



## Clinical trial results:

### Active-Controlled Trial of the Safety and Tolerability of MP29-02 in Subjects with Chronic Allergic or Nonallergic Rhinitis

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2011-001368-23 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 17 June 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 | MP4000 |
|-----------------------|--------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Meda Pharmaceuticals   |
| Sponsor organisation address | 265 Davidson Avenue, Suite 300, Somerset, United States, 08873-4120                        |
| Public contact               | Group leader study managers, 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                       | 05 October 2010 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 17 June 2009    |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 17 June 2009    |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of azelastine hydrochloride and fluticasone propionate combination nasal spray in chronic use daily over a 1-year period.

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                          | 16 January 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 | India: 612 |
| Worldwide total number of subjects   | 612        |
| 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)                     | 1   |
| Adolescents (12-17 years)                 | 36  |
| Adults (18-64 years)                      | 569 |
| From 65 to 84 years                       | 6   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects 12 to 80 years of age with a history of chronic rhinitis symptoms due to perennial allergic rhinitis, perennial nonallergic rhinitis, or VMR who might benefit from continuous therapy with MP29-02 were considered for entry into the study. Subjects who met the study entry criteria were enrolled following an initial 7-day screening period.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Not blinded                    |

### Arms

|  |   |
|--|---|
| Are arms mutually exclusive?           | Yes   |
| <b>Arm title</b>                       | 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               | Intranasal use , Topical use                        |

Dosage and administration details:

Mode of Administration: Topical/intranasal spray

Dose: 137 mcg azelastine hydrochloride and 50 mcg fluticasone propionate/ spray

Regimen: 1 spray per nostril bid (morning [AM] and evening [PM])

Duration of Treatment: 12 months

|  |                              |
|--|------------------------------|
| <b>Arm title</b>                       | 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               | Intranasal use , Topical use |

Dosage and administration details:

Mode of Administration: Topical/intranasal spray

Dose: 50 mcg fluticasone propionate/ spray

Regimen: 2 sprays per nostril qd (AM)

Duration of Treatment: 12 months

| <b>Number of subjects in period 1</b> | MP29-02 nasal spray | Fluticasone nasal spray |
|---------------------------------------|---------------------|-------------------------|
| Started                               | 405                 | 207                     |
| Completed                             | 312                 | 152                     |
| Not completed                         | 93                  | 55                      |
| Consent withdrawn by subject          | 12                  | 8                       |
| Abnormal test procedure results       | 2                   | -                       |
| Treatment failure                     | -                   | 2                       |
| Adverse event, non-fatal              | 11                  | 6                       |
| Other                                 | 2                   | 3                       |
| Administrative problems               | 15                  | 6                       |
| Non-compliance                        | 5                   | 3                       |
| Did not have an end of study CRF page | 5                   | 4                       |
| Lost to follow-up                     | 38                  | 20                      |
| Protocol deviation                    | 3                   | 3                       |

## Baseline characteristics

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | MP29-02 nasal spray |
|-----------------------|---------------------|

|                                |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Fluticasone nasal spray |
|-----------------------|-------------------------|

|                                |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| Reporting group values                | MP29-02 nasal spray | Fluticasone nasal spray | Total |
|---------------------------------------|---------------------|-------------------------|-------|
| Number of subjects                    | 405                 | 207                     | 612   |
| Age categorical<br>Units: Subjects    |                     |                         |       |
| Adolescents (12-17 years)             | 28                  | 8                       | 36    |
| Adults (18-64 years)                  | 373                 | 196                     | 569   |
| 65 years and over                     | 3                   | 3                       | 6     |
| Not recorded                          | 1                   | 0                       | 1     |
| Gender categorical<br>Units: Subjects |                     |                         |       |
| Female                                | 164                 | 97                      | 261   |
| Male                                  | 240                 | 110                     | 350   |
| Not recorded                          | 1                   | 0                       | 1     |

## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | MP29-02 nasal spray                          |
| Reporting group description: -   |  |
| Reporting group title  | Fluticasone nasal spray                      |
| Reporting group description: -   |  |
| Subject analysis set title   | Safety population for MP29-02                |
| Subject analysis set type  | Safety analysis                              |
| Subject analysis set description:<br>Safety population for MP29-02.                |  |
| Subject analysis set title   | Safety population for Fluticasone Propionate |
| Subject analysis set type  | Safety analysis                              |
| Subject analysis set description:<br>Safety population for Fluticasone Propionate. |  |

### Primary: Number of AEs Reported

|   |                                       |
|---|---------------------------------------|
| End point title   | Number of AEs Reported <sup>[1]</sup> |
| End point description:  |                                       |
| End point type  | Primary                               |
| End point timeframe:<br>Safety and tolerability assessments were made at Months 1, 3, 6, 9, and 12. Phone contact was made at Months 2, 4, 5, 7, 8, 10, and 11 during the 12-month evaluation period. |                                       |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis for the safety end point - number of AEs reported - was performed.

| End point values            | Safety population for MP29-02 | Safety population for Fluticasone Propionate |  |  |
|-----------------------------|-------------------------------|--|--|--|
| Subject group type          | Subject analysis set          | Subject analysis set                         |  |  |
| Number of subjects analysed | 404                           | 207  |  |  |
| Units: number of subjects   |                               |  |  |  |
| All Treatment-Emergent AEs  | 653                           | 313  |  |  |
| All Treatment-Related AEs   | 61                            | 46   |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Safety and tolerability assessments were made at Months 1, 3, 6, 9, and 12. Phone contact was made at Months 2, 4, 5, 7, 8, 10, and 11 during the 12-month evaluation period.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 11.1   |

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Fluticasone nasal spray |
|-----------------------|-------------------------|

Reporting group description: -

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | MP29-02 nasal spray |
|-----------------------|---------------------|

Reporting group description: -

| Serious adverse events                               | Fluticasone nasal spray | MP29-02 nasal spray |  |
|--|-------------------------|---------------------|--|
| Total subjects affected by serious adverse events    |                         |                     |  |
| subjects affected / exposed                          | 1 / 207 (0.48%)         | 3 / 404 (0.74%)     |  |
| number of deaths (all causes)                        | 0                       | 0                   |  |
| number of deaths resulting from adverse events       | 0                       | 0                   |  |
| General disorders and administration site conditions |                         |                     |  |
| Pyrexia  |                         |                     |  |
| subjects affected / exposed                          | 0 / 207 (0.00%)         | 1 / 404 (0.25%)     |  |
| occurrences causally related to treatment / all      | 0 / 0                   | 0 / 1               |  |
| deaths causally related to treatment / all           | 0 / 0                   | 0 / 0               |  |
| Infections and infestations                          |                         |                     |  |
| Dengue fever   |                         |                     |  |
| subjects affected / exposed                          | 0 / 207 (0.00%)         | 1 / 404 (0.25%)     |  |
| occurrences causally related to treatment / all      | 0 / 0                   | 0 / 1               |  |
| deaths causally related to treatment / all           | 0 / 0                   | 0 / 0               |  |
| Gastroenteritis                                      |                         |                     |  |
| subjects affected / exposed                          | 1 / 207 (0.48%)         | 0 / 404 (0.00%)     |  |
| occurrences causally related to treatment / all      | 0 / 1                   | 0 / 0               |  |
| deaths causally related to treatment / all           | 0 / 0                   | 0 / 0               |  |
| Appendicitis   |                         |                     |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 207 (0.00%) | 1 / 404 (0.25%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Dehydration                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 207 (0.48%) | 0 / 404 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 2.7 %

| <b>Non-serious adverse events</b>                     | Fluticasone nasal spray | MP29-02 nasal spray |  |
|---|-------------------------|---------------------|--|
| Total subjects affected by non-serious adverse events |                         |                     |  |
| subjects affected / exposed                           | 92 / 207 (44.44%)       | 188 / 404 (46.53%)  |  |
| Nervous system disorders                              |                         |                     |  |
| Headache  |                         |                     |  |
| subjects affected / exposed                           | 28 / 207 (13.53%)       | 50 / 404 (12.38%)   |  |
| occurrences (all)                                     | 28                      | 50                  |  |
| Dysgeusia   |                         |                     |  |
| subjects affected / exposed                           | 1 / 207 (0.48%)         | 11 / 404 (2.72%)    |  |
| occurrences (all)                                     | 1                       | 11                  |  |
| General disorders and administration site conditions  |                         |                     |  |
| Pyrexia   |                         |                     |  |
| subjects affected / exposed                           | 22 / 207 (10.63%)       | 33 / 404 (8.17%)    |  |
| occurrences (all)                                     | 22                      | 33                  |  |
| Respiratory, thoracic and mediastinal disorders       |                         |                     |  |
| Cough   |                         |                     |  |
| subjects affected / exposed                           | 5 / 207 (2.42%)         | 20 / 404 (4.95%)    |  |
| occurrences (all)                                     | 5                       | 20                  |  |
| Nasal congestion                                      |                         |                     |  |
| subjects affected / exposed                           | 8 / 207 (3.86%)         | 12 / 404 (2.97%)    |  |
| occurrences (all)                                     | 8                       | 12                  |  |
| Infections and infestations                           |                         |                     |  |
| Rhinitis  |                         |                     |  |



|                             |                 |                  |  |
|-----------------------------|-----------------|------------------|--|
| subjects affected / exposed | 5 / 207 (2.42%) | 11 / 404 (2.72%) |  |
| occurrences (all)           | 5               | 11               |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 29 November 2007 | Protocol amended to include change in methodology of the study (increase of patients in one treatment arm of the sub-study) |
| 21 January 2008  | Protocol amended to include administrative modifications related to the implementation of the first protocol amendment      |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported