



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
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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
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Arm title	AZLI+IV
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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
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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
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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
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End point description:

End point type	Secondary
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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
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Comparison groups	AZLI+IV v IV+IV
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Number of subjects included in analysis	24
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	> 0.05
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Method	Logrank
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Secondary: Change in CFQ-R Respiratory Domain at Day 14

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

End point type	Secondary
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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
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Dictionary used

Dictionary name	Study dictionary
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Dictionary version	1
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Reporting groups

Reporting group title	AZLI+IV
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Reporting group description: -

Reporting group title	IV+IV
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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