



Clinical trial results:

An exploratory, double-blind, randomised, multicenter, psychopharmacological study in adult patients with moderate to severe asthma to compare two pressurised Metered-Dose Inhalers (pMDIs) on patients' perception of asthma symptoms.

Summary

EudraCT number	2021-001449-11
Trial protocol	IT
Global end of trial date	01 February 2023

Results information

Result version number	v1 (current)
This version publication date	16 February 2024
First version publication date	16 February 2024

Trial information

Trial identification

Sponsor protocol code	CLI-01535AA0-02
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04886999
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Chiesi Farmaceutici S.p.A
Sponsor organisation address	via Palermo, 26/A, PARMA, Italy, 43122
Public contact	Clinical Trial Transparency , Chiesi Farmaceutici S.p.a., clinicaltrials_info@chiesi.com
Scientific contact	Clinical Trial Transparency , Chiesi Farmaceutici S.p.a., clinicaltrials_info@chiesi.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	29 August 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study aimed to assess the perception of symptoms and subject's preferences comparing two inhalers containing the same medication/formulation as Foster® 100/6 µg pMDI, but with different characteristics, in adult subjects whose asthma was already controlled with Foster® 100/6 µg pMDI.

Protection of trial subjects:

The clinical study was performed in accordance with the principles that have their origin in the Declaration of Helsinki, and with local regulations.

The study was carried out in accordance with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) notes for guidance on Good Clinical Practice (GCP) (ICH E6 Version 2).

Investigators insured a close follow-up of safety signals, and that everything has been done to reduce the burden of study procedures (e.g. no painful procedures, etc.).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 February 2022
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	Italy: 81
Worldwide total number of subjects	81
EEA total number of subjects	81

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)	64

From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

81 sbj screened and 78 randomised into 2 study treatment sequences:

- 39 CHF1535 Inhaler A (white)-CHF1535 Inhaler B (pink);
- 39 CHF1535 Inhaler B (pink)-CHF1535 Inhaler A (white).

Of the 78 randomised sbj, 4 discontinued during the baseline period and 74 started the treatment. Data presented in the tables below are referred to those 74 sbj.

Pre-assignment

Screening details:

After signing the informed consent form, subjects were screened at the investigational site during the screening/randomisation visit (V1). On the same day, and after checking all inclusion and exclusion criteria, eligible subjects were randomised into one of two study treatment sequences.

Period 1

Period 1 title	Treatment Period 1, Treatment Period 2 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

The double-blind randomisation ensured that no systematic bias affected the treatment sequence allocation and subject/Investigator perceptions of the study treatments. An Unblinded member of the site was assigned at each site by the Principal Investigator for treatment dispensation, return management, treatment accountability activities; the Unblinded site personnel were distinct from the Blinded Investigator, who performed the other blinded activities such as the collection of the ICF.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence - Inhaler A // Inhaler B

Arm description:

The 2, 2-week treatment periods in the cross-over design were deemed adequate to evaluate the psychopharmacological aspects and assess the subject's preferences and perception of symptoms comparing two inhalers containing the same medication/formulation as Foster® 100/6 µg pMDI but with different characteristics.

The treatment sequence Inhaler A/Inhaler B consists of:

- Baseline treatment with Foster® CHF1535 100/6 µg pMDI, from V1 (Day 1) for a 2-week period;
- First treatment period with CHF1535 100/6 µg pMDI with Inhaler A (white actuator), from V2 (Day 15) to V3 (Day 29);
- Second treatment period with CHF1535 100/6 µg pMDI with Inhaler B (pink actuator), from V3 (Day 29) to V4 (Day 43).

39 subjects were randomized into this treatment sequence, of whom 36 completed the study.

3 subjects discontinued during the baseline period for undergoing adverse events, for consent withdrawal and other reasons.

Arm type	Experimental
Investigational medicinal product name	CHF1535 100/6 µg pMDI fixed dose combination of BDP + FF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

CHF1535 100/6 µg pMDI BDP + FF is a drug pressurised inhaler per actuation. It was given twice daily (BID), 2 puffs in the morning preferably before 10.00 am and 2 puffs in the evening preferably before 10.00 pm.

Arm title	Treatment Sequence - Inhaler B // Inhaler A
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Arm description:

The 2, 2-week treatment periods in the cross-over design were deemed adequate to evaluate the psychopharmacological aspects and assess the subject's preferences and perception of symptoms comparing two inhalers containing the same medication/formulation as Foster® 100/6 µg pMDI but with different characteristics.

The treatment sequence Inhaler B/Inhaler A consists of:

- Baseline treatment with Foster® CHF1535 100/6 µg pMDI, from V1 (Day 1) for a 2-week period;
- First treatment period with CHF1535 100/6 µg pMDI with Inhaler B (pink actuator), from V2 (Day 15) to V3 (Day 29);
- Second treatment period with CHF1535 100/6 µg pMDI with Inhaler A (white actuator), from V3 (Day 29) to V4 (Day 43).

39 subjects were randomized into this treatment sequence, of whom 36 completed the study.

1 subject discontinued during the baseline period due to other reason and 2 subjects discontinued due to withdrawal of consent and other reasons during Treatment period 1, while receiving inhaler B.

Arm type	Experimental
Investigational medicinal product name	CHF1535 100/6 µg pMDI fixed dose combination of BDP + FF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

CHF1535 100/6 µg pMDI BDP + FF is a drug pressurised inhaler per actuation. It was given twice daily (BID), 2 puffs in the morning preferably before 10.00 am and 2 puffs in the evening preferably before 10.00 pm.

Number of subjects in period 1^[1]	Treatment Sequence - Inhaler A // Inhaler B	Treatment Sequence - Inhaler B // Inhaler A
Started	36	38
Completed	36	36
Not completed	0	2
Consent withdrawn by subject	-	1
Other reasons	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 81 subjects enrolled in the trial, 4 screening failures. Of the 78 randomised subjects, 4 discontinued during the baseline period and 74 started the treatment.

Baseline characteristics

Reporting groups

Reporting group title	Treatment Sequence - Inhaler A // Inhaler B
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Reporting group description:

The 2, 2-week treatment periods in the cross-over design were deemed adequate to evaluate the psychopharmacological aspects and assess the subject's preferences and perception of symptoms comparing two inhalers containing the same medication/formulation as Foster® 100/6 µg pMDI but with different characteristics.

The treatment sequence Inhaler A/Inhaler B consists of:

- Baseline treatment with Foster® CHF1535 100/6 µg pMDI, from V1 (Day 1) for a 2-week period;
- First treatment period with CHF1535 100/6 µg pMDI with Inhaler A (white actuator), from V2 (Day 15) to V3 (Day 29);
- Second treatment period with CHF1535 100/6 µg pMDI with Inhaler B (pink actuator), from V3 (Day 29) to V4 (Day 43).

39 subjects were randomized into this treatment sequence, of whom 36 completed the study.

3 subjects discontinued during the baseline period for undergoing adverse events, for consent withdrawal and other reasons.

Reporting group title	Treatment Sequence - Inhaler B // Inhaler A
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Reporting group description:

The 2, 2-week treatment periods in the cross-over design were deemed adequate to evaluate the psychopharmacological aspects and assess the subject's preferences and perception of symptoms comparing two inhalers containing the same medication/formulation as Foster® 100/6 µg pMDI but with different characteristics.

The treatment sequence Inhaler B/Inhaler A consists of:

- Baseline treatment with Foster® CHF1535 100/6 µg pMDI, from V1 (Day 1) for a 2-week period;
- First treatment period with CHF1535 100/6 µg pMDI with Inhaler B (pink actuator), from V2 (Day 15) to V3 (Day 29);
- Second treatment period with CHF1535 100/6 µg pMDI with Inhaler A (white actuator), from V3 (Day 29) to V4 (Day 43).

39 subjects were randomized into this treatment sequence, of whom 36 completed the study.

1 subject discontinued during the baseline period due to other reason and 2 subjects discontinued due to withdrawal of consent and other reasons during Treatment period 1, while receiving inhaler B.

Reporting group values	Treatment Sequence - Inhaler A // Inhaler B	Treatment Sequence - Inhaler B // Inhaler A	Total
Number of subjects	36	38	74
Age categorical Units: Subjects			
Adults (18-64 years)	29	28	57
From 65-84 years	7	10	17
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	47.0	51.6	
standard deviation	± 16.2	± 15.2	-
Gender categorical Units: Subjects			
Female	21	19	40
Male	15	19	34
Race Units: Subjects			
White	36	38	74
Asian	0	0	0
Black or African American	0	0	0

Other	0	0	0
Smoking Status			
Units: Subjects			
Non-smoker	26	20	46
Ex-smoker	9	17	26
Current smoker	1	1	2
BMI			
Units: kg/m2			
arithmetic mean	26.50	26.06	
standard deviation	± 4.36	± 4.30	-
Weight			
Units: kg			
arithmetic mean	75.6	73.9	
standard deviation	± 14.7	± 14.8	-

End points

End points reporting groups

Reporting group title	Treatment Sequence - Inhaler A // Inhaler B
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Reporting group description:

The 2, 2-week treatment periods in the cross-over design were deemed adequate to evaluate the psychopharmacological aspects and assess the subject's preferences and perception of symptoms comparing two inhalers containing the same medication/formulation as Foster® 100/6 µg pMDI but with different characteristics.

The treatment sequence Inhaler A/Inhaler B consists of:

- Baseline treatment with Foster® CHF1535 100/6 µg pMDI, from V1 (Day 1) for a 2-week period;
- First treatment period with CHF1535 100/6 µg pMDI with Inhaler A (white actuator), from V2 (Day 15) to V3 (Day 29);
- Second treatment period with CHF1535 100/6 µg pMDI with Inhaler B (pink actuator), from V3 (Day 29) to V4 (Day 43).

39 subjects were randomized into this treatment sequence, of whom 36 completed the study.

3 subjects discontinued during the baseline period for undergoing adverse events, for consent withdrawal and other reasons.

Reporting group title	Treatment Sequence - Inhaler B // Inhaler A
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Reporting group description:

The 2, 2-week treatment periods in the cross-over design were deemed adequate to evaluate the psychopharmacological aspects and assess the subject's preferences and perception of symptoms comparing two inhalers containing the same medication/formulation as Foster® 100/6 µg pMDI but with different characteristics.

The treatment sequence Inhaler B/Inhaler A consists of:

- Baseline treatment with Foster® CHF1535 100/6 µg pMDI, from V1 (Day 1) for a 2-week period;
- First treatment period with CHF1535 100/6 µg pMDI with Inhaler B (pink actuator), from V2 (Day 15) to V3 (Day 29);
- Second treatment period with CHF1535 100/6 µg pMDI with Inhaler A (white actuator), from V3 (Day 29) to V4 (Day 43).

39 subjects were randomized into this treatment sequence, of whom 36 completed the study.

1 subject discontinued during the baseline period due to other reason and 2 subjects discontinued due to withdrawal of consent and other reasons during Treatment period 1, while receiving inhaler B.

Subject analysis set title	Inhaler A
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Subjects who took the test product CHF1535 100/6 µg pMDI fixed dose combination of BDP + FF via Inhaler A (white actuator), 2 puffs twice daily (BID).

Subject analysis set titles will be selected as labels in all the "endpoint values tables".

Subject analysis set title	Inhaler B
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Subjects who took the reference product CHF1535 100/6 µg pMDI fixed dose combination of BDP + FF via Inhaler B (pink actuator), 2 puffs twice daily (BID).

Subject analysis set titles will be selected as labels in all the "endpoint values tables".

Subject analysis set title	Answer - Inhaler A
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Answer given in study-specific subject's questionnaire.

Subject analysis set titles will be selected as labels in all the "endpoint values tables".

Subject analysis set title	Answer - Inhaler B
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Answer given in study-specific subject's questionnaire.

Subject analysis set titles will be selected as labels in all the "endpoint values tables".

Subject analysis set title	Answer - No Preference
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Subject analysis set type	Intention-to-treat
Subject analysis set description: Answer given in study-specific subject's questionnaire.	
Subject analysis set titles will be selected as labels in all the "endpoint values tables".	
Subject analysis set title	Answer - Yes
Subject analysis set type	Intention-to-treat
Subject analysis set description: Answer given in study-specific subject's questionnaire.	
Subject analysis set titles will be selected as labels in all the "endpoint values tables".	
Subject analysis set title	Answer - No
Subject analysis set type	Intention-to-treat
Subject analysis set description: Answer given in study-specific subject's questionnaire.	
Subject analysis set titles will be selected as labels in all the "endpoint values tables".	
Subject analysis set title	Answer - I do not know
Subject analysis set type	Intention-to-treat
Subject analysis set description: Answer given in study-specific subject's questionnaire.	
Subject analysis set titles will be selected as labels in all the "endpoint values tables".	

Primary: Change from baseline in average VAS score (range 1-100) perceptions of asthma - over the 14 days of treatment - Question #3

End point title	Change from baseline in average VAS score (range 1-100) perceptions of asthma - over the 14 days of treatment - Question #3
End point description: The analysis was performed on the ITT set. The results of VAS score of asthma symptoms were obtained daily from subjects' answers to Question #3 of study-specific subject's questionnaire. Baseline score is the average of the VAS scores collected during the baseline period and change from baseline is calculated over the entire 14-days treatment periods. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint, period by timepoint interaction and treatment by timepoint interaction as fixed effects. Data are presented as adjusted means in each treatment group and their 95% CIs. This endpoint is indicated as PRIMARY ENDPOINT to comply with EudraCT register requirements, but it should be considered as an OTHER PRE-SPECIFIED endpoint like the other endpoints listed.	
End point type	Primary
End point timeframe: Question #3 "How would you score your asthma symptoms yesterday?" was to be answered every morning during the 14-days baseline period and over the two 14-days treatment periods.	

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[1]	73 ^[2]		
Units: score				
arithmetic mean (confidence interval 95%)	2.68 (0.99 to 4.37)	1.63 (-0.06 to 3.32)		

Notes:

[1] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[2] - Number of subjects with available data/Number of subjects in the ITT set: 73/74

Statistical analyses

Statistical analysis title	Change from baseline - 14 days treatment period
Statistical analysis description:	
The analysis was performed on the ITT set. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint and treatment by timepoint interaction as fixed effects. Data are presented as adjusted mean differences with their 95% two-sided Confidence Intervals, and p-value.	
The value N=145, shown below, is generated automatically and is due to innate error of the EudraCT database system.	
Comparison groups	Inhaler A v Inhaler B
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.385
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	3.45

Other pre-specified: Change from baseline in average VAS score (range 1-100) perceptions of asthma - over the 14 days of treatment - Question #4

End point title	Change from baseline in average VAS score (range 1-100) perceptions of asthma - over the 14 days of treatment - Question #4
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End point description:

The analysis was performed on the ITT set. The results of VAS score of asthma symptoms were obtained daily from subjects' answers to Question #4 of study-specific subject's questionnaire. Baseline score is the average of the VAS scores collected during the baseline period and change from baseline is calculated over the entire 14-days treatment periods. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint, period by timepoint interaction and treatment by timepoint interaction as fixed effects. Data are presented as adjusted means in each treatment group and their 95% CIs.

End point type	Other pre-specified
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End point timeframe:

Question #4 "How burdensome was your asthma yesterday?" was to be answered over the entire 14-day treatment period (every morning from the day after V1 to the end of the study at V4).

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[3]	73 ^[4]		
Units: score				
arithmetic mean (confidence interval 95%)	2.62 (0.58 to 4.65)	1.82 (-0.22 to 3.85)		

Notes:

[3] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[4] - Number of subjects with available data/Number of subjects in the ITT set: 73/74

Statistical analyses

Statistical analysis title	Change from baseline - 14 days treatment period
Statistical analysis description:	
An unstructured covariance matrix within period was assumed, and the Kenward-Roger adjustment was used for the degrees of freedom. Data are presented as adjusted mean differences with their 95% two-sided Confidence Intervals, and p-value. The value N=145, shown below, is generated automatically and is due to innate error of the EudraCT database system.	
Comparison groups	Inhaler A v Inhaler B
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.582
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.08
upper limit	3.68

Other pre-specified: Change from baseline in average VAS score (range 1-100) perceptions of asthma - over the 14 days of treatment - Question #5

End point title	Change from baseline in average VAS score (range 1-100) perceptions of asthma - over the 14 days of treatment - Question #5
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End point description:

The analysis was performed on the ITT set. The results of VAS score of asthma symptoms were obtained daily from subjects' answers to Question #5 of study-specific subject's questionnaire. Baseline score is the average of the VAS scores collected during the baseline period and change from baseline is calculated over the entire 14-days treatment periods. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint, period by timepoint interaction and treatment by timepoint interaction as fixed effects. Data are presented as adjusted means in each treatment group and their 95% CIs.

End point type	Other pre-specified
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End point timeframe:

Question #5 "Did your asthma symptoms improve yesterday?" was to be answered over the entire 14-day treatment period (every morning from the day after V1 to the end of the study at V4).

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[5]	73 ^[6]		
Units: score				
arithmetic mean (confidence interval 95%)	0.25 (-1.27 to 1.76)	1.54 (0.02 to 3.05)		

Notes:

[5] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[6] - Number of subjects with available data/Number of subjects in the ITT set: 73/74

Statistical analyses

Statistical analysis title	Change from baseline - 14 days treatment period
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Statistical analysis description:

An unstructured covariance matrix within period was assumed, and the Kenward-Roger adjustment was used for the degrees of freedom. Data are presented as adjusted mean differences with their 95% two-sided Confidence Intervals, and p-value.

The value N=145, shown below, is generated automatically and is due to innate error of the EudraCT database system.

Comparison groups	Inhaler A v Inhaler B
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.234
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	-1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.43
upper limit	0.85

Other pre-specified: Change from baseline in average VAS score (range 1-100) perceptions of asthma - over the 14 days of treatment - Question #6

End point title	Change from baseline in average VAS score (range 1-100) perceptions of asthma - over the 14 days of treatment - Question #6
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End point description:

The analysis was performed on the ITT set. The results of VAS score of asthma symptoms were obtained daily from subjects' answers to Question #6 of study-specific subject's questionnaire. Baseline score is the average of the VAS scores collected during the baseline period and change from baseline is calculated over the entire 14-days treatment periods. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint, period by timepoint interaction and treatment by timepoint interaction as fixed effects. Data are presented as adjusted means in each treatment group and their 95% CIs.

End point type	Other pre-specified
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End point timeframe:

Question #6 "Did your asthma symptoms worsen yesterday?" was to be answered over the entire 14-day treatment period (every morning from the day after V1 to the end of the study at V4).

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[7]	73 ^[8]		
Units: score				
arithmetic mean (confidence interval 95%)	2.53 (0.82 to 4.25)	1.66 (-0.05 to 3.38)		

Notes:

[7] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[8] - Number of subjects with available data/Number of subjects in the ITT set: 73/74

Statistical analyses

Statistical analysis title	Change from baseline - 14 days treatment period
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Statistical analysis description:

An unstructured covariance matrix within period was assumed, and the Kenward-Roger adjustment was used for the degrees of freedom. Data are presented as adjusted mean differences with their 95% two-sided Confidence Intervals, and p-value.

The value N=145, shown below, is generated automatically and is due to innate error of the EudraCT database system.

Comparison groups	Inhaler A v Inhaler B
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.475
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	3.3

Other pre-specified: Change from baseline in average VAS score (range 1-100) - over the first 7 days of treatment - Question #3

End point title	Change from baseline in average VAS score (range 1-100) - over the first 7 days of treatment - Question #3
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End point description:

The analysis was performed on the ITT set. The results of VAS score of asthma symptoms were obtained daily from subjects' answers to Question #3 of study-specific subject's questionnaire. Baseline score is the average of the VAS scores collected during the baseline period and change from baseline is calculated over the first 7 days of treatment. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint, period by timepoint interaction and treatment by timepoint interaction as fixed effects. Data are presented as adjusted means in each treatment group and their 95% CIs.

End point type	Other pre-specified
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End point timeframe:

Question #3 "How would you score your asthma symptoms yesterday?" was to be answered every morning during the 14-days baseline period and over the first 7 days treatment periods.

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[9]	73 ^[10]		
Units: score				
arithmetic mean (confidence interval 95%)	2.91 (1.40 to 4.42)	1.72 (0.22 to 3.22)		

Notes:

[9] - Number of subjects with available data/Number of subjects in the ITT set: 71/72

[10] - Number of subjects with available data/Number of subjects in the ITT set: 73/74

Statistical analyses

Statistical analysis title	Change from baseline - 7 days treatment period
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Statistical analysis description:

The analysis was performed on the ITT set. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint, period by timepoint interaction and treatment by timepoint interaction as fixed effects. Data are presented as adjusted mean differences with their 95% two-sided Confidence Intervals, and p-value.

The value N=144, shown below, is generated automatically and is due to innate error of the EudraCT database system.

Comparison groups	Inhaler A v Inhaler B
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.267
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	3.31

Other pre-specified: Change from baseline in average VAS score (range 1-100) - over the first 7 days of treatment - Question #4

End point title	Change from baseline in average VAS score (range 1-100) - over the first 7 days of treatment - Question #4
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End point description:

The analysis was performed on the ITT set. The results of VAS score of asthma symptoms were obtained daily from subjects' answers to Question #4 of study-specific subject's questionnaire. Baseline score is the average of the VAS scores collected during the baseline period and change from baseline is calculated over the first 7 days of treatment. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint, period by timepoint interaction and treatment by timepoint interaction as fixed effects. Data are presented as adjusted means in each treatment group and their 95% CIs.

End point type	Other pre-specified
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End point timeframe:

Question #4 "How burdensome was your asthma yesterday?" was to be answered over the entire 14-

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[11]	73 ^[12]		
Units: score				
arithmetic mean (confidence interval 95%)	2.82 (0.88 to 4.77)	1.78 (-0.15 to 3.71)		

Notes:

[11] - Number of subjects with available data/Number of subjects in the ITT set: 71/72

[12] - Number of subjects with available data/Number of subjects in the ITT set: 73/74

Statistical analyses

Statistical analysis title	Change from baseline - 7 days treatment period
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Statistical analysis description:

An unstructured covariance matrix within period was assumed, and the Kenward-Roger adjustment was used for the degrees of freedom. Data are presented as adjusted mean differences with their 95% two-sided Confidence Intervals, and p-value.

The value N=144, shown below, is generated automatically and is due to innate error of the EudraCT database system.

Comparison groups	Inhaler A v Inhaler B
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.45
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	3.78

Other pre-specified: Change from baseline in average VAS score (range 1-100) - over the first 7 days of treatment - Question #5

End point title	Change from baseline in average VAS score (range 1-100) - over the first 7 days of treatment - Question #5
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End point description:

The analysis was performed on the ITT set. The results of VAS score of asthma symptoms were obtained daily from subjects' answers to Question #5 of study-specific subject's questionnaire. Baseline score is the average of the VAS scores collected during the baseline period and change from baseline is calculated over the first 7 days of treatment. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint, period by timepoint interaction and treatment by timepoint interaction as fixed effects. Data are presented as adjusted means in each treatment group and their 95% CIs.

End point type	Other pre-specified
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End point timeframe:

Question #5 "Did your asthma symptoms improve yesterday?" was to be answered over the entire 14-

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[13]	73 ^[14]		
Units: score				
arithmetic mean (confidence interval 95%)	0.69 (-1.64 to 3.02)	1.45 (-0.86 to 3.76)		

Notes:

[13] - Number of subjects with available data/Number of subjects in the ITT set: 71/72

[14] - Number of subjects with available data/Number of subjects in the ITT set: 73/74

Statistical analyses

Statistical analysis title	Change from baseline - 7 days treatment period
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Statistical analysis description:

An unstructured covariance matrix within period was assumed, and the Kenward-Roger adjustment was used for the degrees of freedom. Data are presented as adjusted mean differences with their 95% two-sided Confidence Intervals, and p-value.

The value N=144, shown below, is generated automatically and is due to innate error of the EudraCT database system.

Comparison groups	Inhaler A v Inhaler B
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.648
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.04
upper limit	2.53

Other pre-specified: Change from baseline in average VAS score (range 1-100) - over the first 7 days of treatment - Question #6

End point title	Change from baseline in average VAS score (range 1-100) - over the first 7 days of treatment - Question #6
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End point description:

The analysis was performed on the ITT set. The results of VAS score of asthma symptoms were obtained daily from subjects' answers to Question #6 of study-specific subject's questionnaire. Baseline score is the average of the VAS scores collected during the baseline period and change from baseline is calculated over the first 7 days of treatment. A linear mixed model for repeat measures was used, including subject, period, treatment, timepoint, period by timepoint interaction and treatment by timepoint interaction as fixed effects. Data are presented as adjusted means in each treatment group and their 95% CIs.

End point type	Other pre-specified
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End point timeframe:

Question #6 "Did your asthma symptoms worsen yesterday?" was to be answered over the entire 14-

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[15]	73 ^[16]		
Units: score				
arithmetic mean (confidence interval 95%)	2.08 (0.15 to 4.00)	1.94 (0.02 to 3.85)		

Notes:

[15] - Number of subjects with available data/Number of subjects in the ITT set: 71/72

[16] - Number of subjects with available data/Number of subjects in the ITT set: 73/74

Statistical analyses

Statistical analysis title	Change from baseline - 7 days treatment period
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Statistical analysis description:

An unstructured covariance matrix within period was assumed, and the Kenward-Roger adjustment was used for the degrees of freedom. Data are presented as adjusted mean differences with their 95% two sided Confidence Intervals, and p-value.

The value N=144, shown below, is generated automatically and is due to innate error of the EudraCT database system.

Comparison groups	Inhaler A v Inhaler B
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.919
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.58
upper limit	2.86

Other pre-specified: Psychopharmacological aspects - Question #7

End point title	Psychopharmacological aspects - Question #7
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End point description:

The end point evaluates the subject's questionnaire item (VAS score) related to subjects' expected improving before starting the treatment period. This analysis will be applied on Question #7 of the study-specific subject's questionnaire. The analysis was performed for the ITT set. Data are presented as arithmetic mean and standard deviation.

End point type	Other pre-specified
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End point timeframe:

Question #7 "Do you expect any improvement in asthma symptoms with this treatment?" was to be answered at specific study visit timepoints (V2 - day 15, V3 - day 29), before starting the treatment period.

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50 ^[17]	45 ^[18]		
Units: score				
arithmetic mean (standard deviation)	64.5 (± 34.3)	60.8 (± 36.8)		

Notes:

[17] - Number of subjects with available data/Number of subjects in the ITT set: 50/72

[18] - Number of subjects with available data/Number of subjects in the ITT set: 45/74

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Psychopharmacological aspects - Question #8

End point title	Psychopharmacological aspects - Question #8
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End point description:

The end point evaluates the subject's questionnaire item (VAS score) related to subjects' expected worsening before starting the treatment period. This analysis will be applied on Question #8 of the study-specific subject's questionnaire. The analysis was performed for the ITT set. Data are presented as arithmetic mean and standard deviation.

End point type	Other pre-specified
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End point timeframe:

Question #8 "Do you expect any worsening of your asthma symptoms with this treatment?" was to be answered at specific study visit timepoints (V2 - day 15, V3 - day 29), before starting the treatment period.

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50 ^[19]	45 ^[20]		
Units: score				
arithmetic mean (standard deviation)	8.9 (± 17.0)	8.0 (± 16.2)		

Notes:

[19] - Number of subjects with available data/Number of subjects in the ITT set: 50/72

[20] - Number of subjects with available data/Number of subjects in the ITT set: 45/74

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Psychopharmacological aspects - Question #9

End point title	Psychopharmacological aspects - Question #9
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End point description:

The end point evaluates the subject's questionnaire item (VAS score) related to subjects' improvement in overall asthma symptoms at the end of the entire treatment period. This analysis will be applied on Question #9 of the study-specific subject's questionnaire. The analysis was performed for the ITT set. Data are presented as arithmetic mean and standard deviation.

End point type	Other pre-specified
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End point timeframe:

Question #9 "How much do you think this treatment improved your overall asthma symptoms?" was to be answered at specific study visit timepoints (V3 - day 29, V4 - day 43), at the end of the entire treatment period.

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55 ^[21]	51 ^[22]		
Units: score				
arithmetic mean (standard deviation)	41.1 (± 36.5)	44.6 (± 35.8)		

Notes:

[21] - Number of subjects with available data/Number of subjects in the ITT set: 55/72

[22] - Number of subjects with available data/Number of subjects in the ITT set: 51/74

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Psychopharmacological aspects - Question #10

End point title	Psychopharmacological aspects - Question #10
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End point description:

The end point evaluates the subject's questionnaire item (VAS score) related to subjects' worsening in overall asthma symptoms at the end of the entire treatment period. This analysis will be applied on Question #10 of the study-specific subject's questionnaire. The analysis was performed for the ITT set. Data are presented as arithmetic mean and standard deviation.

End point type	Other pre-specified
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End point timeframe:

Question #10 "How much do you think this treatment worsened your overall asthma symptoms?" was to be answered at specific study visit timepoints (V3 - day 29, V4 - day 43), at the end of the entire treatment period.

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55 ^[23]	51 ^[24]		
Units: score				
arithmetic mean (standard deviation)	8.0 (± 14.9)	11.8 (± 17.2)		

Notes:

[23] - Number of subjects with available data/Number of subjects in the ITT set: 55/72

[24] - Number of subjects with available data/Number of subjects in the ITT set: 51/74

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' preference and perception of the devices - over the 14 days of treatment - Question #11

End point title	Subjects' preference and perception of the devices - over the 14 days of treatment - Question #11
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End point description:

Number and percentage of subjects will be reported on the ITT population by treatment group along with their 95%CI. This analysis will be applied on questions #11, #12, #13, #14, #15 and #16 of the study-specific subject's questionnaire collected only at V4.

End point type	Other pre-specified
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End point timeframe:

Questions #11 "Which inhaler did you visually prefer?" was answered before disclosing that the only difference between the two inhalers was the colour of the actuator.

End point values	Answer - Inhaler A	Answer - Inhaler B	Answer - No Preference	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	14	17	27	
Units: %				
arithmetic mean (confidence interval 95%)	24.1 (13.9 to 37.2)	29.3 (18.1 to 42.7)	46.6 (33.3 to 60.1)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' preference and perception of the devices - over the 14 days of treatment - Question #12

End point title	Subjects' preference and perception of the devices - over the 14 days of treatment - Question #12
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End point description:

Number and percentage of subjects will be reported on the ITT population by treatment group along with their 95%CI. This analysis will be applied on questions #11, #12, #13, #14, #15 and #16 of the study-specific subject's questionnaire collected only at V4.

End point type	Other pre-specified
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End point timeframe:

Questions #12 "Which inhaler did you prefer to use?" was answered before disclosing that the only difference between the two inhalers was the colour of the actuator.

End point values	Answer - Inhaler A	Answer - Inhaler B	Answer - No Preference	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	16	22	
Units: %				
arithmetic mean (confidence interval 95%)	34.5 (22.5 to 48.1)	27.6 (16.7 to 40.9)	37.9 (25.5 to 51.6)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' preference and perception of the devices - over the 14 days of treatment - Question #13

End point title	Subjects' preference and perception of the devices - over the 14 days of treatment - Question #13
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End point description:

Number and percentage of subjects will be reported on the ITT population by treatment group along with their 95%CI. This analysis will be applied on questions #11, #12, #13, #14, #15 and #16 of the study-specific subject's questionnaire collected only at V4.

End point type	Other pre-specified
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End point timeframe:

Questions #13 "Do you think that changes were made to the inhalers?" was answered before disclosing that the only difference between the two inhalers was the colour of the actuator.

End point values	Answer - Yes	Answer - No	Answer - I do not know	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	17	14	
Units: %				
arithmetic mean (confidence interval 95%)	46.6 (33.3 to 60.1)	29.3 (18.1 to 42.7)	24.1 (13.9 to 37.2)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' preference and perception of the devices - over the 14 days of treatment - Question #14

End point title	Subjects' preference and perception of the devices - over the 14 days of treatment - Question #14
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End point description:

Number and percentage of subjects will be reported on the ITT population by treatment group along with their 95%CI. This analysis will be applied on questions #11, #12, #13, #14, #15 and #16 of the study-specific subject's questionnaire collected only at V4.

End point type	Other pre-specified
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End point timeframe:

Questions #14 "Do you think the changes we made across the inhalers have impacted your asthma symptoms?" was answered before disclosing that the only difference between the 2 inhalers was the colour of the actuator, among the sbj who answered Yes to Q#13.

End point values	Answer - Yes	Answer - No	Answer - I do not know	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	14	10	3	
Units: %				
arithmetic mean (confidence interval 95%)	51.9 (31.9 to 71.3)	37.0 (19.4 to 57.6)	11.1 (2.4 to 29.2)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' preference and perception of the devices - over the 14 days of treatment - Question #15

End point title	Subjects' preference and perception of the devices - over the 14 days of treatment - Question #15
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End point description:

Number and percentage of subjects will be reported on the ITT population by treatment group along with their 95%CI. This analysis will be applied on questions #11, #12, #13, #14, #15 and #16 of the study-specific subject's questionnaire collected only at V4.

End point type	Other pre-specified
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End point timeframe:

Questions #15 "Based on the information you've received, did it impact your perception of your asthma symptoms?" was answered after disclosure (only at V4).

End point values	Answer - Yes	Answer - No	Answer - I do not know	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	39	7	
Units: %				
arithmetic mean (confidence interval 95%)	20.7 (11.2 to 33.4)	67.2 (53.7 to 79.0)	12.1 (5.0 to 23.3)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' preference and perception of the devices - over the 14 days of treatment - Question #16

End point title	Subjects' preference and perception of the devices - over the 14 days of treatment - Question #16
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End point description:

Number and percentage of subjects will be reported on the ITT population by treatment group along with their 95%CI. This analysis will be applied on questions #11, #12, #13, #14, #15 and #16 of the study-specific subject's questionnaire collected only at V4.

End point type	Other pre-specified
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End point timeframe:

Questions #16 "Which of inhaler A or inhaler B had the biggest impact on the perception of your asthma

symptoms?" was answered after disclosure (only at V4).

End point values	Answer - Inhaler A	Answer - Inhaler B	Answer - No Preference	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	18	13	27	
Units: %				
arithmetic mean (confidence interval 95%)	31.0 (19.5 to 44.5)	22.4 (12.5 to 35.3)	46.6 (33.3 to 60.1)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in average reliever medication use - over the 14 days of treatment - Question #2

End point title	Change from baseline in average reliever medication use - over the 14 days of treatment - Question #2
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End point description:

The analyses will be applied on questions #2 of the study-specific subject's questionnaire collected daily. Average use (puffs/day) during baseline, average use (puffs/day) during treatment period (over the entire 14 treatment days) and change from baseline will be summarized on the ITT population by treatment group.

End point type	Other pre-specified
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End point timeframe:

Question #2 "How many puffs of rescue medication have you taken yesterday?" was to be answered over the entire 14-day treatment period (every morning from the day after V1 to the end of the study at V4).

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[25]	73 ^[26]		
Units: puffs/day				
arithmetic mean (standard deviation)	-0.06 (± 0.69)	-0.04 (± 0.74)		

Notes:

[25] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[26] - Number of subjects with available data/Number of subjects in the ITT set: 73/74

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in AQLQ activity limitation score - after 14 days of treatment

End point title	Change from baseline in AQLQ activity limitation score - after 14 days of treatment
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End point description:

The standardised AQLQ scoring system is used to assess quality of life of asthma subjects in this study. It consists of 32 questions divided in 4 domains and has a 7-point scale to assess subject's condition. Only one response is allowed per question and a subject must answer all the questions.

End point type	Other pre-specified
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End point timeframe:

AQLQ(S) scores was performed over the 14-day period.

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[27]	72 ^[28]		
Units: score				
arithmetic mean (standard deviation)	0.10 (± 0.41)	0.04 (± 0.53)		

Notes:

[27] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[28] - Number of subjects with available data/Number of subjects in the ITT set: 72/74

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in AQLQ symptoms score - after 14 days of treatment

End point title	Change from baseline in AQLQ symptoms score - after 14 days of treatment
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End point description:

The standardised AQLQ scoring system is used to assess quality of life of asthma subjects in this study. It consists of 32 questions divided in 4 domains and has a 7-point scale to assess subject's condition. Only one response is allowed per question and a subject must answer all the questions.

End point type	Other pre-specified
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End point timeframe:

AQLQ(S) scores was performed over the 14-day period.

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[29]	72 ^[30]		
Units: score				
arithmetic mean (standard deviation)	-0.03 (± 0.42)	0.00 (± 0.66)		

Notes:

[29] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[30] - Number of subjects with available data/Number of subjects in the ITT set: 72/74

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in AQLQ emotional function score - after 14 days of treatment

End point title	Change from baseline in AQLQ emotional function score - after 14 days of treatment
End point description: The standardised AQLQ scoring system is used to assess quality of life of asthma subjects in this study. It consists of 32 questions divided in 4 domains and has a 7-point scale to assess subject's condition. Only one response is allowed per question and a subject must answer all the questions.	
End point type	Other pre-specified
End point timeframe: AQLQ(S) scores was performed over the 14-day period.	

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[31]	72 ^[32]		
Units: score				
arithmetic mean (standard deviation)	0.06 (± 0.37)	0.04 (± 0.71)		

Notes:

[31] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[32] - Number of subjects with available data/Number of subjects in the ITT set: 72/74

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in AQLQ environmental stimuli score - after 14 days of treatment

End point title	Change from baseline in AQLQ environmental stimuli score - after 14 days of treatment
End point description: The standardised AQLQ scoring system is used to assess quality of life of asthma subjects in this study. It consists of 32 questions divided in 4 domains and has a 7-point scale to assess subject's condition. Only one response is allowed per question and a subject must answer all the questions.	
End point type	Other pre-specified
End point timeframe: AQLQ(S) scores was performed over the 14-day period.	

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[33]	72 ^[34]		
Units: score				
arithmetic mean (standard deviation)	0.11 (± 0.70)	0.13 (± 0.61)		

Notes:

[33] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[34] - Number of subjects with available data/Number of subjects in the ITT set: 72/74

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in AQLQ overall score - after 14 days of treatment

End point title	Change from baseline in AQLQ overall score - after 14 days of treatment
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End point description:

The standardised AQLQ scoring system is used to assess quality of life of asthma subjects in this study. It consists of 32 questions divided in 4 domains and has a 7-point scale to assess subject's condition. Only one response is allowed per question and a subject must answer all the questions.

End point type	Other pre-specified
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End point timeframe:

AQLQ(S) scores was performed over the 14-day period.

End point values	Inhaler A	Inhaler B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72 ^[35]	72 ^[36]		
Units: score				
arithmetic mean (standard deviation)	0.05 (± 0.37)	0.04 (± 0.53)		

Notes:

[35] - Number of subjects with available data/Number of subjects in the ITT set: 72/72

[36] - Number of subjects with available data/Number of subjects in the ITT set: 72/74

Statistical analyses

Statistical analysis title	Change from baseline AQLQ(S)
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Statistical analysis description:

Change from baseline in the Standardised Asthma Quality of Life Questionnaire score after 14 days of treatment in each treatment periods was analysed for the ITT set by an analysis of variance (ANOVA) model including treatment, period and subject as fixed effects.

Data are presented as adjusted mean differences with their 95% two sided Confidence Intervals, and p-value.

The value N=144, shown below, is generated automatically and is due to innate error of the EudraCT database system.

Comparison groups	Inhaler A v Inhaler B
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.823
Method	ANOVA
Parameter estimate	Adjusted Mean Difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.12

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Safety variables were presented using descriptive statistics. The safety analysis was based on the Safety set using the actual treatment received.

Adverse event reporting additional description:

All AEs are reported by System Organ Class and Preferred Term and are coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 24.0.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24
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Reporting groups

Reporting group title	Inhaler A
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Reporting group description:

CHF1535 100/6 µg pMDI fixed dose combination of BDP + FF via Inhaler A (white actuator), 2 puffs twice daily (BID).

Reporting group title	Inhaler B
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Reporting group description:

CHF1535 100/6 µg pMDI fixed dose combination of BDP + FF via Inhaler B (pink actuator), 2 puffs twice daily (BID).

Serious adverse events	Inhaler A	Inhaler B	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Inhaler A	Inhaler B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 72 (9.72%)	6 / 74 (8.11%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Chest discomfort subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0	1 / 74 (1.35%) 1	
Gastrointestinal disorders Oral discomfort subjects affected / exposed occurrences (all)	1 / 72 (1.39%) 1	0 / 74 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dysphonia subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Rhinitis allergic subjects affected / exposed occurrences (all) Throat irritation subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0 1 / 72 (1.39%) 1 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0 1 / 72 (1.39%) 1	4 / 74 (5.41%) 4 0 / 74 (0.00%) 0 2 / 74 (2.70%) 2 1 / 74 (1.35%) 1 0 / 74 (0.00%) 0	
Musculoskeletal and connective tissue disorders Musculoskeletal chest pain subjects affected / exposed occurrences (all)	1 / 72 (1.39%) 1	0 / 74 (0.00%) 0	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Laryngitis	2 / 72 (2.78%) 2 1 / 72 (1.39%) 1	1 / 74 (1.35%) 1 0 / 74 (0.00%) 0	

subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	
occurrences (all)	1	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