Clinical trial results:
Randomized, Double-Blind Trial of MP29-02 Nasal Spray Compared to Placebo, Azelastine Hydrochloride Nasal Spray, and Fluticasone Propionate Nasal Spray in the Treatment of Patients with Seasonal Allergic Rhinitis

Summary

EudraCT number	2011-001369-42
Trial protocol	Outside EU/EEA
Global end of trial date	13 June 2008

Results information

Result version number	v1 (current)
This version publication date	29 July 2016
First version publication date	29 July 2016

Trial information

Trial identification

Sponsor protocol code	MP4002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00651118
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Meda Pharmaceuticals Inc.
Sponsor organisation address	265 Davidson Avenue, Suite 300, Somerset, United States, NJ 08873-4120
Public contact	Group leader study manager, MEDA Pharma GmbH & Co. KG, +49 617288801, 42b@medapharma.de
Scientific contact	Head Corporate Clinical Affairs, MEDA Pharma GmbH & Co. KG, +49 617288801, 42b@medapharma.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000990-PIP02-10
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	03 May 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 June 2008
Global end of trial reached?	Yes
Global end of trial date	13 June 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare efficacy and safety of azelastine hydrochloride and fluticasone propionate combination nasal spray to placebo and to each product alone.

Protection of trial subjects:

No specific additional measures to minimise pain and distress were required. The patients could withdraw from treatment at any time and for any reason.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 March 2008
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	United States: 832
Worldwide total number of subjects	832
EEA total number of subjects	0

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)	98
Adults (18-64 years)	706
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study began with a 7-day single-blind Placebo Lead-in Period during which subjects recorded symptom scores twice daily in order to qualify for randomization to the double-blind treatment period. On Visit 2 subjects who satisfied the symptom requirements and continued to meet all of the study inclusion/exclusion criteria were randomized.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	MP29-02

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Azelastine hydrochloride and fluticasone propionate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Total Daily Dose: 548 mcg azelastine/200 mcg fluticasone;
1 spray per nostril twice daily;
2-week study

Arm title	Azelastine HCL

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Azelastine hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

1 spray per nostril twice daily;
total daily dose: 548 mcg azelastine;
2-week study

Arm title	Fluticasone

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	Fluticasone propionate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

1 spray per nostril twice daily;
total daily dose: 200 mcg fluticasone;
2-week study

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Same formulation as MP29-02 used with the exception of the active ingredients;
1 spray per nostril twice daily;
2-week study

Number of subjects in period 1	MP29-02	Azelastine HCL	Fluticasone
Started	207	208	207
Completed	198	197	200
Not completed	9	11	7
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	4	1	-
Other	1	2	4
Lost to follow-up	2	1	-
Protocol deviation	2	6	2

Number of subjects in period 1	Placebo
Started	210
Completed	203
Not completed	7
Consent withdrawn by subject	1
Adverse event, non-fatal	1
Other	1
Lost to follow-up	2
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	MP29-02
Reporting group description: -	
Reporting group title	Azelastine HCL
Reporting group description: -	
Reporting group title	Fluticasone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	MP29-02	Azelastine HCL	Fluticasone
Number of subjects	207	208	207
Age categorical Units: Subjects			
Adolescents (12-17 years)	19	28	15
Adults (18-64 years)	183	172	185
65 or older	5	8	7
not reported / not in ITT	0	0	0
Gender categorical Units: Subjects			
Female	142	130	127
Male	65	78	80
not reported / not in ITT	0	0	0

Reporting group values	Placebo	Total	
Number of subjects	210	832	
Age categorical Units: Subjects			
Adolescents (12-17 years)	36	98	
Adults (18-64 years)	165	705	
65 or older	8	28	
not reported / not in ITT	1	1	
Gender categorical Units: Subjects			
Female	132	531	
Male	77	300	
not reported / not in ITT	1	1	

End points

End points reporting groups

Reporting group title	MP29-02
Reporting group description: -	
Reporting group title	Azelastine HCL
Reporting group description: -	
Reporting group title	Fluticasone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Change From Baseline in 12-Hour Reflective Total Nasal Symptom Score over the 14-Day Treatment Period: AM and PM Combined

End point title	Change From Baseline in 12-Hour Reflective Total Nasal Symptom Score over the 14-Day Treatment Period: AM and PM Combined
End point description:	
End point type	Primary
End point timeframe:	
Day 1 PM to day 14 AM	

End point values	MP29-02	Azelastine HCL	Fluticasone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	207	208	207	209[1]
Units: difference in scores				
least squares mean (standard deviation)	-5.61 (± 5.235)	-4.23 (± 4.629)	-4.71 (± 4.678)	-2.92 (± 3.923)

Notes:

[1] - One randomized subject not in the ITT population.

Statistical analyses

Statistical analysis title	Comparison MP29-02 vs Placebo
Comparison groups	MP29-02 v Placebo
Number of subjects included in analysis	416
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [2]
Method	ANCOVA

Notes:

[2] - Pre-specified with multiplicity adjustement (gatekeeping).

Statistical analysis title	Comparison MP29-02 vs Azelastine

Comparison groups	MP29-02 v Azelastine HCL
Number of subjects included in analysis	415
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001 [3]
Method	ANCOVA

Notes:

[3] - Pre-specified with multiplicity adjustement (gatekeeping).

Statistical analysis title	Comparison MP29-02 vs Fluticasone
Comparison groups	MP29-02 v Fluticasone
Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.034 [4]
Method	ANCOVA

Notes:

[4] - Pre-specified with multiplicity adjustement (gatekeeping).

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 2 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0
Reporting groups	
Reporting group title	MP29-02
Reporting group description: 548 mcg azelastine/200 mcg fluticasone	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Fluticasone
Reporting group description: 200 mcg	
Reporting group title	Azelastine HCL
Reporting group description: 548 mcg	

Serious adverse events	MP29-02	Placebo	Fluticasone
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 207 (0.00%)	0 / 210 (0.00%)	0 / 207 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Azelastine HCL		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 208 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	MP29-02	Placebo	Fluticasone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 207 (14.49%)	24 / 210 (11.43%)	32 / 207 (15.46%)
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	5 / 207 (2.42%)	1 / 210 (0.48%)	2 / 207 (0.97%)
occurrences (all)	5	1	2
Headache			
subjects affected / exposed	2 / 207 (0.97%)	4 / 210 (1.90%)	7 / 207 (3.38%)
occurrences (all)	2	4	7
General disorders and administration site conditions			
Mucosal erosion			
subjects affected / exposed	1 / 207 (0.48%)	0 / 210 (0.00%)	2 / 207 (0.97%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 207 (0.48%)	0 / 210 (0.00%)	2 / 207 (0.97%)
occurrences (all)	1	0	2
Respiratory, thoracic and mediastinal disorders			
Nasal discomfort			
subjects affected / exposed	2 / 207 (0.97%)	0 / 210 (0.00%)	2 / 207 (0.97%)
occurrences (all)	2	0	2
Epistaxis			
subjects affected / exposed	3 / 207 (1.45%)	2 / 210 (0.95%)	5 / 207 (2.42%)
occurrences (all)	3	2	5
Sneezing			
subjects affected / exposed	1 / 207 (0.48%)	1 / 210 (0.48%)	0 / 207 (0.00%)
occurrences (all)	1	1	0
Cough			
subjects affected / exposed	2 / 207 (0.97%)	0 / 210 (0.00%)	0 / 207 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 207 (1.93%)	1 / 210 (0.48%)	1 / 207 (0.48%)
occurrences (all)	4	1	1

Non-serious adverse events	Azelastine HCL		

Total subjects affected by non-serious adverse events subjects affected / exposed	26 / 208 (12.50%)		
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 7 / 208 (3.37%) 7 2 / 208 (0.96%) 2		
General disorders and administration site conditions Mucosal erosion subjects affected / exposed occurrences (all)	 0 / 208 (0.00%) 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	 1 / 208 (0.48%) 1		
Respiratory, thoracic and mediastinal disorders Nasal discomfort subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Sneezing subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	 4 / 208 (1.92%) 4 4 / 208 (1.92%) 4 2 / 208 (0.96%) 2 1 / 208 (0.48%) 1		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	 1 / 208 (0.48%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 February 2008	Amendment included changes to some eligibility critiera and some administrative modifications
11 March 2008	Amendment included changes to the methodology, sample size, more specific details on procedures, and some administrative modifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported