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	2011-001370-26
Trial protocol	Outside EU/EEA
Global end of trial date	03 November 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	MP4004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00740792
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, DE 0049 617288801, 42b@medapharma.de
Scientific contact	Head Corporate Clinical Affairs, Meda Pharma GmbH & Co. KG, DE 0049 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	03 November 2008
Global end of trial reached?	Yes
Global end of trial date	03 November 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	14 August 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: 779
Worldwide total number of subjects	779
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)	55
Adults (18-64 years)	710
From 65 to 84 years	14
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 in order to qualify for randomization to the
double-blind 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

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;
14-day double-blind Treatment Period

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
14-day double-blind Treatment Period

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;
14-day double-blind Treatment Period

Arm title	Placebo

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;
Same formulation as MP29-02 with the exception of the active ingredients;
1 spray per nostril twice daily;
14-day double-blind Treatment Period

Number of subjects in period 1	MP29-02	Azelastine HCL	Fluticasone
Started	195	194	189
Completed	183	186	180
Not completed	12	8	9
Consent withdrawn by subject	1	1	-
Abnormal test procedure results	-	1	-
Treatment failure	1	1	-
Adverse event, non-fatal	3	1	1
Protocol violation	-	-	-
Other	5	2	3
Non-compliance	-	-	5
Lost to follow-up	2	1	-
Protocol deviation	-	1	-

Number of subjects in period 1	Placebo
Started	201
Completed	190
Not completed	11
Consent withdrawn by subject	-
Abnormal test procedure results	-
Treatment failure	3

Adverse event, non-fatal	3
Protocol violation	2
Other	3
Non-compliance	-
Lost to follow-up	-
Protocol deviation	-

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	195	194	189
Age categorical Units: Subjects			
Adolescents (12-17 years)	12	12	14
Adults (18-64 years)	176	178	172
65 or older	5	4	3
Not reported / not in ITT	2	0	0
Gender categorical Units: Subjects			
Female	126	128	121
Male	67	66	68
Not reported / not in ITT	2	0	0

Reporting group values	Placebo	Total	
Number of subjects	201	779	
Age categorical Units: Subjects			
Adolescents (12-17 years)	17	55	
Adults (18-64 years)	181	707	
65 or older	2	14	
Not reported / not in ITT	1	3	
Gender categorical Units: Subjects			
Female	119	494	
Male	81	282	
Not reported / not in ITT	1	3	

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	193[1]	193[2]	188[3]	199[4]
Units: difference in scores				
least squares mean (standard deviation)	-5.54 (± 5.183)	-4.54 (± 4.621)	-4.55 (± 5.146)	-3.03 (± 3.932)

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.

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

Statistical analyses

Statistical analysis title	Comparison MP29-02 vs Placebo
Comparison groups	MP29-02 v Placebo
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [5]
Method	ANCOVA

Notes:

[5] - 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	386
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.032 [6]
Method	ANCOVA

Notes:

[6] - 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	381
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.038 [7]
Method	ANCOVA

Notes:

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

Adverse events

Adverse events information

Timeframe for reporting adverse events:

At each visit, the study investigators and/or coordinators questioned subjects as to how they had been feeling since their last visit. If the AE was still present at the time the database was locked, a follow-up report was provided at a later date.

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 - 1 spray per nostril twice daily

Reporting group title	Azelastine HCL

Reporting group description:

548 mcg - 1 spray per nostril twice daily

Reporting group title	Fluticasone

Reporting group description:

200 mcg - 1 spray per nostril twice daily

Reporting group title	Placebo

Reporting group description:

Safety population. 0 mcg - 1 spray per nostril twice daily

Serious adverse events	MP29-02	Azelastine HCL	Fluticasone
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 195 (0.51%)	0 / 194 (0.00%)	0 / 189 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Hepatitis C virus test positive	Additional description: onset 3 weeks after double-blinded period		
subjects affected / exposed	1 / 195 (0.51%)	0 / 194 (0.00%)	0 / 189 (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

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 200 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Infections and infestations			
Hepatitis C virus test positive	Additional description: onset 3 weeks after double-blinded period		
subjects affected / exposed	0 / 200 (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	Azelastine HCL	Fluticasone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 195 (15.90%)	35 / 194 (18.04%)	24 / 189 (12.70%)
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	4 / 195 (2.05%)	14 / 194 (7.22%)	1 / 189 (0.53%)
occurrences (all)	4	14	1
Headache			
subjects affected / exposed	6 / 195 (3.08%)	4 / 194 (2.06%)	5 / 189 (2.65%)
occurrences (all)	6	4	5

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 200 (10.00%)		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 200 (0.50%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 200 (1.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported