



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 using 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 standard deviation | 32.8 ± 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 standard deviation | 41.73 ± 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