Open-Label Phase 2 Trial to Evaluate the Safety and Efficacy of;Aztreonam 75 mg Powder and Solvent for Nebuliser;Solution/Aztreonam for Inhalation Solution (AZLI) in Pediatric;Patients with Cystic Fibrosis (CF) and New Onset Lower Respiratory;Tract Culture Positive for Pseudomonas aeruginosa (PA)

Published: 14-10-2011
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON37937

Source
ToetsingOnline

Brief title
ALPINE (Aztreonam Lysine for Pseudomonas Infection Eradication)

Condition

- Respiratory tract infections

Synonym
Cystic Fibrosis, Lung infection

Research involving
Human

Sponsors and support

Primary sponsor: Gilead Sciences
Source(s) of monetary or material Support: Pharmaceutisch bedrijf

Intervention

Keyword: Aztreonam inhaler, Cystic Fibrosis, Pediatrics, Pseudomonas aeruginosa (PA)

Outcome measures

Primary outcome

The primary objective of this study is to evaluate the proportion of subjects with PA-negative cultures at all time points during a 6-month monitoring period (through Day 196) after cessation of active treatment; microbiological cultures will be obtained at Baseline, Day 28 (end of treatment), Day 56 (1 month after completing AZLI), Day 112 (3 months after completing AZLI), and Day 196 (6 months after completing AZLI). PA-specific antibody titers will be obtained at Baseline, Day 28, and Day 196.

Secondary outcome

Secondary objectives are to evaluate the following:

In subjects >= 6 years of age:

• Change from baseline in FEV1 % predicted at Days 28, 56, 112, and 196;

• Change from baseline in CFQ-R Respiratory Symptoms Score (RSS) at Days 28,

56, 112, and 196.

In all patients:

• Proportion of patients with PA-negative cultures at Days 28, 56, 112 and 196;

• Use of additional (non-study) antipseudomonal antibiotics (as a marker for PA exacerbation);

• Change from baseline in weight, height, and body mass index (BMI) at Days 28, 56, 112, and 196;

In patients < 6 years of age:

• Pharmacokinetics: 1 peak plasma sample will be obtained 1 hour after the first dose of AZLI (Day 1); 1 trough plasma sample will be obtained immediately prior to the last dose of AZLI (Day 28). Plasma aztreonam concentrations at each time point will be summarized (mean, median, standard deviation [SD], minimum, maximum, and number of samples).

Study description

Background summary

Cystic fibrosis (CF) affects an estimated 100,000 people worldwide. In Europe, approximately 29,000 people are estimated to have CF. Approximately 66% of European patients are conservatively estimated to be children (< 18 years of age). CF patients are particularly susceptible to pulmonary infections with organisms such as Pseudomonas aeruginosa (PA), Staphylococcus aureus, Achromobacter species (spp.), Burkholderia spp., Stenotrophomonas maltophilia, and Haemophilus influenzae. Infected patients experience progressive obstruction of the airways and loss of lung function that is due in large part to the inflammatory response to chronic bacterial infection. The most significant bacterial pathogen associated with CF pulmonary disease is PA. PA infection is a significant predictor of mortality and has also been associated with higher rates of pulmonary function decline. In general, pediatric CF patients have a lower incidence of PA airway infection compared to adults.

Initial infection with PA, prior to the development of chronic infection, has been characterized as a window of opportunity for PA eradication. Early and aggressive antibiotic treatment of initial PA infection in young patients with CF has been observed to improve pulmonary function and delay the onset of chronic PA infection, thus increasing survival. As a result, eradication of PA at initial detection is now a treatment strategy used by most CF centers.

Study objective

The purpose of this study is to evaluate whether aztreonam solution for inhalation (AZLI) is safe and effective for the treatment and complete eradication of a lung infection with PA (Pseudomonas aeruginosa) in patients with Cystic Fibrosis (CF) and who are younger than 18 years. People with CF often have lung infections that occur repeatedly and get worse over time. The current treatment with an antibiotic is used to stop or slow down the growth of these bacteria. However the bacterium is not eradicated. The antibiotic may be given orally or i.v., or in the form of an inhalation.
AZLI is an investigative drug for people under the age of 18.
AZLI is registered under the name Cayston ® in Europe and is approved for patients aged 18 years and older who have CF and a lung infection with PA.

Study design

This is an open-label, multi-center study in children (3 months to less than 18 years) with CF and a first fixed lung infection with PA who will be treated 28 days with AZLI inhalation, 3 times daily 75 mg. Participants are followed-up for 6 months after the treatment phase of 28 days to determine whether the PA infection is completely eradicated.
Control visits take place at 4 different timepoints, day 28, day 56, day 112 and day 196. For all subjects blood samples will be taken at visits 2, 3 and 6 and sputum samples will be taken at visits 2, 3, 4, 5 and 6 (or throat swab if sputum cannot be produced). If < 6 years, plasma PK samples will be taken at visits 2 and 3. If 6 years or more, spirometry will be done at all visits. For females of child-bearing potential, urine pregnancy tests will be taken at visits 1, 2, 3 and 4.
The screening phase is variable up to 14 days.
It is possible to complete screening and baseline visits on one day. The maximum duration of the study for participants is approximately 7 months (28 weeks).

AZLI will be taken using the Investigational eFlow® Nebulizer System (eFlow), which is CE marked in the EU and marketed for use with Cayston under the trade name Altera. The eFlow is a reusable device that mixes air with the study drug solution so that it becomes a mist that is inhaled (breathed in). The device works using a porous membrane (thin metal layer with many holes) that vibrates and allows you to inhale AZLI into your lungs. This helps lessen the amount of

drug left in your mouth and throat. AZLI should only be taken using the eFlow. The eFlow must not be used to take any other medication.

Intervention

All patients receive 28 days Aztreonam for inhalation, three times daily 75 Mgr. Depending on the follow-up visit this may be extended up to 32 days.

Study burden and risks

Patients are asked to inhale study medication (AZLI) for 28 days, 3 times a day. Prior to this inhalation a short-acting brochodilatator should be used, which is not always the standard treatment for the patient.
The patient must visit the hospital at least 5 times for follow-up of the study. Each visit will take approximately 3-4 hours.
Besides taking blood samples, completing questionnaires, also **a spirometry could be performed (> 6 years).
Patients who are sexually active must comply with stringent precautions and girls are regularly carried out a pregnancy test.

Contacts

Public
Gilead Sciences

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

• Aged 3 months to less than 18 years.;• Diagnosis of CF as determined by the 1997 CF Consensus Conference criteria: sweat chloride level >= 60 mEq/L by quantitative pilocarpine iontophoresis; or a genotype with 2 identifiable mutations consistent with CF; or an abnormal nasal transepithelial potential difference (NPD), and 1 or more;clinical features consistent with CF.;• Documented new onset of positive lower respiratory tract culture for PA within 30 days of study entry (screening visit) defined as either first lifetime documented PA-positive culture, or PA recovered after at least a 2-year history of PA-negative respiratory cultures (at least 2 cultures per year);• FEV1 >= 80% predicted (for subjects >= 6 years of age).;• Clinically stable with no evidence of significant respiratory symptoms or, if obtained for clinical evaluation, no chest radiograph findings at screening that would require administration of IV antipseudomonal antibiotics, oxygen supplementation, or hospitalization.

Exclusion criteria

• Use of IV or inhaled antipseudomonal antibiotics within 2 years of study entry (screening visit).;• Use of oral antipseudomonal antibiotics within 30 days of study entry (screening visit).;• History of hypersensitivity/adverse reaction to aztreonam, or beta-agonists.;• Use of any investigational drug, or device within 28 days of study entry (screening visit).;• Presence of a condition or abnormality that would compromise the subject*s safety or the quality of study data, in the opinion of the investigator.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-04-2012
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cayston
Generic name:	Aztreonam
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	14-10-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	13-03-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-04-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-08-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-08-2012

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-11-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-01-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-001255-36-NL
CCMO	NL37691.041.11