



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) | EMA-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 (\pm 5.18) | -4.82 (\pm 4.762) | -4.89 (\pm 4.655) | -3.4 (\pm 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 adjustment (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 adjustment (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 adjustment (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 | 8 / 450 (1.78%) | | |
| occurrences (all) | 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