



## Clinical trial results:

### Double Blind, Randomized, Placebo-Controlled, Parallel-Group, Multicenter/Multinational, Efficacy and Safety Study of Desloratadine 5 mg in the Treatment of Subjects With Allergic Rhinitis Who Meet the Criteria for Intermittent Allergic Rhinitis (IAR)

#### Summary

|                          |  |
|--------------------------|--|
| EudraCT number           | 2005-005449-20                               |
| Trial protocol           | FI PT ES DE HU SE GR DK IT BE Outside EU/EEA |
| Global end of trial date | 21 November 2007                             |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 10 February 2016 |
| First version publication date | 17 July 2015     |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | P04683 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |                              |
|------------------------------------|------------------------------|
| ISRCTN number                      | -                            |
| ClinicalTrials.gov id (NCT number) | NCT00406783                  |
| WHO universal trial number (UTN)   | -                            |
| Other trial identifiers            | Protocol number: MK-4117-174 |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Merck Sharp & Dohme Corp.  |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033                               |
| Public contact               | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |
| Sponsor organisation name    | Merck Sharp & Dohme Corp.  |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033                               |
| Public contact               | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |

Notes:

#### Paediatric regulatory details

|  |     |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No  |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No  |
| Does article 46 of REGULATION (EC) No                                | Yes |

|                                |
|--------------------------------|
| 1901/2006 apply to this trial? |
|--------------------------------|

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 21 November 2007 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 21 November 2007 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 21 November 2007 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

This study will investigate the effectiveness of desloratadine in treating subjects with allergic rhinitis (AR) who meet the criteria for intermittent allergic rhinitis.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 28 August 2006 |
| 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 | Netherlands: 2         |
| Country: Number of subjects enrolled | Portugal: 2            |
| Country: Number of subjects enrolled | Spain: 21              |
| Country: Number of subjects enrolled | Sweden: 35             |
| Country: Number of subjects enrolled | Denmark: 2             |
| Country: Number of subjects enrolled | Finland: 9             |
| Country: Number of subjects enrolled | France: 109            |
| Country: Number of subjects enrolled | Germany: 55            |
| Country: Number of subjects enrolled | Greece: 17             |
| Country: Number of subjects enrolled | Hungary: 24            |
| Country: Number of subjects enrolled | Italy: 68              |
| Country: Number of subjects enrolled | Canada: 134            |
| Country: Number of subjects enrolled | Russian Federation: 48 |
| Country: Number of subjects enrolled | Turkey: 21             |
| Worldwide total number of subjects   | 547                    |
| EEA total number of subjects         | 344                    |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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)                 | 20  |
| Adults (18-64 years)                      | 519 |
| From 65 to 84 years                       | 8   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Study sites were part of the Global Allergy and Asthma European Network (GA2LEN).

### Pre-assignment

Screening details:

Approximately eight subjects were to be enrolled at each site, but up to approximately 30 subjects could be enrolled at each site with the sponsor's approval.

### Period 1

|                              |                            |
|------------------------------|----------------------------|
| Period 1 title               | Treatment (overall period) |
| Is this the baseline period? | Yes                        |
| Allocation method            | Randomised - controlled    |
| Blinding used                | Double blind               |
| Roles blinded                | Subject, Investigator      |

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Desloratadine 5 mg |
|------------------|--------------------|

Arm description:

Desloratadine 5 mg, oral, tablet, once daily for 15 days

|  |                            |
|--|----------------------------|
| Arm type                               | Experimental               |
| Investigational medicinal product name | Desloratadine              |
| Investigational medicinal product code |                            |
| Other name                             | SCH 34117, Aeries, MK-4117 |
| Pharmaceutical forms                   | Tablet                     |
| Routes of administration               | Oral use                   |

Dosage and administration details:

Desloratadine 5 mg, oral, tablet, once daily for 15 days

|  |          |
|--|----------|
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

Placebo to Desloratadine, oral, tablet, once daily for 15 days

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Placebo to Desloratadine, oral, tablet, once daily for 15 days

|  |          |
|--|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

Placebo to desloratadine, oral, tablet once daily for 15 days

| <b>Number of subjects in period 1</b> | Desloratadine 5 mg | Placebo |
|---------------------------------------|--------------------|---------|
| Started                               | 276                | 271     |
| Completed                             | 262                | 256     |
| Not completed                         | 14                 | 15      |
| Did not meet protocol eligibility     | -                  | 1       |
| Consent withdrawn by subject          | 1                  | 4       |
| Adverse event, non-fatal              | 4                  | 4       |
| Lost to follow-up                     | 3                  | -       |
| Lack of efficacy                      | 2                  | 3       |
| Protocol deviation                    | 4                  | 3       |

## Baseline characteristics

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Desloratadine 5 mg |
|-----------------------|--------------------|

Reporting group description:

Desloratadine 5 mg, oral, tablet, once daily for 15 days

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo to Desloratadine, oral, tablet, once daily for 15 days

| Reporting group values                                | Desloratadine 5 mg | Placebo | Total |
|---|--------------------|---------|-------|
| Number of subjects                                    | 276                | 271     | 547   |
| Age categorical<br>Units: Subjects                    |                    |         |       |
| In utero  | 0                  | 0       | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                  | 0       | 0     |
| Newborns (0-27 days)                                  | 0                  | 0       | 0     |
| Infants and toddlers (28 days-23 months)              | 0                  | 0       | 0     |
| Children (2-11 years)                                 | 0                  | 0       | 0     |
| Adolescents (12-17 years)                             | 12                 | 8       | 20    |
| Adults (18-64 years)                                  | 262                | 257     | 519   |
| From 65-84 years                                      | 2                  | 6       | 8     |
| 85 years and over                                     | 0                  | 0       | 0     |
| Age continuous<br>Units: years                        |                    |         |       |
| arithmetic mean                                       | 33.8               | 34.6    |       |
| standard deviation                                    | ± 12               | ± 12.8  | -     |
| Gender categorical<br>Units: Subjects                 |                    |         |       |
| Female  | 154                | 164     | 318   |
| Male  | 122                | 107     | 229   |

## End points

### End points reporting groups

|  |                    |
|--|--------------------|
| Reporting group title  | Desloratadine 5 mg |
| Reporting group description:<br>Desloratadine 5 mg, oral, tablet, once daily for 15 days       |                    |
| Reporting group title  | Placebo            |
| Reporting group description:<br>Placebo to Desloratadine, oral, tablet, once daily for 15 days |                    |

### Primary: The Change From Baseline in the 12-hour AM/PM-PRIOR (Reflective) Total 5 Symptom Score (T5SS) From Subject Daily Diaries Averaged Over Treatment Days 1 to 15

|  |   |
|--|---|
| End point title  | The Change From Baseline in the 12-hour AM/PM-PRIOR (Reflective) Total 5 Symptom Score (T5SS) From Subject Daily Diaries Averaged Over Treatment Days 1 to 15 |
| End point description:<br>AM/PM is the average of separate morning (AM) and evening (PM) evaluations. T5SS = the sum of the individual scores for nasal congestion/stuffiness, sneezing, rhinorrhea/nasal discharge, nasal pruritis, and ocular pruritis. Each individual symptom/sign was scored from 0 (none) to 3 (severe). |   |
| End point type   | Primary   |
| End point timeframe:<br>Baseline and Days 1 to 15  |   |

| End point values                    | Desloratadine 5 mg | Placebo            |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 271 <sup>[1]</sup> | 265 <sup>[2]</sup> |  |  |
| Units: Scores on a scale            |                    |                    |  |  |
| least squares mean (standard error) | -3.01 (± 0.21)     | -2.13 (± 0.2)      |  |  |

Notes:

[1] - All randomized participants with a non-missing baseline and at least some post-baseline data.

[2] - All randomized participants with a non-missing baseline and at least some post-baseline data.

### Statistical analyses

|   |                              |
|---|------------------------------|
| Statistical analysis title  | Treatment Difference         |
| Statistical analysis description:<br>Difference in the least squares means between change from baseline in AM/PM PRIOR (reflective) T5SS for participants taking desloratadine over Day 1 to Day 15 of treatment vs. change from baseline in AM/PM PRIOR (reflective) T5SS for participants taking placebo over Day 1 to Day 15 of treatment. Negative differences are in favor of the desloratadine treatment group in the comparison. |                              |
| Comparison groups   | Desloratadine 5 mg v Placebo |

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 536                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | superiority <sup>[3]</sup>     |
| P-value                                 | < 0.001                        |
| Method                                  | ANOVA                          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -0.88                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -1.31                          |
| upper limit                             | -0.46                          |

Notes:

[3] - LS means, SEM, and 95% Confidence Intervals are obtained from an ANOVA model with treatment and site effects.

### Secondary: Change From Baseline in the Rhinoconjunctivitis Quality of Life Questionnaire-Standardized Version (RQLQ-S) at the Final Visit

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in the Rhinoconjunctivitis Quality of Life Questionnaire-Standardized Version (RQLQ-S) at the Final Visit |
|-----------------|--|

End point description:

The RQLQ-S questionnaire consists of 28 questions grouped into 7 domains. Each question is scored on a scale of 0 (not troubled with symptoms) to 6 (extremely troubled with symptoms). The total RQLQ-S score is the average score of the 28 questions which consisted of a total of 7 domains.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and 15 days

| End point values                    | Desloratadine 5 mg | Placebo            |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 250 <sup>[4]</sup> | 248 <sup>[5]</sup> |  |  |
| Units: Scores on a scale            |                    |                    |  |  |
| least squares mean (standard error) | -1.1 (± 0.1)       | -0.73 (± 0.1)      |  |  |

Notes:

[4] - Participant ≥18 years of age and where available in the local language.

[5] - Participants ≥18 years of age and where available in the local language.

### Statistical analyses

|                            |                      |
|----------------------------|----------------------|
| Statistical analysis title | Treatment Difference |
|----------------------------|----------------------|

Statistical analysis description:

Difference in the least squares means between change from baseline in RQLQ-S for participants taking desloratadine at Day 15 of treatment vs. change from baseline in RQLQ-S for participants taking placebo at Day 15 of treatment. Negative differences are in favor of the desloratadine treatment group in the comparison.

|                   |                              |
|-------------------|------------------------------|
| Comparison groups | Desloratadine 5 mg v Placebo |
|-------------------|------------------------------|



|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 498                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | superiority <sup>[6]</sup>     |
| P-value                                 | < 0.001                        |
| Method                                  | ANOVA                          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -0.37                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -0.58                          |
| upper limit                             | -0.17                          |

Notes:

[6] - LS means, SEM, and 95% Confidence Intervals are obtained from an ANOVA model with treatment and site effects.

### Other pre-specified: Total 5 Symptom Score (T5SS) - Average AM/PM PRIOR (Reflective) 12 Hours Diary: BASELINE

|                 |  |
|-----------------|--|
| End point title | Total 5 Symptom Score (T5SS) - Average AM/PM PRIOR (Reflective) 12 Hours Diary: BASELINE |
|-----------------|--|

End point description:

AM/PM is the average of separate morning (AM) and evening (PM) evaluations. T5SS = the sum of the individual scores for nasal congestion/stuffiness, sneezing, rhinorrhea/nasal discharge, nasal pruritis, and ocular pruritis. Each individual symptom/sign was scored from 0 (none) to 3 (severe).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline

| End point values                    | Desloratadine 5 mg | Placebo            |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 271 <sup>[7]</sup> | 265 <sup>[8]</sup> |  |  |
| Units: Scores on a scale            |                    |                    |  |  |
| least squares mean (standard error) | 8.5 (± 0.14)       | 8.33 (± 0.14)      |  |  |

Notes:

[7] - All participants with a non-missing baseline and at least some post-baseline data.

[8] - All participants with a non-missing baseline and at least some post-baseline data.

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Rhinoconjunctivitis Quality of Life Questionnaire-Standardized Version (RQLQ-S: BASELINE)

|                 |   |
|-----------------|---|
| End point title | Rhinoconjunctivitis Quality of Life Questionnaire-Standardized Version (RQLQ-S: BASELINE) |
|-----------------|---|

End point description:

The RQLQ-S questionnaire consists of 28 questions grouped into 7 domains. Each question is scored on a scale of 0 (not troubled with symptoms) to 6 (extremely troubled with symptoms). The total RQLQ-S score is the average score of the 28 questions which consisted of a total of 7 domains.

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

---

End point timeframe:

Baseline

---

| End point values                    | Desloratadine<br>5 mg | Placebo             |  |  |
|-------------------------------------|-----------------------|---------------------|--|--|
| Subject group type                  | Reporting group       | Reporting group     |  |  |
| Number of subjects analysed         | 250 <sup>[9]</sup>    | 248 <sup>[10]</sup> |  |  |
| Units: Scores on a scale            |                       |                     |  |  |
| least squares mean (standard error) | 2.96 ( $\pm$ 0.08)    | 2.8 ( $\pm$ 0.08)   |  |  |

Notes:

[9] - All participants  $\geq 18$  years of age and where available in the local language.

[10] - All participants  $\geq 18$  years of age and where available in the local language.

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to Day 15

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Desloratadine 5 mg |
|-----------------------|--------------------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events                            | Desloratadine 5 mg | Placebo         |  |
|---|--------------------|-----------------|--|
| Total subjects affected by serious adverse events |                    |                 |  |
| subjects affected / exposed                       | 0 / 276 (0.00%)    | 0 / 271 (0.00%) |  |
| number of deaths (all causes)                     | 0                  | 0               |  |
| number of deaths resulting from adverse events    | 0                  | 0               |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events                            | Desloratadine 5 mg | Placebo          |  |
|---|--------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                    |                  |  |
| subjects affected / exposed                           | 18 / 276 (6.52%)   | 17 / 271 (6.27%) |  |
| Nervous system disorders                              |                    |                  |  |
| Headache  |                    |                  |  |
| subjects affected / exposed                           | 18 / 276 (6.52%)   | 17 / 271 (6.27%) |  |
| occurrences (all)                                     | 23                 | 21               |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment  |
|--------------|--|
| 14 June 2006 | This amendment provided an updated version of a study questionnaire.   |
| 05 June 2007 | This amendment changed criteria for subject discontinuation from the study and changed the grading scale for a study assessment. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported