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	2011-001371-39
Trial protocol	Outside EU/EEA
Global end of trial date	26 August 2009

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	MP4006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00883168
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	04 May 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 August 2009
Global end of trial reached?	Yes
Global end of trial date	26 August 2009
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	08 April 2009
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: 1801
Worldwide total number of subjects	1801
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)	199
Adults (18-64 years)	1557
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study began with a 7-day single-blind treatment period during which subjects recorded symptom scores twice daily in order to qualify for randomization to the doubleblind treatment period. On Visit 2 subjects who satisfied the symptom severity 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 nasal spray

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Azelastine hydrochloride and fluticasone propionate
Investigational medicinal product code	MP29-02
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Azelastine HCl 548mcg / fluticasone propionate 200mcg;
1 spray per nostril twice daily;
14-day treatment period.

Arm title	Azelastine nasal spray

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:

Azelastine HCl 548mcg;
1 spray per nostril twice daily;
14-day treatment period.

Arm title	Fluticasone nasal spray

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:

Fluticasone propionate 200mcg;
1 spray per nostril twice daily;
14-day treatment period.

Arm title	Placebo nasal spray
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo nasal spray
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Placebo nasal spray, 0 mcg;
1 spray per nostril twice daily;
14-day treatment period.

Number of subjects in period 1	MP29-02 nasal spray	Azelastine nasal spray	Fluticasone nasal spray
Started	451	449	450
Completed	434	430	431
Not completed	17	19	19
Consent withdrawn by subject	2	1	2
Treatment failure	-	-	2
Adverse event, non-fatal	3	4	3
Other	2	2	2
Administrative problems	1	-	-
Non-compliance	1	4	5
Lost to follow-up	2	1	1
Protocol deviation	6	7	4

Number of subjects in period 1	Placebo nasal spray
Started	451
Completed	433
Not completed	18
Consent withdrawn by subject	1
Treatment failure	2
Adverse event, non-fatal	5
Other	2
Administrative problems	-
Non-compliance	4
Lost to follow-up	-

Protocol deviation	4

Baseline characteristics

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

Reporting group values	MP29-02 nasal spray	Azelastine nasal spray	Fluticasone nasal spray
Number of subjects	451	449	450
Age categorical Units: Subjects			
Adolescents (12-17 years)	57	38	56
Adults (18-64 years)	382	390	390
65 or older	9	17	4
Not reported / not in ITT	3	4	0
Gender categorical Units: Subjects			
Female	277	271	280
Male	171	174	170
Not reported / not in ITT	3	4	0

Reporting group values	Placebo nasal spray	Total	
Number of subjects	451	1801	
Age categorical Units: Subjects			
Adolescents (12-17 years)	46	197	
Adults (18-64 years)	387	1549	
65 or older	15	45	
Not reported / not in ITT	3	10	
Gender categorical Units: Subjects			
Female	269	1097	
Male	179	694	
Not reported / not in ITT	3	10	

End points

End points reporting groups

Reporting group title	MP29-02 nasal spray
Reporting group description: -	
Reporting group title	Azelastine nasal spray
Reporting group description: -	
Reporting group title	Fluticasone nasal spray
Reporting group description: -	
Reporting group title	Placebo nasal spray
Reporting group description: -	

Primary: Change from Baseline in 12-Hour Reflective TNSS over the 14-Day Treatment Period: AM and PM Combined

End point title	Change from Baseline in 12-Hour Reflective TNSS 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 nasal spray	Azelastine nasal spray	Fluticasone nasal spray	Placebo nasal spray
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	448[1]	443[2]	450	448[3]
Units: difference in scores				
least squares mean (standard deviation)	-5.53 (± 5.18)	-4.82 (± 4.762)	-4.89 (± 4.655)	-3.4 (± 4.342)

Notes:

[1] - Total number of intent-to-treat subjects with available data.

[2] - Total number of intent-to-treat subjects with available data.

[3] - Total number of intent-to-treat subjects with available data.

Statistical analyses

Statistical analysis title	Comparison MP29-02 vs Placebo
Comparison groups	MP29-02 nasal spray v Placebo nasal spray
Number of subjects included in analysis	896
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [4]
Method	ANCOVA

Notes:

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

Statistical analysis title	Comparison MP29-02 vs Azelastine
Comparison groups	MP29-02 nasal spray v Azelastine nasal spray
Number of subjects included in analysis	891
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.016 [5]
Method	ANCOVA

Notes:

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

Statistical analysis title	Comparison MP29-02 vs Fluticasone
Comparison groups	MP29-02 nasal spray v Fluticasone nasal spray
Number of subjects included in analysis	898
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.029 [6]
Method	ANCOVA

Notes:

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

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The Treatment Period consisted of three clinic visits: (1) Randomization at Day 1, (2) Day 7 interim visit, and (3) Day 14 Final Study
Visit or Early Termination Visit. Appropriate assessments to evaluate the safety of the study drugs at each study visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	MP29-02 nasal spray
Reporting group description: -	
Reporting group title	Placebo nasal spray
Reporting group description: -	
Reporting group title	Azelastine nasal spray
Reporting group description: -	
Reporting group title	Fluticasone nasal spray

Reporting group description: -

Serious adverse events	MP29-02 nasal spray	Placebo nasal spray	Azelastine nasal spray
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 451 (0.22%)	1 / 451 (0.22%)	0 / 449 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
lacerated right hand			
subjects affected / exposed	1 / 451 (0.22%)	0 / 451 (0.00%)	0 / 449 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
pyogenic arthritis of the right elbow			
subjects affected / exposed	0 / 451 (0.00%)	1 / 451 (0.22%)	0 / 449 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Fluticasone nasal spray		
Total subjects affected by serious adverse events			

subjects affected / exposed	0 / 450 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
lacerated right hand			
subjects affected / exposed	0 / 450 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
pyogenic arthritis of the right elbow			
subjects affected / exposed	0 / 450 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	MP29-02 nasal spray	Placebo nasal spray	Azelastine nasal spray
Total subjects affected by non-serious adverse events			
subjects affected / exposed	75 / 451 (16.63%)	55 / 451 (12.20%)	63 / 449 (14.03%)
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	21 / 451 (4.66%)	0 / 451 (0.00%)	23 / 449 (5.12%)
occurrences (all)	21	0	23
Headache			
subjects affected / exposed	10 / 451 (2.22%)	4 / 451 (0.89%)	14 / 449 (3.12%)
occurrences (all)	10	4	14

Non-serious adverse events	Fluticasone nasal spray		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 450 (12.22%)		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 450 (0.22%)		
occurrences (all)	1		
Headache			

subjects affected / exposed occurrences (all)	8 / 450 (1.78%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2009	for changes see amendment 2
25 March 2009	To ensure subjects are moderately to severely symptomatic and highly sensitive to a current pollen. Amended protocols included changes to the methodology, increase in study sites and sample size, changes to some inclusion criteria, 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