Clinical trial results:
Use of Buventol Easyhaler and Bufomix Easyhaler as Relievers in Methacholine Challenge Testing and Inspiratory Flow Profiles during Induced Bronchoconstriction in Adult Subjects

Summary

EudraCT number	2021-001573-22
Trial protocol	FI
Global end of trial date	30 June 2023

Results information

Result version number	v1 (current)
This version publication date	08 June 2024
First version publication date	08 June 2024

Trial information

Trial identification

Sponsor protocol code	0010032

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05084222
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Orion Corporation
Sponsor organisation address	Orionintie 1, Espoo, Finland, 02100
Public contact	Clinical Trial Information Desk, Orion Corporation, +358 104261, clinicaltrials@orionpharma.com
Scientific contact	Clinical Trial Information Desk, Orion Corporation, +358 104261, clinicaltrials@orionpharma.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	30 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2023
Global end of trial reached?	Yes
Global end of trial date	30 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To show non-inferiority of Buventol Easyhaler to Ventoline Evohaler in treatment of induced bronchoconstriction

Protection of trial subjects:

The participants were monitored by the site personnel during the whole study. All study treatments were administered at the study site under the supervision of the site personnel. Additional salbutamol was administered in case bronchoconstriction did not recover at the specified time frame. If the participant still did not reach the desired level of FEV1, a physician was called upon, and, if needed, the participant was treated on clinical grounds. Adequate medical expertise and facilities to handle possible emergency situations were available during the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 November 2021
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	Finland: 180
Worldwide total number of subjects	180
EEA total number of subjects	180

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)	151
From 65 to 84 years	29

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 601 adult subjects were screened and 180 were randomised to the study in two study sites in Finland.

Pre-assignment

Screening details:

The methacholine challenge testing was performed and participants who experienced forced expired volume in 1 second (FEV1) drop ≥ 20% compared to post-diluent spirometry were included.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

NA, open label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Bufomix Easyhaler

Arm description:

Two inhalations were administered from Bufomix Easyhaler 160/4.5 µg resulting in dose of 320/9 µg of budesonide and formoterol, respectively.

Arm type	Experimental
Investigational medicinal product name	budesonide and formoterol fumarate dihydrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations were administered from Bufomix Easyhaler 160/4.5 µg resulting in dose of 320/9 µg of budesonide and formoterol, respectively. The dose was repeated once if needed.

Arm title	Buventol Easyhaler

Arm description:

400 µg of salbutamol from Buventol Easyhaler was administered as two 200 µg inhalations.

Arm type	Experimental
Investigational medicinal product name	salbutamol sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

400 µg of salbutamol from Buventol Easyhaler was administered as two 200 µg inhalations. The dose was repeated once if needed.

Arm title	Ventoline Evohaler

Arm description:

400 µg of salbutamol from Ventoline Evohaler was administered via Volumatic spacer.

Arm type	Active comparator

Investigational medicinal product name	salbutamol sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

400 µg of salbutamol from Ventoline Evohaler was administered via Volumatic spacer. A single dose was administered to the spacer and the participant inhaled it before the next dose. This resulted in 4 cycles of administration. The dose was repeated once if needed.

Number of subjects in period 1	Bufomix Easyhaler	Buventol Easyhaler	Ventoline Evohaler
Started	60	60	60
Completed	60	60	60

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	180	180	
Age categorical Units: Subjects			
Adults (18-64 years)	151	151	
From 65-84 years	29	29	
Gender categorical Units: Subjects			
Female	124	124	
Male	56	56	

End points

End points reporting groups

Reporting group title	Bufomix Easyhaler
Reporting group description:	
Two inhalations were administered from Bufomix Easyhaler 160/4.5 µg resulting in dose of 320/9 µg of budesonide and formoterol, respectively.	
Reporting group title	Buventol Easyhaler
Reporting group description:	
400 µg of salbutamol from Buventol Easyhaler was administered as two 200 µg inhalations.	
Reporting group title	Ventoline Evohaler
Reporting group description:	
400 µg of salbutamol from Ventoline Evohaler was administered via Volumatic spacer.	

Primary: FEV1

End point title	FEV1
End point description:	
Mean change in forced expired volume in 1 second (FEV1) from post-diluent to FEV1 after the first study treatment dose.	
End point type	Primary
End point timeframe:	
FEV1 was measured 10 minutes after study treatment dosing.	

End point values	Bufomix Easyhaler	Buventol Easyhaler	Ventoline Evohaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	60	60	
Units: L				
geometric mean (confidence interval 95%)	2.760 (2.675 to 2.846)	2.840 (2.750 to 2.930)	2.923 (2.837 to 3.009)	

Statistical analyses

Statistical analysis title	FEV1 after treatment, change from baseline
Statistical analysis description:	
analysis of covariance between Buventol Easyhaler and Ventoline Evohaler	
Comparison groups	Buventol Easyhaler v Ventoline Evohaler
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.083

Confidence interval	
level	95 %
sides	1-sided
lower limit	-0.146

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse events were collected during the whole study.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Bufomix Easyhaler
Reporting group description: Two inhalations were administered from Bufomix Easyhaler 160/4.5 µg resulting in dose of 320/9 µg of budesonide and formoterol, respectively.	
Reporting group title	Buventol Easyhaler
Reporting group description: 400 µg of salbutamol from Buventol Easyhaler was administered as two 200 µg inhalations.	
Reporting group title	Ventoline Evohaler
Reporting group description: 400 µg of salbutamol from Ventoline Evohaler was administered via Volumatic spacer.	

Serious adverse events	Bufomix Easyhaler	Buventol Easyhaler	Ventoline Evohaler
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 60 (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: 0 %

Non-serious adverse events	Bufomix Easyhaler	Buventol Easyhaler	Ventoline Evohaler
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 60 (8.33%)	1 / 60 (1.67%)	2 / 60 (3.33%)
General disorders and administration site conditions			
Obstruction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	1 / 60 (1.67%) 1	1 / 60 (1.67%) 1
Musculoskeletal and connective tissue disorders Pain in jaw subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 January 2023	Another study site was added. Collection of concomitant treatments for AEs before and during MC test was added. Collection of age was added. Recording of smoking status was added as it was missing from the original protocol by mistake. Smoking status is important information to characterise the patients.
22 May 2023	Recording of spirometric inspiratory values (PIF and inspiratory volume) from already performed spirometries to develop a statistical prediction model to estimate PIF via Easyhaler was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported