An Open-Label, Randomized, Phase 3 Trial to Evaluate the Efficacy and Safety of Aztreonam 75 mg Powder and Diluent for Nebuliser Solution (AZLI) versus Tobramycin Nebuliser Solution (TNS) in an Intermittent Aerosolized Antibiotic Regimen, in subjects with Cystic Fibrosis followed by an Open Label, Single Arm Extension

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The primary objective of this study is to assess the comparative safety and efficacy ofAztreonam Lysine for Inhalation (AZLI) and Tobramycin Nebuliser Solution (TNS) in adultand pediatric cystic fibrosis (CF) patients aged 6 years or older with...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON35394

Source
ToetsingOnline

Brief title
GS-US-205-0110

Condition

- Bacterial infectious disorders
- Congenital respiratory tract disorders

Synonym
Cystic Fibrosis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: antibiotics, efficacy and safety, lunginfection, patients with Cystic Fibrosis

Outcome measures

Primary outcome

The primary study endpoint was change in patient-reported respiratory symptoms

between

Days 0 and 28, as determined by the CFQ-R respiratory domain.

The primary efficacy endpoint is the relative change in FEV1 percent predicted

at Day 28 compared to baseline.

Secondary outcome

Secondary endpoints

The key secondary endpoints are:

- Change from baseline in the Cystic Fibrosis Questionnaire - Revised (CFQ-R)

Respiratory Symptoms Scale at Day 28

- Relative change from baseline in FEy1 percent of predicted at Week 20 (end of

last treatment course of AZLI or TNS)

- Use of additional (non-protocol specified) antipseudomonal antibiotics during

the course of the study

- Hospitalizations during the course of the study

- Change in PA CFUs in sputum at the end of each on-drug cycle Additional

efficacy endpoints to be evaluated are:

- Changes from baseline in FEV1 , FVC and FEF 25-75 at each study visit

- Change from baseline in other domains as assessed by the CFQ-R at each visit

- Changes from baseline in weight and Body Mass Index (BMI) at each visit

- Missed school/work days during the course of the study

- Treatment Satisfaction Questionnaire for Medication (TSQM) at Day 28 and

either Day 140 or ET

Study description

Background summary

CF patients are particularly susceptible to pulmonary infections with organisms including Pseudomonas aeruginosa (PA),
PA-infected patients also experience episodes of acute pulmonary exacerbation, which is characterized by worsening respiratory symptoms and an acute decline in lung function. The central role of PA in CF lung disease has led to testing of intensive therapy with antipseudomonal antibiotics to suppress infection."
In patients with well-established infections,
this approach will lead to decreases in sputum PA density. Although these decreases are usually short lived, lung function benefits from antibiotic therapy are maintained over extended periods of time. 7

Study objective

The primary objective of this study is to assess the comparative safety and efficacy of
Aztreonam Lysine for Inhalation (AZLI) and Tobramycin Nebuliser Solution (TNS)

in adult
and pediatric cystic fibrosis (CF) patients aged 6 years or older with pulmonary Pseudomonas aeruginosa (PA) infection

Study design

This is a Phase 3, open-label, randomized, parallel group, multicenter study to be conducted
at approximately 50 centers in Europe. If needed in order to complete enrollment,
approximately 10 additional study centers within Europe, or in the US, Canada and Australia
may be added. The total study period will be 26 weeks with 9 scheduled clinic visits (see
Figure 1). Visit 1 will begin a 14-day screening period. At Visit 2, qualifying patients will
be randomly assigned to treatment.
Treatment will be started at Visit 2 with either AML or TNS. Patients will return on Day 14
of their first course for Visit 3 and on Day 28 for Visit 4. After completion of Visit 4,
patients will return every 28 days for Visits 5 through 9.

Intervention

- Three cycles of AML 75 mg TID for 28 days, followed by no treatment for 28 days
- Three cycles of TNS 300 mg BID for 28 days, followed by no treatment for 28 days

Study burden and risks

Burden and risk will be in comparison to standard of therapy. In the standard of therapy there will also be long function tests and medication to be administered.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Subjects must meet all of the following inclusion criteria to be eligible for participation in the randomized portion of this study.
* Males or females aged 6 years and older
* Subjects with CF as diagnosed by one of the following:
* Documented sweat chloride * 60 mEq/L by quantitative pilocarpine iontophoresis test, or
* Documented sweat sodium * 60 mmol/L, or
* Two well characterized genetic mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, or
* Abnormal nasal potential difference with accompanying symptoms characteristic of CF
* Documented PA in an expectorated sputum or throat swab culture within 3 months prior to Visit 1 or at Visit 1
* Subjects must be able to provide written informed consent/assent prior to any study related procedures; parent/guardian must be able to give written informed consent as necessary prior to any study related procedure
* Subjects must have received previous treatment with aerosolized antibiotics without demonstration of drug intolerance

* FEV1 * 75% predicted at Visit 1
* Ability to perform reproducible pulmonary function tests
* Chest radiograph at Visit 1 without significant acute findings (e.g., infiltrates [lobar or diffuse interstitial], pleural effusion, pneumothorax); or chest radiograph or MRI obtained within the 180 days prior to Visit 1 without acute findings and no significant intercurrent illness; chronic, stable findings (e.g., chronic scarring or atelectasis) are allowed

Exclusion criteria

* Current use of oral corticosteroids in doses exceeding the equivalent of 10 mg prednisone a day or 20 mg prednisone every other day
* History of sputum or throat swab culture yielding B. cepacia in the previous 2 years
* Current requirement for daily continuous oxygen supplementation or requirement for more than 2 L/minute at night
* Administration of any investigational drug or device within 28 days of Visit 1 or within 6 half-lives of the investigational drug (whichever is longer)
* Known local or systemic hypersensitivity to monobactam antibiotics
* Known allergies/intolerance to tobramycin
* Inability to tolerate inhalation of a short acting *2 agonist
* Changes in or initiation of chronic azithromycin treatment within 28 days prior to Visit 1
* Administration of antipseudomonal antibiotics by inhalation, intravenous or oral routes within the 14 days prior to Randomization/Visit 2
* Changes in antimicrobial, bronchodilator (BD), dornase alfa, or corticosteroid medications within 7 days prior to Visit 1
* Changes in physiotherapy technique or schedule within 7 days prior to Visit 1
* History of lung transplantation
* Abnormal renal or hepatic function or serum chemistry at Visit 1, defined as:
* AST, ALT > 5 times upper limit of normal range (ULN)
* Creatinine > 2 times ULN
* Positive pregnancy test at Visit 1; all women of childbearing potential will be tested
* Female of childbearing potential who is lactating or is not (in the opinion of the investigator) practicing an acceptable method of birth control; female subjects who utilize hormonal contraceptives as one of their birth control methods must have used the same method for at least 3 months before study dosing
* Any serious or active medical or psychiatric illness, which in the opinion of the investigator, would interfere with subject treatment, assessment, or compliance with the protocol

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-12-2008
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aztreonam Lysine
Generic name:	Aztreonam
Product type:	Medicine
Brand name:	Tobi
Generic name:	Tobramycine Nebuliser solution
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	24-04-2008
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	10-06-2008
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	26-11-2008
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	27-01-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	30-01-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	10-06-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	16-07-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	06-10-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	02-12-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	12-03-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	12-04-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	27-09-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2007-004277-26-NL
CCMO	NL22498.098.08