

**Clinical trial results:**

MULTICENTRE, RANDOMISED, DOUBLE-BLIND, PARALLEL GROUP, PLACEBO-CONTROLLED STUDY ON THE THERAPEUTIC EFFICACY AND SAFETY OF BECLOMETHASONE DIPROPIONATE SUSPENSION FOR INHALATION 800 micrograms TWICE DAILY VS PLACEBO ADDED TO ANTIBIOTIC THERAPY IN PATIENTS WITH ACUTE RHINOSINUSITIS

Summary

EudraCT number	2011-001459-35
Trial protocol	IT
Global end of trial date	27 January 2014

Results information

Result version number	v1 (current)
This version publication date	11 July 2016
First version publication date	09 August 2015

Trial information**Trial identification**

Sponsor protocol code	MC/PR/1400/007/11
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01691677
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Chiesi Farmaceutici Spa
Sponsor organisation address	Via Palermo 26/A, Parma, Italy, 43122
Public contact	CTT Manager, Chiesi Farmaceutici, clinicaltrials_info@chiesi.com
Scientific contact	CTT Manager, Chiesi Farmaceutici, 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	27 January 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 January 2014
Global end of trial reached?	Yes
Global end of trial date	27 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that BDP suspension for inhalation twice a day for 14 days added to antibiotic therapy improves clinical success rate and accelerates recovery in patients with acute rhinosinusitis.

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	24 January 2013
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: 166
Worldwide total number of subjects	166
EEA total number of subjects	166

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)	164
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 166 patients were randomised to receive the assigned treatment: 83 were assigned to the nebulised BDP group and 83 were assigned to the Placebo group. Nine patients, 2 (2.4% of randomised) in the BDP group and 7 (8.4%) in the Placebo group, discontinued the study.

Period 1

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

Blinding implementation details:

The realization of the double blind design was made it possible by the use of a BDP suspension for nebulization placebo UDV, which was totally indistinguishable from the respective active in terms of size, shape, colour and mode of inhalation

Arms

Are arms mutually exclusive?	Yes
Arm title	Test treatment

Arm description:

Beclomethasone dipropionate (BDP) suspension for nebulization (Clenil per Aerosol, Chiesi Farmaceutici S.p.A.) 800 µg/2 mL one administration b.i.d. for 14 days.

Arm type	Experimental
Investigational medicinal product name	BDP
Investigational medicinal product code	
Other name	beclomethasone dipropionate
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Beclomethasone dipropionate (BDP) suspension for nebulization (Clenil per Aerosol, Chiesi Farmaceutici S.p.A.) 800 µg/2 mL one administration b.i.d. for 14 days.

Arm title	Reference treatment
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Arm description:

Matched BDP placebo solution for nebulisation, 2 ml one administration b.i.d. for 14 days

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Matched BDP placebo solution for nebulisation, 2 ml one administration b.i.d. for 14 days

Number of subjects in period 1	Test treatment	Reference treatment
Started	83	83
Completed	81	76
Not completed	2	7
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	1
Lost to follow-up	1	5
Lack of efficacy	-	1

Baseline characteristics

Reporting groups

Reporting group title	Test treatment
Reporting group description: Beclomethasone dipropionate (BDP) suspension for nebulization (Clenil per Aerosol, Chiesi Farmaceutici S.p.A.) 800 µg/2 mL one administration b.i.d. for 14 days.	
Reporting group title	Reference treatment
Reporting group description: Matched BDP placebo solution for nebulisation, 2 ml one administration b.i.d. for 14 days	

Reporting group values	Test treatment	Reference treatment	Total
Number of subjects	83	83	166
Age categorical			
Units: Subjects			
Adults (18-64 years)	82	82	164
From 65-84 years	1	1	2
Age continuous			
Units: years			
arithmetic mean	0	0	
standard deviation	± 0	± 0	-
Gender categorical			
Units: Subjects			
Female	46	54	100
Male	37	29	66

Subject analysis sets

Subject analysis set title	BDP - safety population
Subject analysis set type	Safety analysis
Subject analysis set description: All randomised subjects who took at least one dose of study medication.	
Subject analysis set title	Placebo - safety population
Subject analysis set type	Safety analysis
Subject analysis set description: All randomised subjects who took at least one dose of study medication.	
Subject analysis set title	BDP - ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomised patients with post-baseline data and completing at least the first week of treatment (i.e. attending visit 2).	
Subject analysis set title	Placebo - ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomised patients with post-baseline data and completing at least the first week of treatment (i.e. attending visit 2).	

Reporting group values	BDP - safety population	Placebo - safety population	BDP - ITT population
Number of subjects	82	78	81
Age categorical Units: Subjects			
Adults (18-64 years)	81	77	80
From 65-84 years	1	1	1
Age continuous Units: years			
arithmetic mean	39.84	40.56	39.89
standard deviation	± 11.67	± 12.62	± 11.74
Gender categorical Units: Subjects			
Female	45	51	44
Male	37	27	37

Reporting group values	Placebo - ITT population		
Number of subjects	77		
Age categorical Units: Subjects			
Adults (18-64 years)	76		
From 65-84 years	1		
Age continuous Units: years			
arithmetic mean	40.38		
standard deviation	± 12.6		
Gender categorical Units: Subjects			
Female	50		
Male	27		

End points

End points reporting groups

Reporting group title	Test treatment
Reporting group description: Beclomethasone dipropionate (BDP) suspension for nebulization (Clenil per Aerosol, Chiesi Farmaceutici S.p.A.) 800 µg/2 mL one administration b.i.d. for 14 days.	
Reporting group title	Reference treatment
Reporting group description: Matched BDP placebo solution for nebulisation, 2 ml one administration b.i.d. for 14 days	
Subject analysis set title	BDP - safety population
Subject analysis set type	Safety analysis
Subject analysis set description: All randomised subjects who took at least one dose of study medication.	
Subject analysis set title	Placebo - safety population
Subject analysis set type	Safety analysis
Subject analysis set description: All randomised subjects who took at least one dose of study medication.	
Subject analysis set title	BDP - ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomised patients with post-baseline data and completing at least the first week of treatment (i.e. attending visit 2).	
Subject analysis set title	Placebo - ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomised patients with post-baseline data and completing at least the first week of treatment (i.e. attending visit 2).	

Primary: Clinical success at Day 7

End point title	Clinical success at Day 7
End point description: Clinical success is defined as a patient report of cured or much improved throughout the treatment period or the untreated follow-up period.	
End point type	Primary
End point timeframe: The overall sinus symptoms were assessed through patient reports at Day 7 (Visit 2), at Day 14 (Visit 3) during the treatment phase, and at Day 21 (Visit 4) and at Day 28 (Visit 5) during the phone follow-up phase.	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	81	77		
Units: number of subject	30	24		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.437
Method	Chi-squared

Primary: Clinical success at Day 14

End point title	Clinical success at Day 14
End point description:	Clinical success is defined as a patient report of cured or much improved throughout the treatment period or the untreated follow-up period.
End point type	Primary
End point timeframe:	The overall sinus symptoms were measured through patient reports at Day 7 (Visit 2), at Day 14 (Visit 3) during the treatment phase, and at Day 21 (Visit 4) and at Day 28 (Visit 5) during the phone follow-up phase.

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	81	77		
Units: number of subject	49	47		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.944
Method	Chi-squared

Primary: Clinical success at Day 21

End point title	Clinical success at Day 21
End point description:	Clinical success is defined as a patient report of cured or much improved throughout the treatment period or the untreated follow-up period
End point type	Primary

End point timeframe:

The overall sinus symptoms were measured through patient reports at Day 7 (Visit 2), at Day 14 (Visit 3) during the treatment phase, and at Day 21 (Visit 4) and at Day 28 (Visit 5) during the phone follow-up phase.

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	81	77		
Units: number of subject	55	53		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	Placebo - ITT population v BDP - ITT population
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9
Method	Chi-squared

Primary: Clinical success at Day 28

End point title	Clinical success at Day 28
End point description:	Clinical success is defined as a patient report of cured or much improved throughout the treatment period or the untreated follow-up period.
End point type	Primary
End point timeframe:	The overall sinus symptoms were measured through patient reports at Day 7 (Visit 2), at Day 14 (Visit 3) during the treatment phase, and at Day 21 (Visit 4) and at Day 28 (Visit 5) during the phone follow-up phase.

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	81	77		
Units: number of subject	58	55		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98
Method	Chi-squared

Secondary: Time from baseline to a status of clinical success

End point title	Time from baseline to a status of clinical success
End point description:	
End point type	Secondary
End point timeframe:	
The overall sinus symptoms were evaluated at Day 7 (Visit 2), at Day 14 (Visit 3) during the treatment phase, and at Day 21 (Visit 4) and at Day 28 (Visit 5) during the phone follow-up phase	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	81	77		
Units: days				
median (confidence interval 95%)	12 (11 to 15)	14 (11 to 19)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox regression analysis
Point estimate	0.986
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.682
upper limit	1.426

Secondary: Change from baseline to Visit 2 in overall sinus symptoms

End point title	Change from baseline to Visit 2 in overall sinus symptoms
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End point description:

End point type	Secondary
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End point timeframe:

The overall sinus symptoms were evaluated by the investigator at Day 7 (Visit 2), at Day 14 (Visit 3) during the treatment phase, and at Day 21 (Visit 4) and at Day 28 (Visit 5) during the phone follow-up phase

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	69		
Units: digit				
arithmetic mean (standard deviation)	-3.2 (± 2.5)	-2.7 (± 2.1)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1214
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.5658
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2837
upper limit	0.152

Secondary: Change from baseline to Visit 3 in overall sinus symptoms

End point title	Change from baseline to Visit 3 in overall sinus symptoms
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End point description:

End point type	Secondary
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End point timeframe:

The overall sinus symptoms were evaluated by the investigator at Day 7 (Visit 2), at Day 14 (Visit 3) during the treatment phase, and at Day 21 (Visit 4) and at Day 28 (Visit 5) during the phone follow-up phase

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	69		
Units: digit				
arithmetic mean (standard deviation)	-4.4 (± 3.2)	-4.8 (± 2.6)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6216
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.1961
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5878
upper limit	0.98

Secondary: Change from baseline to Visit 2 in headache sinus symptom

End point title	Change from baseline to Visit 2 in headache sinus symptom
End point description:	
This parameter was assessed using a VAS	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 2	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	70		
Units: score				
arithmetic mean (standard deviation)	-2.7 (± 2.5)	-2.6 (± 2.6)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6579
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.1612
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8793
upper limit	0.5569

Secondary: Change from baseline to Visit 3 in headache sinus symptom

End point title	Change from baseline to Visit 3 in headache sinus symptom
End point description:	
This parameter was assessed using a VAS	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 3	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	68		
Units: score				
arithmetic mean (standard deviation)	-3.6 (± 3.4)	-4.1 (± 3.1)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3107
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.3845

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3626
upper limit	1.1315

Secondary: Change from baseline to Visit 2 in facial pain sinus symptom

End point title Change from baseline to Visit 2 in facial pain sinus symptom

End point description:

This parameter was assessed using a VAS

End point type Secondary

End point timeframe:

The assessment was performed during treatment phase, at Visit 2

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	69		
Units: score				
arithmetic mean (standard deviation)	-2.1 (± 2.3)	-2.3 (± 2.3)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7927
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.08783
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5718
upper limit	0.7474

Secondary: Change from baseline to Visit 3 in facial pain sinus symptom

End point title Change from baseline to Visit 3 in facial pain sinus symptom

End point description:

This parameter was assessed using a VAS

End point type Secondary

End point timeframe:

The assessment was performed during treatment phase, at Visit 3

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67	68		
Units: score				
arithmetic mean (standard deviation)	-3 (\pm 3)	-3.6 (\pm 3)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1184
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.5349
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1383
upper limit	1.2082

Secondary: Change from baseline to Visit 2 in facial pressure sinus symptom

End point title Change from baseline to Visit 2 in facial pressure sinus symptom

End point description:

This parameter was assessed using a VAS

End point type Secondary

End point timeframe:

The assessment was performed during treatment phase, at Visit 2

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	70		
Units: score				
arithmetic mean (standard deviation)	-2.1 (± 2.4)	-2.4 (± 2.4)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7298
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.1169
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5509
upper limit	0.7846

Secondary: Change from baseline to Visit 3 in facial pressure sinus symptom

End point title	Change from baseline to Visit 3 in facial pressure sinus symptom
End point description:	
This parameter was assessed using a VAS	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 3	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	68		
Units: score				
arithmetic mean (standard deviation)	-3.1 (± 3)	-3.8 (± 3.1)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2933
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.3695
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3232
upper limit	1.0621

Secondary: Change from baseline to Visit 2 in nasal congestion sinus symptom

End point title	Change from baseline to Visit 2 in nasal congestion sinus symptom
End point description:	
This parameter was assessed using a VAS	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 2	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	70		
Units: score				
arithmetic mean (standard deviation)	-3.6 (± 2.8)	-3 (± 2.4)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1355
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.5964

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3818
upper limit	0.189

Secondary: Change from baseline to Visit 3 in nasal congestion sinus symptom

End point title	Change from baseline to Visit 3 in nasal congestion sinus symptom
End point description:	This parameter was assessed using a VAS
End point type	Secondary
End point timeframe:	The assessment was performed during treatment phase, at Visit 3

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	69		
Units: score				
arithmetic mean (standard deviation)	-4.8 (± 3.3)	-4.9 (± 2.7)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8481
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.07905
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7358
upper limit	0.8939

Secondary: Change from baseline to Visit 2 in nasal discharge sinus symptom

End point title	Change from baseline to Visit 2 in nasal discharge sinus symptom
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End point description:

This parameter was assessed using a VAS

End point type Secondary

End point timeframe:

The assessment was performed during treatment phase, at Visit 2

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	69		
Units: score				
arithmetic mean (standard deviation)	-2.9 (± 2.9)	-2.6 (± 2.7)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2808
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.4263
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2049
upper limit	0.3523

Secondary: Change from baseline to Visit 3 in nasal discharge sinus symptom

End point title Change from baseline to Visit 3 in nasal discharge sinus symptom

End point description:

This parameter was assessed using a VAS

End point type Secondary

End point timeframe:

The assessment was performed during treatment phase, at Visit 3

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	69		
Units: score				
arithmetic mean (standard deviation)	-4.2 (± 3.9)	-4.4 (± 3)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7968
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.09944
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8617
upper limit	0.6629

Secondary: Change from baseline to Visit 2 in olfactory disturbance sinus symptom

End point title	Change from baseline to Visit 2 in olfactory disturbance sinus symptom
End point description:	
This parameter was assessed using a VAS	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 2	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	69		
Units: score				
arithmetic mean (standard deviation)	-2.6 (± 3)	-2.2 (± 2.4)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2263
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.4385
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1518
upper limit	0.2749

Secondary: Change from baseline to Visit 3 in olfactory disturbance sinus symptom

End point title	Change from baseline to Visit 3 in olfactory disturbance sinus symptom
End point description:	
This parameter was assessed using a VAS	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 3	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67	67		
Units: score				
arithmetic mean (standard deviation)	-3.6 (± 3.7)	-3.5 (± 3.2)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8414
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.07302

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6472
upper limit	0.7933

Secondary: Change from baseline to Visit 2 in the level of work performance

End point title	Change from baseline to Visit 2 in the level of work performance
End point description:	This parameter was assessed using a VAS
End point type	Secondary
End point timeframe:	During treatment phase: at Visit 2 and Visit 3

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	56		
Units: score				
arithmetic mean (standard deviation)	15.3 (\pm 32.2)	17.3 (\pm 30.8)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9887
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.063
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8704
upper limit	8.7444

Secondary: Change from baseline to Visit 3 in the level of work performance

End point title	Change from baseline to Visit 3 in the level of work performance
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End point description:

This parameter was assessed using a VAS

End point type Secondary

End point timeframe:

The assessment was performed during treatment phase, at Visit 3

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	56	56		
Units: score				
arithmetic mean (standard deviation)	16.5 (± 43)	24 (± 39.5)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2696
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-6.165
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.1752
upper limit	4.8454

Secondary: Missed working time over the study

End point title Missed working time over the study

End point description:

This parameter was assessed using a VAS

End point type Secondary

End point timeframe:

From visit 1 to visit 3

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	81	77		
Units: days				
arithmetic mean (standard deviation)	0.967 (± 2.037)	0.915 (± 1.762)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absence of relapses over the study

End point title	Absence of relapses over the study
End point description:	
End point type	Secondary
End point timeframe:	
Over the study	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	81	77		
Units: number of subject	80	74		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.358
Method	Fisher exact

Secondary: Number of relapses

End point title	Number of relapses
End point description:	
<p>Relapse was observed in 2 (2.6%) patients in the Placebo group at Day 7, in 1 (1.3%) patient in the Placebo group at Day 14 and at Day 21, and in 1 patient in either group (1.2% in the BDP group and 1.3% in the Placebo group) at Day 28. One patient (1.2%) in the BDP group and 3 (3.9%) in the Placebo group had at least one relapse during the study.</p>	

End point type	Secondary
End point timeframe:	
Through overall trial	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	81	77		
Units: number of subject	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to visit 2 in the level of nasal mucociliary transport time

End point title	Change from baseline to visit 2 in the level of nasal mucociliary transport time
End point description:	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 2	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	28		
Units: min				
arithmetic mean (standard deviation)	-3.96 (± 6.69)	-2.35 (± 4.74)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1898
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-1.1454

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8757
upper limit	0.5849

Secondary: Change from baseline to Visit 3 in the level of nasal mucociliary transport time

End point title	Change from baseline to Visit 3 in the level of nasal mucociliary transport time
End point description:	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 3	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	28		
Units: min				
arithmetic mean (standard deviation)	-5.16 (± 6.66)	-3.69 (± 5.29)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2658
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.9266
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5687
upper limit	0.7234

Secondary: Change from baseline to Visit 2 in total inspiratory nasal resistance

End point title	Change from baseline to Visit 2 in total inspiratory nasal
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resistance

End point description:

End point type	Secondary
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End point timeframe:

The assessment was performed during treatment phase, at Visit 2

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: Pa/mL/s				
arithmetic mean (standard deviation)	-0.18 (± 0.1)	-0.11 (± 0.12)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1142
Method	ANOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.06933
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1567
upper limit	0.01808

Secondary: Change from baseline to Visit 3 in total inspiratory nasal resistance

End point title	Change from baseline to Visit 3 in total inspiratory nasal resistance
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End point description:

End point type	Secondary
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End point timeframe:

The assessment was performed during treatment phase, at Visit 3

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	13		
Units: Pa/mL/s				
arithmetic mean (standard deviation)	-0.27 (± 0.12)	-0.22 (± 0.16)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2033
Method	ANOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.05455
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1409
upper limit	0.03182

Secondary: Change from baseline to Visit 2 in total expiratory nasal resistance

End point title	Change from baseline to Visit 2 in total expiratory nasal resistance
End point description:	
End point type	Secondary
End point timeframe:	The assessment was performed during treatment phase, at Visit 2

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	13		
Units: Pa/mL/s				
arithmetic mean (standard deviation)	-0.15 (± 0.1)	-0.1 (± 0.1)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1599
Method	ANOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.05759
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1397
upper limit	0.02452

Secondary: Change from baseline to Visit 3 in total expiratory nasal resistance

End point title	Change from baseline to Visit 3 in total expiratory nasal resistance
End point description:	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 3	

End point values	BDP - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	13		
Units: Pa/mL/s				
arithmetic mean (standard deviation)	-0.27 (± 0.14)	-0.2 (± 0.17)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - ITT population v Placebo - ITT population
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1523
Method	ANOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.0668

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1603
upper limit	0.02672

Secondary: Change from baseline in heart rate at Visit 2

End point title	Change from baseline in heart rate at Visit 2
End point description:	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 2	

End point values	BDP - safety population	Placebo - safety population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	68		
Units: bmp				
arithmetic mean (standard deviation)	-0.4 (± 5.3)	0 (± 4)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - safety population v Placebo - safety population
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8062
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.1831
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6558
upper limit	1.2896

Secondary: Change from baseline in heart rate at Visit 3

End point title	Change from baseline in heart rate at Visit 3
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End point description:

End point type	Secondary
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End point timeframe:

The assessment was performed during treatment phase, at Visit 3

End point values	BDP - safety population	Placebo - safety population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	68		
Units: bpm				
arithmetic mean (standard deviation)	-0.3 (± 5.6)	0.3 (± 4.4)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - safety population v Placebo - safety population
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6721
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.3246
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8374
upper limit	1.1883

Secondary: Change from baseline in SBP at Visit 2

End point title	Change from baseline in SBP at Visit 2
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End point description:

End point type	Secondary
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End point timeframe:

The assessment was performed during treatment phase, at Visit 2

End point values	BDP - safety population	Placebo - safety population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	69		
Units: mmHg				
arithmetic mean (standard deviation)	-0.1 (± 7.1)	-0.1 (± 7.8)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - safety population v Placebo - safety population
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3174
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	1.181
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1462
upper limit	3.5082

Secondary: Change from baseline in SBP at Visit 3

End point title	Change from baseline in SBP at Visit 3
End point description:	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 3	

End point values	BDP - safety population	Placebo - safety population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	69		
Units: mmHg				
arithmetic mean (standard deviation)	-1.5 (± 8.4)	0.3 (± 7.1)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - safety population v Placebo - safety population
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2063
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-1.4817
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7889
upper limit	0.8255

Secondary: Change from baseline in DBP at Visit 2

End point title	Change from baseline in DBP at Visit 2
End point description:	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 2	

End point values	BDP - safety population	Placebo - safety population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	69		
Units: mmHg				
arithmetic mean (standard deviation)	-1.4 (± 5.7)	-0.3 (± 5.6)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	BDP - safety population v Placebo - safety population
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4927
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.6137

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3781
upper limit	1.1507

Secondary: Change from baseline in DBP at Visit 3

End point title	Change from baseline in DBP at Visit 3
End point description:	
End point type	Secondary
End point timeframe:	
The assessment was performed during treatment phase, at Visit 3	

End point values	BDP - safety population	Placebo - safety population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	69		
Units: mmHg				
arithmetic mean (standard deviation)	-1.5 (± 6)	-0.4 (± 5.8)		

Statistical analyses

Statistical analysis title	BDP vs placebo
Comparison groups	Placebo - safety population v BDP - safety population
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6112
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.4685
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2871
upper limit	1.35

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Visit 1 (Day 0, screening-baseline), Visit 2 (Day 7), Visit 3 (Day 14) during the treatment phase, and Visit 4 (Day 21) and Visit 5 (Day 28) during the phone follow-up phase.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Test treatment
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Reporting group description:

Beclomethasone dipropionate (BDP) suspension for nebulization (Clenil per Aerosol, Chiesi Farmaceutici S.p.A.) 800 µg/2 mL one administration b.i.d. for 14 days.

Reporting group title	Reference treatment
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Reporting group description:

Matched BDP placebo solution for nebulisation, 2 ml one administration b.i.d. for 14 days

Serious adverse events	Test treatment	Reference treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 82 (0.00%)	0 / 78 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Test treatment	Reference treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 82 (6.10%)	4 / 78 (5.13%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 82 (3.66%)	2 / 78 (2.56%)	
occurrences (all)	6	8	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 82 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Gastrointestinal disorders			

Gastroesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 82 (1.22%) 1	0 / 78 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	1 / 82 (1.22%) 1	0 / 78 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	0 / 82 (0.00%) 0	1 / 78 (1.28%) 1	
Vomiting subjects affected / exposed occurrences (all)	0 / 82 (0.00%) 0	1 / 78 (1.28%) 1	
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 82 (0.00%) 0	1 / 78 (1.28%) 4	
Infections and infestations Oral candidiasis subjects affected / exposed occurrences (all)	1 / 82 (1.22%) 1	0 / 78 (0.00%) 0	
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 82 (0.00%) 0	1 / 78 (1.28%) 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.

No limitations or caveats are applicable to this summary.

Notes: