VitalBE

Value of inhaled treatment with aztreonam lysine in bronchiectasis

BACKGROUND and OVERVIEW

BACKGROUND

- Bronchiectasis is a common disease with no licensed therapies
- Previous studies of inhaled antibiotics have probably failed because the patients were too “mild”
- The VitalBE study has been designed to test an established antibiotic in the “right” population

IMP

- Aztreonam is a beta-lactam antibiotic with broad spectrum activity against the pathogens causing disease in bronchiectasis

- It is a licensed treatment via inhalation for treatment of cystic fibrosis

HYPOTHESIS

12 months treatment with Aztreonam lysine for inhalation will be safe and well tolerated, and will result in a significant increase in the time to first pulmonary exacerbation in participants with bronchiectasis and a history of frequent exacerbations.

PRIMARY OBJECTIVES

To evaluate the safety and tolerability of Aztreonam lysine

- Outcome Measures/Endpoints - Recording of adverse events, serious adverse events and trial treatment withdrawals between groups

- Timepoint(s) - Reported at any time point in the trial

To determine the effect of Aztreonam Lysine on time to first pulmonary exacerbation

- Outcome Measures/Endpoints - Time to first exacerbation

- Timepoint - Single event per participant over 12 months

SECONDARY OBJECTIVES

To determine the effect of Aztreonam lysine on the frequency of exacerbations over 12 months

- Outcome Measures/Endpoints:
  Frequency of exacerbations
- Timepoint(s)
  count data over 12 months

To determine the effect of Aztreonam lysine on quality of life

- Outcome Measures/Endpoints:
  1. St Georges Respiratory Questionnaire
  2. Bronchiectasis Health Questionnaire
  3. Quality of Life Bronchiectasis Questionnaire (QOL-B)
- Timepoint(s)
  Continuous variable

SECONDARY OBJECTIVES cont.

To determine the effect of Aztreonam lysine on pulmonary function

- Outcome Measures/Endpoints - FEV1
- Timepoint(s) - Continuous variables at 0, 6 and 12 months

Change in minimum inhibitory concentration of protocol defined bacteria to aztreonam

- Outcome Measures/Endpoints - MIC
- Timepoint(s) - Baseline, 6 months and 12 months

Monitoring of emergent pathogens

- Outcome Measures/Endpoints - Sputum culture results (emergent pathogen is defined as a new organism isolated in sputum culture which was not defined at baseline)
- Timepoint(s) - 6 months and 12 months (Visits 5 & 6)

Table 3: Exploratory Objectives and Outcome Measures

Exploratory Objective:	Outcome Measure:	Timepoints measured
To determine the impact of Aztreonam lysine on the time to first exacerbation, including all clinically treated exacerbations	Time to first exacerbation (protocol defined and non-protocol defined)	Up to 12 months
To determine the impact of compliance on the efficacy of Aztreonam lysine	Compliance recorded and repeat measurement of efficacy end-points in those complying with >80% of doses	Compliance assessments at all trial visits
To store blood and sputum samples for future biomarker and molecular microbiology studies	Biomarker measurement Microbiome studies Antibiotic resistance studies	Future work
To determine the effect of Aztreonam lysine on different exacerbation subtypes	Exacerbations subtyped into those associated with viruses, new bacteria or non-infectious exacerbations	Count data over 12 months