Clinical trial results:
Expanded Access Program for Aztreonam Lysine for Inhalation in Canadian Patients with Cystic Fibrosis and Pseudomonas aeruginosa Airway Infection Who Have Limited Treatment Options and are at Risk for Disease Progression

Summary

EudraCT number	2015-000397-36
Trial protocol	Outside EU/EEA
Global end of trial date	27 November 2012

Results information

Result version number	v1 (current)
This version publication date	22 March 2016
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	EA-US-205-0122

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00989807
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 November 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2012
Global end of trial reached?	Yes
Global end of trial date	27 November 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to provide expanded access to AZLI 75 mg prior to its commercial availability and establishment of reimbursement programs through Provincial Ministries of Health to patients in Canada with CF and PA airway infection who have limited treatment options and are at risk for disease progression.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 February 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 45
Worldwide total number of subjects	45
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	3
Adults (18-64 years)	41
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Canada. The first participant was screened on 08 February 2010. The last study visit occurred on 27 November 2012.

Pre-assignment

Screening details:

45 participants were screened.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All participants

Arm description:

Aztreonam for inhalation solution (AZLI) 3 times daily in 56-day cycles (28 days on treatment followed by 28 days off treatment).

Arm type	Experimental
Investigational medicinal product name	Aztreonam for inhalation solution
Investigational medicinal product code	
Other name	AZLI, Cayston®
Pharmaceutical forms	Powder for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

AZLI 75 mg administered 3 times daily usung the eFlow nebulizer

Number of subjects in period 1	All participants
Started	45
Completed	34
Not completed	11
Adverse event, non-fatal	3
Participant request to discontinue	3
Not specified	3
Participant non-compliance	2

Baseline characteristics

Reporting groups	
Reporting group title	All participants
Reporting group description:	
Aztreonam for inhalation solution (AZLI) 3 times daily in 56-day cycles (28 days on treatment followed by 28 days off treatment).	

Reporting group values	All participants	Total	
Number of subjects	45	45	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	32.8		
standard deviation	± 12.65	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	20	20	
Race Units: Subjects			
Caucasian	40	40	
Asian or Pacific Islander	1	1	
Other	4	4	
FEV1 % predicted			
FEV1 % predicted is defined as FEV1 % of the patient divided by the average FEV1 % in the population for any person of similar age, sex and body composition.			
Units: percentage of FEV1 % predicted			
arithmetic mean	41.73		
standard deviation	± 17.376	-	

End points

End points reporting groups

Reporting group title	All participants

Reporting group description:

Aztreonam for inhalation solution (AZLI) 3 times daily in 56-day cycles (28 days on treatment followed by 28 days off treatment).

Primary: Percentage of participants experiencing any serious adverse event

End point title	Percentage of participants experiencing any serious adverse event[1]

End point description:

End point type	Primary

End point timeframe:

From date of first dose to study discontinuation (average 73 weeks) plus 30 days

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed.

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: percentage of participants				
number (not applicable)	55.6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From date of first dose to study discontinuation (average 73 weeks) plus 30 days

Adverse event reporting additional description:

All AEs are reported by system order class and preferred term as determined by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	All participants

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Per protocol, non-serious adverse events were not collected in this expanded access study.

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 45 (55.56%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Lung transplant			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Distal intestinal obstruction syndrome			

subjects affected / exposed	2 / 45 (4.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Lung disorder				
subjects affected / exposed	13 / 45 (28.89%)			
occurrences causally related to treatment / all	0 / 31			
deaths causally related to treatment / all	0 / 1			
Infective pulmonary exacerbation of cystic fibrosis				
subjects affected / exposed	7 / 45 (15.56%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 0			
Lung infection pseudomonal				
subjects affected / exposed	3 / 45 (6.67%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 45 (4.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Chronic respiratory failure				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystic fibrosis lung				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia cytomegaloviral				

subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia escherichia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory tract infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 45 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported