Clinical trial results:
Urine concentrations of vilanterol after inhaled administration of vilanterol/fluticasone furoate: Defining a urine threshold and decision limit for vilanterol in doping control analysis

Summary

EudraCT number	2018-002529-48
Trial protocol	DK
Global end of trial date	14 December 2020

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	WADA2018vil

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Center for Aktiv Sundhed, Rigshospitalet
Sponsor organisation address	Rigshospitalet afsnit 7641, Blegdamsvej 9, 2100 København Ø, Copenhagen, Denmark,
Public contact	CFAS, Center for Aktiv Sundhed, Rigshospitalet, eriksorenhalvardhansen@gmail.com
Scientific contact	CFAS, Center for Aktiv Sundhed, Rigshospitalet, eriksorenhalvardhansen@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	14 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 December 2020
Global end of trial reached?	Yes
Global end of trial date	14 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine urine concenctrations of vilanterol and its metabolites after therapeutic and supratherapeutic use.

Protection of trial subjects:

The subjects had a bed to rest. No more measures were needed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2020
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: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligibility criteria were physically active males or females (at least 5 hours physical activity weekly), aged 18-39 years.
42 individuals were screened and 25 included. 6 individuals dropped out during the study, resulting in 19 individuals completing all 4 trials.

Period 1

Period 1 title	Trial 1 - 25 µg inhalation
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Trial 1 - 25 µg

Arm description:

Due to the limits of reporting results, this "arm" represents the first trial of the four trials. The study only has 1 arm, which completes four trial periods.

Arm type	Experimental
Investigational medicinal product name	Relvar ElliptaTM, 22/184 µg vilanterol/fluticasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

The study consisted of four trials. During trials 1 and 3, participants inhaled a single dose (25 µg; Trial 1) or four doses (100 µg; Trial 3). After the single-dose trials (Trial 1 and 3), participants received an inhaler for home administration of the study drug. Trials 2 and 4 were preceded by a repeated dosing regime of once-daily inhalation of 25 µg (7d25 µg; Trial 2) or 100 µg (7d100 µg; Trial 4) for 6 days. Trials were separated by at least a 1-week washout. Home administrations were monitored by staff via online video tools to maximize drug compliance and assess inhalation technique.

Number of subjects in period 1	Trial 1 - 25 µg
Started	25
Completed	25

Period 2

Period 2 title	Trial 2 - 7d 25 µg
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not Blinded

Arms

Arm title	Trial 2 - 7d 25 µg

Arm description:

Due to the limits of reporting results, this "arm" represents the second trial of the four trials. The study only has 1 arm, which completes four trial periods.

Arm type	Experimental
Investigational medicinal product name	Relvar ElliptaTM, 22/184 µg vilanterol/fluticasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

The study consisted of four trials. During trials 1 and 3, participants inhaled a single dose (25 µg; Trial 1) or four doses (100 µg; Trial 3). After the single-dose trials (Trial 1 and 3), participants received an inhaler for home administration of the study drug. Trials 2 and 4 were preceded by a repeated dosing regime of once-daily inhalation of 25 µg (7d25 µg; Trial 2) or 100 µg (7d100 µg; Trial 4) for 6 days. Trials were separated by at least a 1-week washout. Home administrations were monitored by staff via online video tools to maximize drug compliance and assess inhalation technique.

Number of subjects in period 2	Trial 2 - 7d 25 µg
Started	25
Completed	21
Not completed	4
Consent withdrawn by subject	3
non-compliance	1

Period 3

Period 3 title	Trial 3 - 100 µg
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not blinded

Arms

Arm title	Trial 3 - 100 µg

Arm description:

Due to the limits of reporting results, this "arm" represents the third trial of the four trials. The study only has 1 arm, which completes four trial periods.

Arm type	Experimental
Investigational medicinal product name	Relvar ElliptaTM, 22/184 µg vilanterol/fluticasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

The study consisted of four trials. During trials 1 and 3, participants inhaled a single dose (25 µg; Trial 1) or four doses (100 µg; Trial 3). After the single-dose trials (Trial 1 and 3), participants received an inhaler for home administration of the study drug. Trials 2 and 4 were preceded by a repeated dosing regime of once-daily inhalation of 25 µg (7d25 µg; Trial 2) or 100 µg (7d100 µg; Trial 4) for 6 days. Trials were separated by at least a 1-week washout. Home administrations were monitored by staff via online video tools to maximize drug compliance and assess inhalation technique.

Number of subjects in period 3	Trial 3 - 100 µg
Started	21
Completed	20
Not completed	1
Consent withdrawn by subject	1

Period 4

Period 4 title	Trial 4 - 7d 100 µg
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not blinded

Arms

Arm title	Trial 4 - 7d 100 µg

Arm description:

Due to the limits of reporting results, this "arm" represents the fourth trial of the four trials. The study only has 1 arm, which completes four trial periods.

Arm type	Experimental
Investigational medicinal product name	Relvar ElliptaTM, 22/184 µg vilanterol/fluticasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

The study consisted of four trials. During trials 1 and 3, participants inhaled a single dose (25 µg; Trial 1) or four doses (100 µg; Trial 3). After the single-dose trials (Trial 1 and 3), participants received an

inhaler for home administration of the study drug. Trials 2 and 4 were preceded by a repeated dosing regime of once-daily inhalation of 25 µg (7d25 µg; Trial 2) or 100 µg (7d100 µg; Trial 4) for 6 days. Trials were separated by at least a 1-week washout. Home administrations were monitored by staff via online video tools to maximize drug compliance and assess inhalation technique.

Number of subjects in period 4	Trial 4 - 7d 100 µg
Started	20
Completed	19
Not completed	1
Covid-19	1

Baseline characteristics

Reporting groups

Reporting group title	Trial 1 - 25 µg inhalation

Reporting group description: -

Reporting group values	Trial 1 - 25 µg inhalation	Total	
Number of subjects	25	25	
Age categorical Units: Subjects			
18-39	25	25	
Gender categorical Units: Subjects			
Female	9	9	
Male	16	16	

End points

End points reporting groups

Reporting group title	Trial 1 - 25 µg
Reporting group description:	
Due to the limits of reporting results, this "arm" represents the first trial of the four trials. The study only has 1 arm, which completes four trial periods.	
Reporting group title	Trial 2 - 7d 25 µg
Reporting group description:	
Due to the limits of reporting results, this "arm" represents the second trial of the four trials. The study only has 1 arm, which completes four trial periods.	
Reporting group title	Trial 3 - 100 µg
Reporting group description:	
Due to the limits of reporting results, this "arm" represents the third trial of the four trials. The study only has 1 arm, which completes four trial periods.	
Reporting group title	Trial 4 - 7d 100 µg
Reporting group description:	
Due to the limits of reporting results, this "arm" represents the fourth trial of the four trials. The study only has 1 arm, which completes four trial periods.	

Primary: Urine values of Vilanterol

End point title	Urine values of Vilanterol[1]
End point description:	
The mean of maximum urine concentrations (Cmax) of parent vilanterol, with the min-max range, is presented here.	
End point type	Primary
End point timeframe:	
Urine values was collected -1 to 72 hours after inhalation of vilanterol	

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: This study presents urine values of vilanterol and its metabolites after inhalation of relvar elipta. Only minor statistical analyses was made in the presentation of those values.

End point values	Trial 1 - 25 µg	Trial 3 - 100 µg	Trial 2 - 7d 25 µg	Trial 4 - 7d 100 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	20	21	19
Units: ng X mL				
arithmetic mean (full range (min-max))	1.2 (0.2 to 4.1)	6.2 (1.4 to 14.3)	2.0 (0.3 to 4.8)	22.4 (6.4 to 42.1)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
At the beginning of each trial day or by self-reporting.	
Assessment type	Systematic

Dictionary used	
Dictionary name	Study dictionary
Dictionary version	1

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

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: I do not have access to records of non-serious adverse events. This will be typed in later.

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