Randomized, Double-Blind, Phase 3B Trial to Evaluate the Safety and Efficacy of 2 Treatment Regimens of Aztreonam 75 mg Powder and Solvent for Nebulizer Solution / Aztreonam for Inhalation Solution (AZLI) in Pediatric Subjects with Cystic Fibrosis (CF) and New Onset Respiratory Tract Pseudomonas aeruginosa (PA) Infection/Colonization

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To evaluate the safety and efficacy of a 14-day course vs a 28 day course of AZLI 75 mg three times a day (TID) in subjects with new onset PA respiratory tract colonization/infection as determined by PA eradication over a 28-day post treatment...

Ethical review	Approved WMO
Status	Completed
Health condition type	Respiratory disorders congenital
Study type	Interventional

Summary

ID

NL-OMON50497

Source
ToetsingOnline

Brief title
ALPINE 2

Condition

- Respiratory disorders congenital
- Bacterial infectious disorders

Synonym
cystic fibrosis, Mucoviscidosis

Research involving
Human

Sponsors and support

Primary sponsor: Gilead Sciences
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Aztreonamlysine, Cystic Fibrosis, Pseudomonas infection

Outcome measures

Primary outcome

To evaluate the safety and efficacy of a 14-day course vs a 28-day course of AZLI 75 mg three times a day (TID) in subjects with new onset PA respiratory tract colonization/infection as determined by PA eradication over a 28-day post-treatment follow-up period.

Secondary outcome

* To evaluate the time from primary eradication to PA recurrence over a 108-week post-treatment follow-up period

* To compare the efficacy of AZLI 75 mg TID for 14 days vs historical pooled tobramycin nebulizer solution (TNS) two times a day (BID) for 28 days as determined by PA eradication over a 28-day post-treatment follow-up period

* To evaluate the time to PA recurrence for a sub-group of subjects matching the population in the TNS ELITE Study over a 108-week post-treatment follow-up

period

Study description

Background summary

Chronic PA infection has devastating consequences for CF patients, in terms of persistent pulmonary symptoms, frequent acute pulmonary exacerbations often requiring hospitalization and treatment with IV antibiotics, and progressive lung function. Prior to the establishment of chronic infection, there is an opportunity to eradicate new onset PA infection with inhaled anti-pseudomonal antibiotic treatment, with the goal of delaying the onset of chronic PA infection. This can preserve lung function, reduce symptom progression, and prolong survival.
The PA eradication rates in previous study have demonstrated the ability of a 28-day treatment course of AZLI to eradicate new onset PA infection, with rates comparable to other regimens of inhaled antibiotics.
If the 2 treatment arms are shown to be similar in the ability to eradicate new onset PA, this will support shorter treatment duration for initial eradication treatment with AZLI, and will be of benefit to pediatric CF patients (and parents/caregivers) in terms of reduced treatment burden and improved adherence to this treatment regimen.

Study objective

To evaluate the safety and efficacy of a 14-day course vs a 28 day course of AZLI 75 mg three times a day (TID) in subjects with new onset PA respiratory tract colonization/infection as determined by PA eradication over a 28-day post treatment follow-up period.

Study design

This is a randomized, double-blind, multi-center study in pediatric subjects age 3 months to less than 18 years with CF and newly detected PA respiratory tract colonization/infection. The study schedule will consist of a minimum of 13 visits: Screening, Day 1 (Baseline and Randomization), Day 29, Weeks 6, 8, 16, and at 12 week intervals thereafter through Week 112. Subjects may be screened up to 14 days prior to the Baseline visit to determine eligibility for participation in the study. Screening and Baseline may occur on the same day for subjects.
Initial Eradication Phase (Primary Endpoint):
At the Baseline visit (Day 1), eligible subjects will be randomized to a 28-day course of AZLI 75 mg TID or a 14-day course of AZLI 75 mg TID followed by a 14 day course of placebo TID. Note: For the purpose of this protocol, AZLI and

placebo will both be considered *study drug treatment*. After completing study drug treatment, subjects will be followed through Week 8 for safety and recurrence of PA (cultures obtained at Day 29, Week 6, and Week 8).
Follow-Up Culture Phase:
Following the end of the Initial Eradication Phase, subjects will continue in the Follow-Up Culture Phase, with study visits and PA cultures obtained at week 16 and then every 12 weeks for 112 weeks total study duration.
Re-Treatment Phase:
Subjects with PA recurrence after study drug treatment should be re treated with a standard of care antipseudomonal antibiotic regimen at the discretion of the Investigator.
For the first PA recurrence, subjects will be followed and re-cultured at the end of re treatment, 4 weeks post re-treatment, and every 12 weeks thereafter through Week 112. If subjects have subsequent PA recurrences post re-treatment they will be treated at the Investigator*s discretion and have continued follow-up cultures collected every 12 weeks through Week 112.
The total study period will be 112 weeks (4 weeks study drug treatment + 4 weeks Initial Eradication Phase + 104 weeks Follow Up Culture Phase).

Intervention

There is a 50% chance to receive AZLI for 28 days and a 50% chance to receive AZLI for 14 days and placebo for another 14 days.

Study burden and risks

The sudy drug and study procedures are associated with certain risks. These are described in the ICF. The study drug and the study procedures and the combination thereof, can also lead to other, unknown risks. The subjects are carefully monitored. If necessary, the study drug dosage will be decreased or administration wil be stopped.

Contacts

Public
Gilead Sciences

Lakeside Drive 333
Foster City 94404
US
Scientific
Gilead Sciences

Lakeside Drive 333

Foster City 94404
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Male or female aged 3 months to less than 18 years
* Diagnosis of CF as determined by the 2008 CF Consensus Conference criteria:
o Sweat chloride level * 60 mEq/L by quantitative pilocarpine iontophoresis;
o or a genotype with 2 identifiable mutations consistent with CF;
o or an abnormal nasal transepithelial potential difference (NPD), and 1 or more clinical features consistent with CF
* Documented new onset of positive respiratory tract culture for PA within 30 days of Screening 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 who can reliably perform spirometry assessments)
* Clinically stable with no evidence of either acute significant respiratory symptoms 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 Screening
* Use of oral antipseudomonal antibiotics for a respiratory event within 30 days of study entry (Screening visit)
* History or intolerance to inhaled short acting *2 agonists
* History of lung transplantation

* Current requirement for daily continuous oxygen supplementation or requirement of more than 2 L/minute at night
* Hospitalization for a respiratory event within 30 days prior to Screening
* Changes in bronchodilator, corticosteroid, dornase alfa, or hypertonic saline medications within 7 days prior to Screening; for subjects on a stable regimen of hypertonic saline (28 days on/28 days off), beginning or ending a cycle of hypertonic saline is allowed
* Changes in physiotherapy technique or schedule within 7 days prior to Screening
* Abnormal renal or hepatic function results at most recent test within the previous 12 months, defined as
o AST or ALT >5 times upper limit of normal (ULN), or
o Serum creatinine > 2 times ULN for age
* Presence of a condition or abnormality that would compromise the subject*s safety or the quality of the study data, in the opinion of the Investigator
* Known hypersensitivity to aztreonam, its metabolites, or formulation excipients in AZLI

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	15-11-2018
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AZLI 75 mg
Generic name:	Aztreonam 75 mg
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	29-08-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-05-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-11-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-01-2019
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-01-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-02-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2016-002749-42-NL
CCMO	NL60140.078.17

Study results

Date completed: 23-09-2021

Results posted: 01-04-2022

First publication
24-02-2022