Clinical trial results:
Effect of acetazolamide on the incidence of high altitude pulmonary edema at 4559 m

Summary

EudraCT number	2017-005166-22
Trial protocol	AT
Global end of trial date	08 August 2019

Results information

Result version number	v1 (current)
This version publication date	11 November 2019
First version publication date	11 November 2019

Trial information

Trial identification

Sponsor protocol code	M2018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	UK für Anästhesiologie und Intensivmedizin
Sponsor organisation address	Muellner Hauptstr. 48, Salzburg, Austria, 5020
Public contact	Sekretariat, UK für Anästhesiologie und allgemeine Intensivmedizin, 0043 057255 57794, ma.berger@salk.at
Scientific contact	Sekretariat, UK für Anästhesiologie und allgemeine Intensivmedizin, 0043 057255 57794, ma.berger@salk.at

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	25 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 August 2019
Global end of trial reached?	Yes
Global end of trial date	08 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Does acetazolamide reduce the incidence of high altitude pulmoanry edema after rapid and active ascent to 4559 m?

Protection of trial subjects:

Subjects were assessed at least once a day with respect to their physical condition. An investigator was available for the subjects 24 hours per day.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	10 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	13
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

physical fitness (VO2max), history of HAPE

Pre-assignment period milestones

Number of subjects started	22[1]
Number of subjects completed	13

Pre-assignment subject non-completion reasons

Reason: Number of subjects	exclusion after preinvestigation: 9

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 9 dropouts after pre-investigation was completed

Period 1

Period 1 title	High altitude part
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	PL1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

T.I.D.

Arm title	Verum Arm

Arm description:

Acetazolamide

Arm type	Active comparator
Investigational medicinal product name	PR1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

250 mg T.I.D.

Number of subjects in period 1	Placebo	Verum Arm
Started	6	7
Completed	6	7

Period 2	
Period 2 title	Pre-investigation
Is this the baseline period?	Yes[2]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst
Arms	
Are arms mutually exclusive?	Yes
Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	PL1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: T.I.D.	
Arm title	Verum Arm
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	PR1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 250 mg T.I.D.	

Notes:

[2] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: We mixed up the order while entering the data. We entered the high altitude data prior to the baseline investigation data.

Number of subjects in period 2	Placebo	Verum Arm
Started	6	7
Completed	6	7

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Verum Arm
Reporting group description: -	

Reporting group values	Placebo	Verum Arm	Total
Number of subjects	6	7	13
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	7	13
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	57	56	
standard deviation	± 6	± 5	-
Gender categorical Units: Subjects			
Female	1	1	2
Male	5	6	11
High altitude pulmonary edema susceptibility			
History of HAPE was assessed			
Units: Subjects			
HAPE - S	6	7	13

Subject analysis sets	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo	
Subject analysis set title	Verum Arm
Subject analysis set type	Full analysis
Subject analysis set description: Verum Arm	

Reporting group values	Placebo	Verum Arm	
Number of subjects	6	7	
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)	6	7	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	57	56	
standard deviation	± 6	± 5	
Gender categorical Units: Subjects			
Female	1	1	
Male	5	6	
High altitude pulmonary edema susceptibility			
History of HAPE was assessed			
Units: Subjects			
HAPE - S	6	7	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Verum Arm
Reporting group description: Acetazolamide	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Verum Arm
Reporting group description: -	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo	
Subject analysis set title	Verum Arm
Subject analysis set type	Full analysis
Subject analysis set description: Verum Arm	

Primary: Incidence of HAPE

End point title	Incidence of HAPE
End point description:	
End point type	Primary
End point timeframe: 3 days at high altitude	

End point values	Placebo	Verum Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: full numbers	4	3		

Statistical analyses

Statistical analysis title	Incidence HAPE
Comparison groups	Placebo v Verum Arm
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Chi-squared corrected

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: whole study duration	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Verum Arm
Reporting group description: -	

Serious adverse events	Placebo	Verum Arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (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: 1 %

Non-serious adverse events	Placebo	Verum Arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	

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: No adverse events to report.

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