Clinical trial results:
A Single-Dose, Open-Label, Randomized, 3-way Crossover, Clinical Pharmacology Study of CHF 1535 100/6 pMDI (fixed combination of Beclomethasone Dipropionate 100 g plus Formoterol Fumarate 6 g) with or without Spacer Device versus the free Combination of Licensed Beclomethasone pMDI and Formoterol pMDI in Asthmatic Adolescent Patients and One Open-Arm for Adult Patients as Control Group treated with CHF 1535 100/6 pMDI.

Summary

EudraCT number	2011-005108-14
Trial protocol	PL
Global end of trial date	24 August 2012

Results information

Result version number	v1 (current)
This version publication date	10 November 2017
First version publication date	10 November 2017

Trial information

Trial identification

Sponsor protocol code	CCD-1104-PR-0062

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01803087
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., Chiesi Farmaceutici S.p.A., +39 0521 2791, ClinicalTrials_info@chiesi.com
Scientific contact	Clinical Trial Transparency, Chiesi Farmaceutici S.p.A., Chiesi Farmaceutici S.p.A., +39 0521 2791, ClinicalTrials_info@chiesi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000548-PIP01-09
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 March 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 August 2012
Global end of trial reached?	Yes
Global end of trial date	24 August 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate, in adolescents, the systemic exposure to B17MP (active metabolite of BDP) as AUC0-t, after inhalation of CHF 1535 100/6 pMDI with and without spacer device (AeroChamber Plus™) in comparison with the already licensed free combination of BDP pMDI and Formoterol pMDI without spacer.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice (GCP) guidelines and local law requirements. Other than routine care, no specific measures for protection of trial subjects were implemented.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2012
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	Poland: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	30
Adults (18-64 years)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from subjects attending the outpatient's hospital clinics or independent Clinical Research Organisation. Subjects were selected and randomised according to the inclusion criteria.

Pre-assignment

Screening details:

In total, 30 adolescents and 30 adults were screened. No subjects failed screening; all 30 adolescents were randomised to one of 3 treatment sequences (TEST 1/REF/TEST 2, TEST 2/TEST 1/REF, REF/TEST 2/TEST 1), i.e., 10 subjects per treatment sequence, and received study drugs, and all 30 adults received a single dose of control drug (CTR)

Period 1

Period 1 title	Overall trial by sequence (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

As this is an open-label study, blinding is not applicable.

Arms

Are arms mutually exclusive?	Yes
Arm title	TEST 1/REF/TEST 2

Arm description:

Adolescent subjects took the following single-day treatments in sequence:
• TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI for a (total dose of BDP 400 µg / formoterol fumarate [FF] 24 µg);
• REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI for a total dose of BDP 400 µg + FF 24 µg.
• TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using AeroChamber Plus™ for a total dose of BDP 400 µg / FF 24 µg);
The 3 single-day treatment periods were separated by a wash-out period of minimum 7 and maximum 21 days.
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Arm type	Experimental
Investigational medicinal product name	CHF 1535
Investigational medicinal product code	
Other name	beclomethasone dipropionate (BDP), formoterol fumarate (FF), Foster
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

CHF 1535 100/6 pMDI, 4 puffs (total dose of BDP 400 µg / FF 24 µg) CHF 1535 100/6 pMDI, without (TEST 1) or with (TEST 2) AeroChamber Plus™

Investigational medicinal product name	beclomethasone dipropionate + formoterol fumarate
Investigational medicinal product code	
Other name	BDP, FF
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Free combination of BDP pMDI plus FF pMDI, 4 + 4 puffs (total dose of BDP 400 µg + FF 24 µg)

Arm title	TEST 2/TEST 1/REF

Arm description:

Adolescent subjects took the following single-day treatments in sequence:
• TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using AeroChamber Plus™ for a total dose of BDP 400 µg / FF 24 µg);
• TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI for a (total dose of BDP 400 µg / formoterol fumarate [FF] 24 µg);
• REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI for a total dose of BDP 400 µg + FF 24 µg.
The 3 single-day treatment periods were separated by a wash-out period of minimum 7 and maximum 21 days.
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Arm type	Experimental
Investigational medicinal product name	CHF 1535
Investigational medicinal product code	
Other name	beclomethasone dipropionate (BDP), formoterol fumarate (FF), Foster
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

CHF 1535 100/6 pMDI, 4 puffs (total dose of BDP 400 µg / FF 24 µg) CHF 1535 100/6 pMDI, without (TEST 1) or with (TEST 2) AeroChamber Plus™

Investigational medicinal product name	beclomethasone dipropionate + formoterol fumarate
Investigational medicinal product code	
Other name	BDP, FF
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Free combination of BDP pMDI plus FF pMDI, 4 + 4 puffs (total dose of BDP 400 µg + FF 24 µg)

Arm title	REF/TEST 2/TEST 1

Arm description:

Adolescent subjects took the following single-day treatments in sequence:
• REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI for a total dose of BDP 400 µg + FF 24 µg.
• TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using AeroChamber Plus™ for a total dose of BDP 400 µg / FF 24 µg);
• TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI for a (total dose of BDP 400 µg / formoterol fumarate [FF] 24 µg);
The 3 single-day treatment periods were separated by a wash-out period of minimum 7 and maximum 21 days.
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Arm type	Experimental
Investigational medicinal product name	CHF 1535
Investigational medicinal product code	
Other name	beclomethasone dipropionate (BDP), formoterol fumarate (FF), Foster
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

CHF 1535 100/6 pMDI, 4 puffs (total dose of BDP 400 µg / FF 24 µg) CHF 1535 100/6 pMDI, without (TEST 1) or with (TEST 2) AeroChamber Plus™

Investigational medicinal product name	beclomethasone dipropionate + formoterol fumarate
Investigational medicinal product code	
Other name	BDP, FF
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Free combination of BDP pMDI plus FF pMDI, 4 + 4 puffs (total dose of BDP 400 µg + FF 24 µg)

Arm title	CONTROL

Arm description:

Adult patients (N=30) receiving a single dose of control drug (CTR) = 4 puffs of fixed combination CHF 1535 100/6 pMDI, for a total dose of BDP 400 µg / FF 24 µg).
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period. A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Arm type	Active comparator
Investigational medicinal product name	Foster
Investigational medicinal product code	
Other name	CHF 1535 100/6 pMDI, beclomethasone / formoterol fixed combination
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

In one single-day treatment visit, subjects (all adults) were to take 4 puffs of fixed combination CHF 1535 100/6 pMDI (CONTROL
treatment – CTR) for a total dose of BDP 400 µg / FF 24 µg.

Number of subjects in period 1	TEST 1/REF/TEST 2	TEST 2/TEST 1/REF	REF/TEST 2/TEST 1
Started	10	10	10
Completed	9	10	10
Not completed	1	0	0
Protocol deviation	1	-	-

Number of subjects in period 1	CONTROL
Started	30
Completed	30
Not completed	0
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	TEST 1/REF/TEST 2

Reporting group description:

Adolescent subjects took the following single-day treatments in sequence:
• TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI for a (total dose of BDP 400 µg / formoterol fumarate [FF] 24 µg);
• REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI for a total dose of BDP 400 µg + FF 24 µg.
• TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using AeroChamber Plus™ for a total dose of BDP 400 µg / FF 24 µg);
The 3 single-day treatment periods were separated by a wash-out period of minimum 7 and maximum 21 days.
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Reporting group title	TEST 2/TEST 1/REF

Reporting group description:

Adolescent subjects took the following single-day treatments in sequence:
• TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using AeroChamber Plus™ for a total dose of BDP 400 µg / FF 24 µg);
• TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI for a (total dose of BDP 400 µg / formoterol fumarate [FF] 24 µg);
• REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI for a total dose of BDP 400 µg + FF 24 µg.
The 3 single-day treatment periods were separated by a wash-out period of minimum 7 and maximum 21 days.
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Reporting group title	REF/TEST 2/TEST 1

Reporting group description:

Adolescent subjects took the following single-day treatments in sequence:
• REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI for a total dose of BDP 400 µg + FF 24 µg.
• TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using AeroChamber Plus™ for a total dose of BDP 400 µg / FF 24 µg);
• TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI for a (total dose of BDP 400 µg / formoterol fumarate [FF] 24 µg);
The 3 single-day treatment periods were separated by a wash-out period of minimum 7 and maximum 21 days.
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Reporting group title	CONTROL

Reporting group description:

Adult patients (N=30) receiving a single dose of control drug (CTR) = 4 puffs of fixed combination CHF 1535 100/6 pMDI, for a total dose of BDP 400 µg / FF 24 µg).
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Reporting group values	TEST 1/REF/TEST 2	TEST 2/TEST 1/REF	REF/TEST 2/TEST 1
Number of subjects	10	10	10
Age categorical Units: Subjects			
Adolescents (12-17 years)	10	10	10
Adults (18-64 years)	0	0	0

Age continuous			
Units: years			
median	16	14	16
full range (min-max)	12 to 17	12 to 17	12 to 16
Gender categorical			
Note: The sequence TEST 1/REF/ TEST 2 included one subject who discontinued the study due to a major protocol deviation.			
Units: Subjects			
Female	6	5	5
Male	4	5	5

Reporting group values	CONTROL	Total	
Number of subjects	30	60	
Age categorical			
Units: Subjects			
Adolescents (12-17 years)	0	30	
Adults (18-64 years)	30	30	
Age continuous			
Units: years			
median	40		
full range (min-max)	18 to 64	-	
Gender categorical			
Note: The sequence TEST 1/REF/ TEST 2 included one subject who discontinued the study due to a major protocol deviation.			
Units: Subjects			
Female	14	30	
Male	16	30	

End points

End points reporting groups

Reporting group title	TEST 1/REF/TEST 2

Reporting group description:

Adolescent subjects took the following single-day treatments in sequence:
• TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI for a (total dose of BDP 400 µg / formoterol fumarate [FF] 24 µg);
• REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI for a total dose of BDP 400 µg + FF 24 µg.
• TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using AeroChamber Plus™ for a total dose of BDP 400 µg / FF 24 µg);
The 3 single-day treatment periods were separated by a wash-out period of minimum 7 and maximum 21 days.
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Reporting group title	TEST 2/TEST 1/REF

Reporting group description:

Adolescent subjects took the following single-day treatments in sequence:
• TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using AeroChamber Plus™ for a total dose of BDP 400 µg / FF 24 µg);
• TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI for a (total dose of BDP 400 µg / formoterol fumarate [FF] 24 µg);
• REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI for a total dose of BDP 400 µg + FF 24 µg.
The 3 single-day treatment periods were separated by a wash-out period of minimum 7 and maximum 21 days.
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Reporting group title	REF/TEST 2/TEST 1

Reporting group description:

Adolescent subjects took the following single-day treatments in sequence:
• REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI for a total dose of BDP 400 µg + FF 24 µg.
• TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using AeroChamber Plus™ for a total dose of BDP 400 µg / FF 24 µg);
• TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI for a (total dose of BDP 400 µg / formoterol fumarate [FF] 24 µg);
The 3 single-day treatment periods were separated by a wash-out period of minimum 7 and maximum 21 days.
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Reporting group title	CONTROL

Reporting group description:

Adult patients (N=30) receiving a single dose of control drug (CTR) = 4 puffs of fixed combination CHF 1535 100/6 pMDI, for a total dose of BDP 400 µg / FF 24 µg).
Before the one-day single dose treatment period (Visit 2), the study included a two-days run-in period.
A follow-up phone contact was performed within 7-10 days after treatment Visit 2.

Subject analysis set title	TEST 1 - PK/PD population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects from the safety population excluding subjects without any valid PK/PD (i.e., potassium and glucose) measurement or with major protocol deviations significantly affecting PK/PD.

Subject analysis set title	TEST 2 - PK/PD population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects from the safety population excluding subjects without any valid PK/PD (i.e., potassium and glucose) measurement or with major protocol deviations significantly affecting PK/PD.

Subject analysis set title	REF - PK/PD population

Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects from the safety population excluding subjects without any valid PK/PD (i.e., potassium and glucose) measurement or with major protocol deviations significantly affecting PK/PD.

Subject analysis set title	CTR - PK/PD population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects from the safety population excluding subjects without any valid PK/PD (i.e., potassium and glucose) measurement or with major protocol deviations significantly affecting PK/PD.

Primary: B17MP Cmax

End point title	B17MP Cmax

End point description:

The value and time of the maximum drug concentration (Cmax and tmax) were indicators for the rate of absorption.

End point type	Primary

End point timeframe:

At Visit 2, Visit 3 and Visit 4

End point values	TEST 1 - PK/PD population	TEST 2 - PK/PD population	REF - PK/PD population	CTR - PK/PD population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	29	29	30
Units: pg/mL				
arithmetic mean (standard deviation)	1056 (± 1137)	1044 (± 439)	1116 (± 508)	1052 (± 465)

Statistical analyses

Statistical analysis title	TEST 1 vs REF
Comparison groups	TEST 1 - PK/PD population v REF - PK/PD population
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Parameter estimate	adjusted geometric means ratio
Point estimate	84.38
Confidence interval	
level	90 %
sides	2-sided
lower limit	70.22
upper limit	101.38

Notes:

[1] - B17MP Cmax was log-transformed and submitted to a linear model with treatment, sequence, period and subject within sequence as fixed effects.

Statistical analysis title	TEST 2 vs REF
Comparison groups	TEST 2 - PK/PD population v REF - PK/PD population

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Parameter estimate	adjusted geometric means ratio
Point estimate	97
Confidence interval	
level	90 %
sides	2-sided
lower limit	80.92
upper limit	116.27

Notes:

[2] - B17MP Cmax was log-transformed and submitted to a linear model with treatment, sequence, period and subject within sequence as fixed effects.

Statistical analysis title	TEST 2 vs TEST 1
Comparison groups	TEST 1 - PK/PD population v TEST 2 - PK/PD population
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Parameter estimate	adjusted geometric means ratio
Point estimate	114.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	95.67
upper limit	138.13

Notes:

[3] - B17MP Cmax was log-transformed and submitted to a linear model with treatment, sequence, period and subject within sequence as fixed effects

Statistical analysis title	TEST 1 vs CTR
Comparison groups	TEST 1 - PK/PD population v CTR - PK/PD population
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence[4]
Parameter estimate	adjusted geometric means ratio
Point estimate	90.83
Confidence interval	
level	90 %
sides	2-sided
lower limit	72.46
upper limit	113.84

Notes:

[4] - B17MP Cmax was log-transformed and submitted to a linear model with treatment, sequence, period and subject within sequence as fixed effects

Primary: B17MP AUC0-t

End point title	B17MP AUC0-t

End point description:

After single administration, the area under the plasma concentration versus time curve up to the last quantifiable concentration (AUC0-t) was used to measure the extent of absorption.

End point type	Primary

End point timeframe:
At Visit 2, Visit 3 and Visit 4

End point values	TEST 1 - PK/PD population	TEST 2 - PK/PD population	REF - PK/PD population	CTR - PK/PD population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	29	29	30
Units: pg.h/mL				
arithmetic mean (standard deviation)	2798 (± 846)	2724 (± 957)	3028 (± 965)	3107 (± 980)

Statistical analyses

Statistical analysis title	TEST 1 vs REF
Comparison groups	TEST 1 - PK/PD population v REF - PK/PD population
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	equivalence[5]
Parameter estimate	adjusted geometric means ratio
Point estimate	91.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	81.64
upper limit	102.97

Notes:

[5] - B17MP AUC0-t was log-transformed and submitted to a linear model with treatment, sequence, period and subject within sequence as fixed effects.

Statistical analysis title	TEST 2 vs REF
Comparison groups	TEST 2 - PK/PD population v REF - PK/PD population
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence[6]
Parameter estimate	adjusted geometric means ratio
Point estimate	89.63
Confidence interval	
level	90 %
sides	2-sided
lower limit	79.93
upper limit	100.5

Notes:

[6] - B17MP AUC0-t was log-transformed and submitted to a linear model with treatment, sequence, period and subject within sequence as fixed effects.

Statistical analysis title	TEST 2 vs TEST 1
Comparison groups	TEST 1 - PK/PD population v TEST 2 - PK/PD population

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	equivalence[7]
Parameter estimate	adjusted geometric means ratio
Point estimate	97.76
Confidence interval	
level	90 %
sides	2-sided
lower limit	87.05
upper limit	109.78

Notes:

[7] - B17MP AUC0-t was log-transformed and submitted to a linear model with treatment, sequence, period and subject within sequence as fixed effects.

Statistical analysis title	TEST 1 vs CTR
Comparison groups	TEST 1 - PK/PD population v CTR - PK/PD population
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence[8]
Parameter estimate	adjusted geometric means ratio
Point estimate	90.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	78.39
upper limit	103.65

Notes:

[8] - B17MP AUC0-t was log-transformed and submitted to a linear model with treatment, sequence, period and subject within sequence as fixed effects.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
At each clinic visit from Visit 0 (pre-screening visit) to follow-up (phone call)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	TEST1
Reporting group description:	
TEST 1: 4 puffs of fixed combination CHF 1535 100/6 pMDI (total dose of BDP 400 µg / FF 24 µg);	
Reporting group title	TEST2
Reporting group description:	
TEST 2: 4 puffs of fixed combination CHF 1535 100/6 pMDI using the AeroChamber Plus™ spacer device (total dose of BDP 400 µg / FF 24 µg);	
Reporting group title	REF treatment
Reporting group description:	
REF: 4 + 4 puffs of free combination of BDP pMDI plus FF pMDI (total dose of BDP 400 µg + FF 24 µg);	
Reporting group title	CTR Adults
Reporting group description:	
CTR: 4 puffs of a fixed combination CHF 1535 100/6 pMDI (total dose of BDP 400 µg / FF 24 µg).	

Serious adverse events	TEST1	TEST2	REF treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 29 (0.00%)	0 / 29 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	CTR Adults		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 3.3 %

Non-serious adverse events	TEST1	TEST2	REF treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)	1 / 29 (3.45%)	3 / 29 (10.34%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 30 (0.00%)	0 / 29 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 30 (0.00%)	0 / 29 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 30 (0.00%)	0 / 29 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	CTR Adults		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 30 (13.33%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Tremor			

subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 2 / 30 (6.67%) 2		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

There are no limitations nor caveats applicable to this summary of results.

Notes: