive a new copy of the PIS, be re-consented and given a new Participant ID number.
- Details of **all** participants **consented** to the trial to be recorded on the Enrolment and Randomisation Log.

Arranging next visit – timelines (inclusion criteria)

Ensure that the following timelines will be met on the day of visit 2:

- Visit must be arranged within 35 days of Visit 1
- A sputum sample that is culture or PCR positive for *P. aeruginosa* or other Gram-negative respiratory pathogens within 35 days prior to visit 2
- History of at least 3 exacerbations in the previous 12 months
- *Pseudomonas aeruginosa* or other Gram-negative respiratory pathogen detected in sputum or bronchoalveolar lavage on at least 1 occasion in the previous 12 months
- Ensure a negative serum pregnancy test **at screening** for women of childbearing potential

Arranging next visit – timelines (exclusion criteria)

Ensure that the following timelines will be met on the day of visit 2:

- 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
- Treatment of an exacerbation and receiving antibiotic treatment within 4 weeks prior to randomization.
- Pregnant or lactating females.

Visit 2 Baseline/Randomisation (approx. 2 hours)

- Establish participant identity
- Confirm continued consent
- Inclusion/exclusion criteria check
- Adverse event recording
- Concomitant medication check
- Vital signs
- Urine pregnancy test, if required
- Exacerbation recording
- Sputum samples
- Eligibility confirmed by delegated doctor
- Randomisation
- IMP Dispensed
- First Dose
- Sputum samples
- Questionnaires

- All NHS lab results must be reviewed by doctor on Delegation Log
- Eligibility to be assessed once all blood and sputum results have been reviewed
- Assessment of eligibility must be carried out by doctor on Delegation Log

- Date of randomisation should be added to the Enrolment and Randomisation Log.

Trial Medication

Trial medication is given in 28 day cycles with participants taking 28 days of trial medication followed by 28 days not taking trial medication for the 12 months of the trial.

See Trial Medication Guide for mixing Aztreonam/placebo 75mg with the saline.

Nebuliser and handset

Each participant will be given an eFlow nebuliser machine and Altera nebuliser handset which must be used with the trial medication.

The nebuliser machine and handsets must only be used with the trial medication and must not be used for other inhaled medications. The trial medication must only be taken via the supplied nebuliser and handset and not with any other nebuliser machine.

The nebuliser machine will be supplied to the research team and should be given to the participant after randomisation.

A new nebuliser handset should be used for each 28-day cycle of treatment, these will be supplied along with their trial medication from pharmacy. Handsets should be disposed of at home by the participant or in clinical waste at the hospital via the research team. They should not be returned to pharmacy.

Participants must be shown how to use the nebuliser and handset during the administration of the first dose of trial medication at visit 2 see Trial Medication Guide and video “Mixing and storing your Cayston” (from 1 min 11 secs to 2 min 46 secs only)

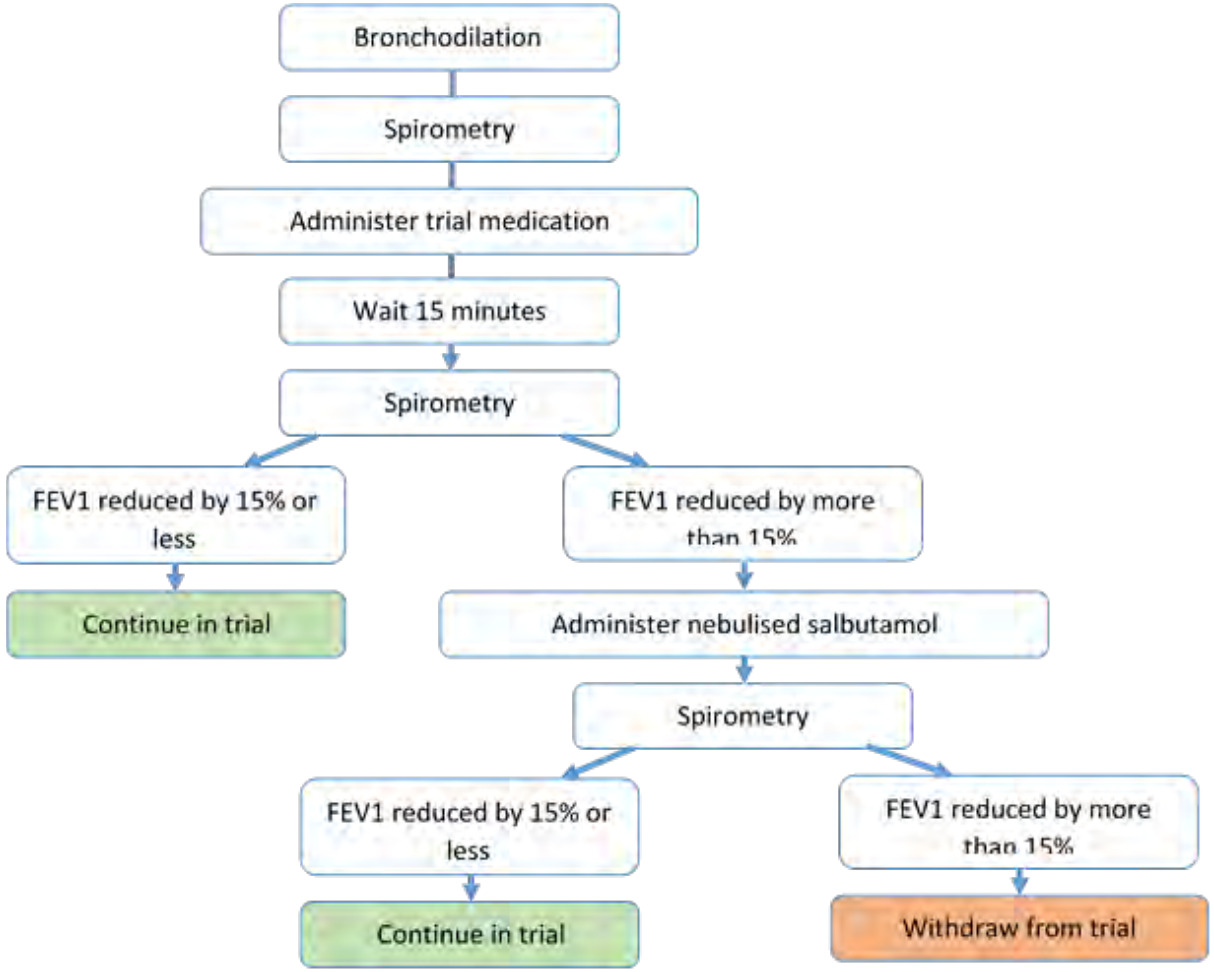
First dose of trial medication

It is possible that participants may experience bronchospasm with the trial medication therefore participants will receive their first dose of trial medication at visit 2. Research staff could keep the empty vial from the first dose in the box for accountability purposes.

The first dose of trial medication should be given to the participant at visit 2.

After Randomisation collect the allocated trial medication from the Clinical Trial Pharmacy

Ask the participant to set up their nebuliser system as per video and trial medication guide



Participant Pack:

When randomised participants should be given the following to take away:

- Trial bag
- Trial Medication – 28 days' supply, (3 packs)(first dose taken at this visit)
- Nebuliser controller unit
- Nebuliser handset
- Trial Medication Guide
- Contact Card
- Participant Appointment Sheet
- Copy of Informed Consent Form
- Questionnaires – QoL-B to complete between Visits 2 and 5

Visit 3 – Month 1 (4 weeks) & Visit 4 – Month 3 (12 weeks) Telephone call

- Establish participant identity
- Confirm continued consent
- Adverse event recording
- Concomitant medication check
- Exacerbation recording
- Questionnaires

Visit 5 – Month 6 (24 weeks)

- Establish participant identity
- Confirm continued consent
- Adverse event recording
- Concomitant medication check
- Vital Signs
- Urine pregnancy test, if required
- Sputum
- Spirometry
- Exacerbation recording
- Research Blood Sample
- Return of used/unused IMP vials
- QoL-B questionnaires completed between Visit 2 -5
- Questionnaires

Visit 6 – Month 12 (48 weeks)

- Establish participant identity
- Confirm continued consent
- Adverse event recording
- Concomitant medication check
- Exacerbation recording
- Vital signs
- Urine pregnancy test, if required
- Research Blood Sample
- Sputum
- Spirometry
- Return of used/unused IMP vials
- QoL-B questionnaires completed between Visit 5 -6
- Questionnaires

Unscheduled visit (as required)

- Establish participant identity
- Confirm continued consent
- Adverse event recording
- Concomitant medication check
- Exacerbation recording
- Vital signs
- Urine pregnancy test, if required
- Research blood sample
- Sputum
- Spirometry
- Questionnaires