Clinical trial results:
Exercise induced bronchoconstriction in children – a single dose of montelukast as alternative to regular daily doses.

Summary

EudraCT number	2011-003652-39
Trial protocol	DK
Global end of trial date	26 August 2018

Results information

Result version number	v1 (current)
This version publication date	14 February 2023
First version publication date	14 February 2023

Trial information

Trial identification

Sponsor protocol code	30689

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Non-Commercial
Sponsor organisation address	Palle Juul- Jensens Boulevard 99, Aarhus N, Denmark, 8200
Public contact	Karen Schow Jensen, Karen Schow Jensen, +45 61718432, karenschowjensen@gmail.com
Scientific contact	Karen Schow Jensen, Karen Schow Jensen, 61718432 61718432, karenschowjensen@gmail.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?	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?	Yes
Primary completion date	26 August 2018
Global end of trial reached?	Yes
Global end of trial date	26 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will compare the effect of a single dose of montelukast and regular daily use of montelukast in children with exercise induced bronchoconstriction.

Breathing will be measured by a spirometer before exercising and measured again several times after exercising.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards.
Patients could receive an inhaled short-acting beta-agonist for distressing symptoms during or after exercise challenge at the discretion of the investigator.

Background therapy:

Background medicine: inhaled corticosteroid therapy (equivalent to max 400-800mikg budesonide daily or equipotent doses).

Evidence for comparator: -

Actual start date of recruitment	01 March 2013
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	Denmark: 19
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	7
Adolescents (12-17 years)	12

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening criteria: Proven exercise-induced asthma with a decrease in FEV1 of >12%
Number of subjects screened: 44
Subjects were excluded during screening because they did not prove to have exercise-induced asthma with a decrease in FEV1 of >12% at the screening test

Pre-assignment period milestones

Number of subjects started	19
Number of subjects completed	19

Period 1

Period 1 title	Period 1 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Subjects were randomised to receive placebo for 7 days in the evening and a morning placebo dose the last day in treatment period 1 or treatment period 2 or treatment period 3 in a counterbalanced order.

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Placebo: placebo 7 days in the evening and a morning placebo dose the last day

Arm title	Single dose of montelukast

Arm description:

Subjects were randomised to receive placebo for 7 days in the evening and a morning single dose of montelukast the last day in treatment period 1 or treatment period 2 or treatment period 3 in a counterbalanced order.

Arm type	Experimental
Investigational medicinal product name	montelukast, single
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Single dose of montelukast: placebo 7 days in the evening and a morning dose of montelukast the last day

Arm title	Montelukast

Arm description:

Subjects were randomised to receive montelukast for 7 days in the evening and a morning dose of placebo the last day in treatment period 1 or treatment period 2 or treatment period 3 in a counterbalanced order.

Arm type	Active comparator
Investigational medicinal product name	montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Montelukast: Montelukast 7 days in the evening and a morning placebo dose the last day

Number of subjects in period 1	Placebo	Single dose of montelukast	Montelukast
Started	19	19	19
Completed	19	19	19

Baseline characteristics

Reporting groups

Reporting group title	Period 1

Reporting group description: -

Reporting group values	Period 1	Total	
Number of subjects	19	19	
Age categorical			
Since the design is crossover, there are 19 participants in each group, but the total number of participants is also 19.			
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)	7	7	
Adolescents (12-17 years)	12	12	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Since the design is crossover, there are 19 participants in each group, but the total number of participants is also 19.			
Units: Subjects			
Female	5	5	
Male	14	14	

Subject analysis sets

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Completers analysis population included all randomized participants who received the study drug in all three periods

Subject analysis set title	Single dose Montelukast
Subject analysis set type	Full analysis

Subject analysis set description:

Completers analysis population included all randomized participants who received the study drug in all three periods

Subject analysis set title	Montelukast
Subject analysis set type	Full analysis

Subject analysis set description:

Completers analysis population included all randomized participants who received the study drug in all three periods

Reporting group values	Placebo	Single dose Montelukast	Montelukast
Number of subjects	19	19	19
Age categorical			
Since the design is crossover, there are 19 participants in each group, but the total number of participants is also 19.			
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)	7	7	7
Adolescents (12-17 years)	12	12	12
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Since the design is crossover, there are 19 participants in each group, but the total number of participants is also 19.			
Units: Subjects			
Female	5	5	5
Male	14	14	14

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects were randomised to receive placebo for 7 days in the evening and a morning placebo dose the last day in treatment period 1 or treatment period 2 or treatment period 3 in a counterbalanced order.	
Reporting group title	Single dose of montelukast
Reporting group description:	
Subjects were randomised to receive placebo for 7 days in the evening and a morning single dose of montelukast the last day in treatment period 1 or treatment period 2 or treatment period 3 in a counterbalanced order.	
Reporting group title	Montelukast
Reporting group description:	
Subjects were randomised to receive montelukast for 7 days in the evening and a morning dose of placebo the last day in treatment period 1 or treatment period 2 or treatment period 3 in a counterbalanced order.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Completers analysis population included all randomized participants who received the study drug in all three periods	
Subject analysis set title	Single dose Montelukast
Subject analysis set type	Full analysis
Subject analysis set description:	
Completers analysis population included all randomized participants who received the study drug in all three periods	
Subject analysis set title	Montelukast
Subject analysis set type	Full analysis
Subject analysis set description:	
Completers analysis population included all randomized participants who received the study drug in all three periods	

Primary: Maximum Percent Fall in FEV1 After Exercise Challenge at 2 Hours Postdose

End point title	Maximum Percent Fall in FEV1 After Exercise Challenge at 2 Hours Postdose
End point description:	
Maximum Percent Fall in FEV1 was defined as the % change from pre-exercise baseline FEV1 to the lowest FEV1 within 20 minutes after exercise. Spirometry measurements were taken prior to each exercise challenge and immediately, 3, 5, 10, 15, & 20 minutes after each exercise challenge. The 2-hour exercise challenges occurred 2 hours after the last dose of study medication. The calculation used to produce the results was [100*(1-(X/Y))] where X= the lowest FEV1 within 20 mins after exercise & Y= pre-exercise baseline FEV1.	
End point type	Primary
End point timeframe:	
Pre-exercise baseline and 0-20 minutes after the exercise challenge performed 2 hours post-dose	

End point values	Placebo	Single dose Montelukast	Montelukast	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: FEV1 % change				
arithmetic mean (standard error)	14.6 (± 2.4)	9.0 (± 1.6)	13.0 (± 2.8)	

Statistical analyses

Statistical analysis title	Comparison between single montelukast vs. placebo
Comparison groups	Placebo v Single dose Montelukast
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority[1]
Parameter estimate	Mean difference (final values)
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	11
Variability estimate	Standard error of the mean
Dispersion value	2.6

Notes:

[1] - Since the design is crossover, the total number of participants is 19.

Primary: Maximum Percent Fall in FEV1 After Exercise Challenge at 5 Hours Postdose

End point title	Maximum Percent Fall in FEV1 After Exercise Challenge at 5 Hours Postdose

End point description:

Maximum Percent Fall in FEV1 was defined as the % change from pre-exercise baseline FEV1 to the lowest FEV1 within 20 minutes after exercise. Spirometry measurements were taken prior to each exercise challenge and immediately, 3, 5, 10, 15, & 20 minutes after each exercise challenge. The 5-hour exercise challenges occurred 5 hours after the last dose of study medication. The calculation used to produce the results was [100*(1-(X/Y))] where X= the lowest FEV1 within 20 mins after exercise & Y= pre-exercise baseline FEV1.

End point type	Primary

End point timeframe:

Pre-exercise baseline and 0-20 minutes after the exercise challenge performed 5 hours post-dose

End point values	Placebo	Single dose Montelukast	Montelukast	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: FEV1				
arithmetic mean (standard error)	10.7 (± 2.4)	6.7 (± 1.4)	8.7 (± 1.9)	

Statistical analyses

Statistical analysis title	Comparison between single montelukast vs. placebo
Comparison groups	Placebo v Single dose Montelukast
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority[2]
Parameter estimate	Mean difference (final values)
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	9.6
Variability estimate	Standard error of the mean
Dispersion value	2.7

Notes:

[2] - Since the design is crossover, the total number of participants is 19.

Primary: Maximum Percent Fall in FEV1 After Exercise Challenge at 8 Hours Postdose

End point title	Maximum Percent Fall in FEV1 After Exercise Challenge at 8 Hours Postdose

End point description:

Maximum Percent Fall in FEV1 was defined as the % change from pre-exercise baseline FEV1 to the lowest FEV1 within 20 minutes after exercise. Spirometry measurements were taken prior to each exercise challenge and immediately, 3, 5, 10, 15, & 20 minutes after each exercise challenge. The 8-hour exercise challenges occurred 8 hours after the last dose of study medication. The calculation used to produce the results was [100*(1-(X/Y))] where X= the lowest FEV1 within 20 mins after exercise & Y= pre-exercise baseline FEV1.

End point type	Primary

End point timeframe:

Pre-exercise baseline and 0-20 minutes after the exercise challenge performed 8 hours post-dose

End point values	Placebo	Single dose Montelukast	Montelukast	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: FEV1				
arithmetic mean (standard error)	10.5 (± 2.1)	7.6 (± 1.4)	7.7 (± 1.8)	

Statistical analyses

Statistical analysis title	Comparison between single montelukast vs. placebo
Comparison groups	Placebo v Single dose Montelukast
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority[3]
Parameter estimate	Mean difference (final values)
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	6.6
Variability estimate	Standard error of the mean
Dispersion value	1.8

Notes:

[3] - Since the design is crossover, the total number of participants is 19.

Primary: Maximum Percent Fall in FEV1 After Exercise Challenge at 11 Hours Postdose

End point title	Maximum Percent Fall in FEV1 After Exercise Challenge at 11 Hours Postdose

End point description:

Maximum Percent Fall in FEV1 was defined as the % change from pre-exercise baseline FEV1 to the lowest FEV1 within 20 minutes after exercise. Spirometry measurements were taken prior to each exercise challenge and immediately, 3, 5, 10, 15, & 20 minutes after each exercise challenge. The 11-hour exercise challenges occurred 11 hours after the last dose of study medication. The calculation used to produce the results was [100*(1-(X/Y))] where X= the lowest FEV1 within 20 mins after exercise & Y= pre-exercise baseline FEV1.

End point type	Primary

End point timeframe:

Pre-exercise baseline and 0-20 minutes after the exercise challenge performed11 hours post-dose

End point values	Placebo	Single dose Montelukast	Montelukast	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: FEV1				
arithmetic mean (standard error)	12.9 (± 2.4)	11.1 (± 1.9)	8.4 (± 1.8)	

Statistical analyses

Statistical analysis title	Since the design is crossover, the total number of
Comparison groups	Single dose Montelukast v Placebo

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority[4]
Parameter estimate	Mean difference (final values)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	6.6
Variability estimate	Standard error of the mean
Dispersion value	2.3

Notes:

[4] - Since the design is crossover, the total number of participants is 19.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events assessment at every visit

Adverse event reporting additional description:

At every visit participants were interviewed about eventual adverse effect of the medicine.

Participants were closely monitored for potential injuries in relation to exercise challenge tests.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	single dose montelukast
Reporting group description: -	
Reporting group title	Montelukast
Reporting group description: -	

Serious adverse events	Placebo	single dose montelukast	Montelukast
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Placebo	single dose montelukast	Montelukast
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 19 (21.05%)	3 / 19 (15.79%)	4 / 19 (21.05%)
Nervous system disorders			
headache			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Gastrointestinal disorders			
stomach ache			

subjects affected / exposed	1 / 19 (5.26%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
vomiting			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 19 (0.00%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	0	2	0

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