



Clinical trial results:

Aztreonam for inhalation for the treatment of acute exacerbations in cystic fibrosis. An open-label, randomised, cross-over pilot study of AZLI plus intravenous Colistin versus standard dual intravenous therapy.

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2016-002832-34 |
| Trial protocol | GB |
| Global end of trial date | 27 September 2019 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 28 October 2020 |
| First version publication date | 28 October 2020 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | AZLI2016DN001 |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02894684 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Liverpool Heart and Chest Hospital |
| Sponsor organisation address | Thomas Drive, Liverpool, United Kingdom, L17 4LH |
| Public contact | Freddy Frost, Liverpool Heart & Chest Hospital, freddy.frost@lhch.nhs.uk |
| Scientific contact | Freddy Frost, Liverpool Heart & Chest Hospital, 0044 01516001616, freddy.frost@lhch.nhs.uk |

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? | No |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 13 May 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 September 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Is using Cayston plus one standard intravenous antibiotic as effective as two standard intravenous antibiotics in the treatment of an acute chest infections in people with cystic fibrosis?

Protection of trial subjects:

Pragmatic design dovetailed beside standard practice

Background therapy:

Chest physiotherapy, mucolytics, oral corticosteroids.

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 01 January 2017 |
| 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 | United Kingdom: 16 |
| Worldwide total number of subjects | 16 |
| EEA total number of subjects | 16 |

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) | 0 |
| Adults (18-64 years) | 16 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Recruited between January 2017 and January 2019

Pre-assignment

Screening details:

n.a

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 16 |
| Number of subjects completed | 16 |

Period 1

| | |
|------------------------------|------------------------------------|
| Period 1 title | Day 14 comparison (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

| | |
|------------------|---------|
| Arm title | AZLI+IV |
|------------------|---------|

Arm description:

AZLI+IV

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | AZLI+IV |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for concentrate for solution for infusion, Concentrate for nebuliser solution |
| Routes of administration | Inhalation use, Intravenous use |

Dosage and administration details:

TDS

| | |
|------------------|-------|
| Arm title | IV+IV |
|------------------|-------|

Arm description:

IV+IV

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Colistimethate+ one other IV |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for injection |
| Routes of administration | In vitro use |

Dosage and administration details:

As per protocol

| Number of subjects in period 1 | AZLI+IV | IV+IV |
|---------------------------------------|---------|-------|
| Started | 12 | 16 |
| Completed | 12 | 16 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Day 14 comparison |
|-----------------------|-------------------|

Reporting group description: -

| Reporting group values | Day 14 comparison | Total | |
|--|-------------------|-------|--|
| Number of subjects | 16 | 16 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 16 | 16 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 29 | | |
| inter-quartile range (Q1-Q3) | 24.5 to 32.5 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 1 | 1 | |
| Male | 15 | 15 | |

End points

End points reporting groups

| | |
|------------------------------|---------|
| Reporting group title | AZLI+IV |
| Reporting group description: | |
| AZLI+IV | |
| Reporting group title | IV+IV |
| Reporting group description: | |
| IV+IV | |

Primary: Change in FEV1 at Day 14

| | |
|--|--------------------------|
| End point title | Change in FEV1 at Day 14 |
| End point description: | |
| Paired comparison of between treatment differences for change in FEV1 at 14 days | |
| End point type | Primary |
| End point timeframe: | |
| 14 days | |

| End point values | AZLI+IV | IV+IV | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 12 | | |
| Units: % predicted | | | | |
| arithmetic mean (standard deviation) | 13.5 (± 11) | 8.8 (± 10.1) | | |

Statistical analyses

| | |
|---|-----------------------|
| Statistical analysis title | Paired comparison |
| Comparison groups | IV+IV v AZLI+IV |
| Number of subjects included in analysis | 24 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (net) |
| Point estimate | 4.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.1 |
| upper limit | 7.2 |

Secondary: Time to next exacerbation

| | |
|-----------------|---------------------------|
| End point title | Time to next exacerbation |
|-----------------|---------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Time to Next Exacerbation

| End point values | AZLI+IV | IV+IV | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 12 | | |
| Units: Days | 140 | 152 | | |

Statistical analyses

| | |
|----------------------------|----------|
| Statistical analysis title | Log rank |
|----------------------------|----------|

| | |
|-------------------|-----------------|
| Comparison groups | AZLI+IV v IV+IV |
|-------------------|-----------------|

| | |
|---|----|
| Number of subjects included in analysis | 24 |
|---|----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|--------|
| P-value | > 0.05 |
|---------|--------|

| | |
|--------|---------|
| Method | Logrank |
|--------|---------|

Secondary: Change in CFQ-R Respiratory Domain at Day 14

| | |
|-----------------|--|
| End point title | Change in CFQ-R Respiratory Domain at Day 14 |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

14 days

| End point values | AZLI+IV | IV+IV | | |
|---------------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 12 | | |
| Units: CFQ-R out of 100 | | | | |
| median (inter-quartile range (Q1-Q3)) | 11.4 (11.1 to 18.1) | 8.3 (-1.4 to 18.1) | | |

Statistical analyses

| Statistical analysis title | Paired analysis |
|---|-------------------------|
| Comparison groups | AZLI+IV v IV+IV |
| Number of subjects included in analysis | 24 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.73 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Pseudomonas aeruginosa load on Day 14

| | |
|------------------------|---------------------------------------|
| End point title | Pseudomonas aeruginosa load on Day 14 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | 14 days |

| End point values | AZLI+IV | IV+IV | | |
|---------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 16 | | |
| Units: Log10 CFU/ml | | | | |
| median (inter-quartile range (Q1-Q3)) | 3.3 (1.8 to 4.3) | 5.0 (3.2 to 5.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: White cell count at Day 14

| | |
|------------------------|----------------------------|
| End point title | White cell count at Day 14 |
| End point description: | |
| End point type | Secondary |

End point timeframe:

14 days

| End point values | AZLI+IV | IV+IV | | |
|---------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 16 | | |
| Units: 10 ⁹ /ml | | | | |
| median (inter-quartile range (Q1-Q3)) | 12.8 (9.2 to 16.1) | 11.7 (7.9 to 14.6) | | |

Statistical analyses

| Statistical analysis title | Paired comparison |
|---|-------------------------|
| Comparison groups | AZLI+IV v IV+IV |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.73 |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Median difference (net) |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.1 |
| upper limit | 4.5 |

Secondary: C-Reactive Protein at Day 14

End point title C-Reactive Protein at Day 14

End point description:

End point type Secondary

End point timeframe:

14 days

| End point values | AZLI+IV | IV+IV | | |
|---------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 16 | | |
| Units: mg/L | | | | |
| median (inter-quartile range (Q1-Q3)) | 4.0 (4.0 to 5.8) | 4.0 (4.0 to 4.0) | | |

Statistical analyses

| Statistical analysis title | Paired comparison |
|---|-------------------------|
| Comparison groups | AZLI+IV v IV+IV |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4 |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Median difference (net) |
| Point estimate | 4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9 |
| upper limit | 26 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1, 7 and 14

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|------------------|
| Dictionary name | Study dictionary |
|-----------------|------------------|

| | |
|--------------------|---|
| Dictionary version | 1 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | AZLI+IV |
|-----------------------|---------|

Reporting group description: -

| | |
|-----------------------|-------|
| Reporting group title | IV+IV |
|-----------------------|-------|

Reporting group description: -

| Serious adverse events | AZLI+IV | IV+IV | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 16 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | AZLI+IV | IV+IV | |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 12 (50.00%) | 8 / 16 (50.00%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 2 / 16 (12.50%) | |
| occurrences (all) | 0 | 2 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 16 (6.25%) | |
| occurrences (all) | 0 | 1 | |
| Bloating | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 16 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|---|-----------------|-----------------|--|
| disorders | | | |
| Drop in Lung function | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 4 / 16 (25.00%) | |
| occurrences (all) | 3 | 4 | |
| Excessive Cough | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 16 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| MSK pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 16 (6.25%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 16 (6.25%) | |
| occurrences (all) | 2 | 1 | |
| Raised CRP | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 2 / 16 (12.50%) | |
| occurrences (all) | 1 | 2 | |

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