Clinical trial results:
EFFECT OF ELECTRONIC MONITORING AND FEEDBACK ON ADHERENCE TO EASYHALER CONTROLLER MEDICATION IN PATIENTS WITH ASTHMA

Summary

EudraCT number	2019-003082-17
Trial protocol	DE
Global end of trial date	24 April 2024

Results information

Result version number	v1 (current)
This version publication date	26 April 2025
First version publication date	26 April 2025

Trial information

Trial identification

Sponsor protocol code	3103017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04869384
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Orion Corporation
Sponsor organisation address	Orionintie 1, Espoo, Finland, 02200
Public contact	Clinical Trial Information Desk, Orion Corporation Orion Pharma, +358 104261, clinicaltrials@orionpharma.com
Scientific contact	Clinical Trial Information Desk, Orion Corporation Orion Pharma, +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	24 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2024
Global end of trial reached?	Yes
Global end of trial date	24 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to compare mean weekly adherence to controller medication between the intervention group using Connected Easyhaler and the control group (active usual care) during the last 6 weeks of the study.

Protection of trial subjects:

Use of Connected Easyhaler was not considered to add any safety concern compared to normal use of inhalers. The trial enrolled adult asthmatic patients with suboptimal asthma control who were currently receiving inhaled budesonide, budesonide/formoterol combination or salmeterol/fluticasone propionate combination as their controller medication. Adverse events were collected from the time that a trial participant signed the IC form until the end-of-trial visit at 6 months.
Salbutamol was used as rescue medication as needed.

Background therapy:

In addition to study medication, the use of possible other asthma medications was permitted and the dose continued as before the trial.

Evidence for comparator: -

Actual start date of recruitment	23 June 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	Germany: 158
Worldwide total number of subjects	158
EEA total number of subjects	158

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)	157
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 171 participants were screened for the trial in Germany, with 78 participants being randomised into the Intervention group and 80 participants randomised into the Usual Care group.

Pre-assignment

Screening details:

Male and female participants, aged 18-65 years with asthma, ACT score 19 or less, were recruited. Participant must have been used their control medication (budesonide, budesonide/formoterol combination or salmeterol/fluticasone) at constant dose for at least 3 months before screening, and to be able to switch to Easyhaler.

Pre-assignment period milestones

Number of subjects started	158
Number of subjects completed	158

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:

This was an open-label trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

Participants in the Intervention group had sensors attached to their controller and reliever medication inhalers and the mobile application installed to their mobile phones. The sensors monitored use of medications by capturing date, time and number of uses. The participants in this group got reminders (sound and/or light) on the controller medication use via sensor and mobile application. In addition, there were push notifications via mobile application. At study visits, the adherence data accumulated since the previous visit was reviewed by the investigator/nurse using the Provider Portal and discussed with the subject.

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

Dosage and administration details:

Individual dosing instructed by the treating physician.

Investigational medicinal product name	Budesonide/Formoterol Easyhaler
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Individual dosing instructed by the treating physician.

Investigational medicinal product name	Salmeterol/Fluticasone propionate Easyhaler
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Individual dosing instructed by the treating physician.

Investigational medicinal product name	Salbutamol Easyhaler
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Reliever medication, used as needed (in accordance with SmPC).

Arm title	Usual Care

Arm description:

Participants in the Usual Care group had sensors attached to their controller and reliever medication inhalers and the mobile application installed to their mobile phones as in the Intervention group. They were told that the sensors monitor how much the inhalers are used; however, the reminders/alarms of the sensors were disabled, and the participants or health care professionals could not review information collected from the sensor via the mobile application.

Arm type	Active comparator
Investigational medicinal product name	Budesonide Easyhaler
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Individual dosing instructed by the treating physician.

Investigational medicinal product name	Salbutamol Easyhaler
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Reliever medication, used as needed (in accordance with SmPC).

Investigational medicinal product name	Salmeterol/Fluticasone propionate Easyhaler
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Individual dosing instructed by the treating physician.

Investigational medicinal product name	Budesonide/Formoterol Easyhaler
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Individual dosing instructed by the treating physician.

Number of subjects in period 1	Intervention	Usual Care
Started	78	80
Completed	77	77
Not completed	1	3
Consent withdrawn by subject	1	3

Baseline characteristics

Reporting groups

Reporting group title	Intervention

Reporting group description:

Participants in the Intervention group had sensors attached to their controller and reliever medication inhalers and the mobile application installed to their mobile phones. The sensors monitored use of medications by capturing date, time and number of uses. The participants in this group got reminders (sound and/or light) on the controller medication use via sensor and mobile application. In addition, there were push notifications via mobile application. At study visits, the adherence data accumulated since the previous visit was reviewed by the investigator/nurse using the Provider Portal and discussed with the subject.

Reporting group title	Usual Care

Reporting group description:

Participants in the Usual Care group had sensors attached to their controller and reliever medication inhalers and the mobile application installed to their mobile phones as in the Intervention group. They were told that the sensors monitor how much the inhalers are used; however, the reminders/alarms of the sensors were disabled, and the participants or health care professionals could not review information collected from the sensor via the mobile application.

Reporting group values	Intervention	Usual Care	Total
Number of subjects	78	80	158
Age categorical Units: Subjects			
Adults (18-64 years)	78	79	157
From 65-84 years	0	1	1
Gender categorical Units: Subjects			
Female	42	51	93
Male	36	29	65

End points

End points reporting groups

Reporting group title	Intervention

Reporting group description:

Participants in the Intervention group had sensors attached to their controller and reliever medication inhalers and the mobile application installed to their mobile phones. The sensors monitored use of medications by capturing date, time and number of uses. The participants in this group got reminders (sound and/or light) on the controller medication use via sensor and mobile application. In addition, there were push notifications via mobile application. At study visits, the adherence data accumulated since the previous visit was reviewed by the investigator/nurse using the Provider Portal and discussed with the subject.

Reporting group title	Usual Care

Reporting group description:

Participants in the Usual Care group had sensors attached to their controller and reliever medication inhalers and the mobile application installed to their mobile phones as in the Intervention group. They were told that the sensors monitor how much the inhalers are used; however, the reminders/alarms of the sensors were disabled, and the participants or health care professionals could not review information collected from the sensor via the mobile application.

Primary: Mean weekly adherence to controller medication

End point title	Mean weekly adherence to controller medication

End point description:

The primary efficacy variable was mean weekly adherence to controller medication (the percentage of doses taken of the doses prescribed) during the last 6 weeks of treatment. The use of controller medication was recorded by the sensor attached to the inhaler in both groups. The adherence was compared between participants who did and did not receive reminders and feedback on their medication use via Connected Easyhaler.

End point type	Primary

End point timeframe:

The last 6 weeks of treatment of the 6 month treatment period.

End point values	Intervention	Usual Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	80		
Units: percent				
least squares mean (confidence interval 95%)	79.07 (72.1 to 86.05)	57.36 (50.24 to 65.47)		

Statistical analyses

Statistical analysis title	Comparison of change in adherence from baseline

Statistical analysis description:

Comparison of change in adherence from baseline between the groups.

Comparison groups	Intervention v Usual Care

Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	21.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.75
upper limit	31.68

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the time that a trial participant signed the IC form until the end-of-trial visit at 6 months.

Adverse event reporting additional description:

The adverse events reported during the run-in period were included.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Intervention

Reporting group description:

Participants in the Intervention group had sensors attached to their controller and reliever medication inhalers and the mobile application installed to their mobile phones. The sensors monitored use of medications by capturing date, time and number of uses. The participants in this group got reminders (sound and/or light) on the controller medication use via sensor and mobile application. In addition, there were push notifications via mobile application. At study visits, the adherence data accumulated since the previous visit was reviewed by the investigator/nurse using the Provider Portal and discussed with the subject.

Reporting group title	Usual Care

Reporting group description:

Participants in the Usual Care group had sensors attached to their controller and reliever medication inhalers and the mobile application installed to their mobile phones as in the Intervention group. They were told that the sensors monitor how much the inhalers are used; however, the reminders/alarms of the sensors were disabled, and the participants or health care professionals could not review information collected from the sensor via the mobile application.

Serious adverse events	Intervention	Usual Care	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 78 (2.56%)	1 / 80 (1.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
ANKLE FRACTURE			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
WRIST FRACTURE			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

MATERNAL EXPOSURE DURING PREGNANCY			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INCISIONAL HERNIA			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Intervention	Usual Care	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 78 (30.77%)	29 / 80 (36.25%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MELANOCYTIC NAEVUS			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
ACCIDENT			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
BONE CONTUSION			
subjects affected / exposed	0 / 78 (0.00%)	2 / 80 (2.50%)	
occurrences (all)	0	2	
CONTUSION			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
CRANIOCEREBRAL INJURY			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
FOOT FRACTURE			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
HEAD INJURY			

subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
IMMUNISATION REACTION			
subjects affected / exposed	4 / 78 (5.13%)	2 / 80 (2.50%)	
occurrences (all)	4	2	
LIGAMENT RUPTURE			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
LIMB INJURY			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
Surgical and medical procedures			
INTERNAL FIXATION OF FRACTURE			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
CERVICOBRACHIAL SYNDROME			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
HEADACHE			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	

Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	5 / 78 (6.41%)	5 / 80 (6.25%)	
occurrences (all)	7	6	
DYSPHONIA			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
SKIN IRRITATION			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 78 (0.00%)	2 / 80 (2.50%)	
occurrences (all)	0	2	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
TENDONITIS			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
BRONCHITIS BACTERIAL			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
CANDIDA INFECTION			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
CORONAVIRUS INFECTION			

subjects affected / exposed	1 / 78 (1.28%)	1 / 80 (1.25%)	
occurrences (all)	1	1	
COVID-19			
subjects affected / exposed	10 / 78 (12.82%)	10 / 80 (12.50%)	
occurrences (all)	10	10	
GASTROINTESTINAL INFECTION			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
NASOPHARYNGITIS			
subjects affected / exposed	7 / 78 (8.97%)	6 / 80 (7.50%)	
occurrences (all)	8	6	
MASTITIS			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
JOINT ABSCESS			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
LARYNGITIS			
subjects affected / exposed	2 / 78 (2.56%)	1 / 80 (1.25%)	
occurrences (all)	2	1	
SKIN INFECTION			
subjects affected / exposed	1 / 78 (1.28%)	0 / 80 (0.00%)	
occurrences (all)	1	0	
ROOT CANAL INFECTION			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 78 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2020	Amendment 1. Changes requested by German regulatory authority BfArM: -Further rationale for patient selection was added to the protocol to justify the inclusion of participants with ACT score ≤19 (5-19). -The use of other asthma mediation was clarified. -Time period for the use of the controller medication at constant dose from at least 1 month was extended to 3 months prior to the screening visit. -A summary of pertinent safety information was included. -The 6-week phone call was removed in order not to create bias. -Pregnancy testing was included to screening for WOCBP -The requirement for WOCBP to use adequate contraception was included. -Paradoxical bronchospasm was added as an example for discontinuing the trial treatment for a participant. -Criteria for discontinuation of the trial were added. -The use of Salbutamol Easyhaler as a reliever medication was clarified. -A new section containing potent inhibitors of CYP3A was added. -Trial procedures at screening were clarified. -It was clarified that participants can call Propeller customer support if they have any questions or concerns related to the sensor or the application. -More detailed information on spirometric measurements was given. -Clarification for pregnancy during the trial was added. -Text concerning discontinuation of the trial was reorganised and added under section 4.7. -Detailed information on contraception methods considered acceptable in this trial based on the Clinical Trial Facilitation Group recommendation was added.
28 May 2020	The amended protocol was created to implement changes requested by German central ethics committee. -Primary objective was clarified. - Secondary objectives were clarified. -Timeline the participant had used an investigational drug was determined more precisely. -Exclusion of individuals who are subordinate to the Sponsor or institutionalised as a result of an administrative or court order were added. -Race as a data to be collected was removed. -Protocol deviation as a reason for participant’s discontinuation was removed -A reason for discontinuing the trial was added. -Ratio for distribution into treatment groups were added. -Easyhaler inhaler technique checking and training missing from randomisation visit was added. -Data related to variable Healthcare utilisation related to asthma to be collected from CRF was removed. -Data related to variable Number of missing working or trial days due to asthma symptoms to be collected from CRF was removed. -Clarification that non-compliance is not considered as a protocol deviation for per-protocol population was added. -Statistical analysis for the primary endpoint was described in more detail. -Clarification related to secondary variable adherence to controller medication was added.

24 November 2020	An amendment to a protocol was created and implemented due to Covid-19 pandemic. -Obtaining baseline data about adherence was added. -Benefit-risk assessment was updated to include the possible risks associated with Covid-19. -The smart phone versions supported were updated. -Time from previous upper or lower respiratory infection was prolonged from 7 to 14 days due to possible covid-19 infection. -The need to return Easyhaler inhalers at every visit was removed because post-randomisation visits (Visit 3 and Visit 4) could have been carried out remotely (a telephone visit, home visit or video call) due to restrictions related to covid-19. -Asthma symptom control was removed as it was accidentally included into the original protocol. Assessment of asthma control according to GINA was considered at the time of protocol development but left out as ACT was included. This correction was missed in the previous amendments. -The precautions due to Covid-19 pandemic and possible protocol assessments during remote visits were added. -Clarifications into data collection was added.
02 March 2021	An amendment was created to implement the changes requested by German central ethics committee. -Additional covid-19 precautions including covid-19 testing were added. -Trial dates (start and complete) were updated due to Covid-19.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported