



## Clinical trial results:

### ELABORATION OF A PATIENT-FRIENDLY TREATMENT STRATEGY WITH CAPSAICIN NASAL SPRAY IN PATIENTS WITH IDIOPATHIC RHINITIS

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2014-003914-10   |
| Trial protocol           | BE               |
| Global end of trial date | 31 December 2018 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 07 January 2021 |
| First version publication date | 07 January 2021 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | sept2014 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02288156 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | UZLeuven                                     |
| Sponsor organisation address | Herestraat 49, Leuven, Belgium, 3000         |
| Public contact               | UZ Leuven, UZ Leuven, Leen.cools@uzleuven.be |
| Scientific contact           | UZ Leuven, UZ Leuven, leen.cools@uzleuven.be |

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 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 01 December 2019 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 31 December 2018 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 31 December 2018 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate if the two novel treatment modalities show non-inferiority compared to the current treatment modality of capsaicin nasal treatment in 120 patients with IR. The gathered data of this single center trial can be used to guide the decision on the set-up and the design of a larger multi-center trial being powered to prove non-inferiority.

Protection of trial subjects:

On the application day, the nasal mucosa was anesthetized before the first 2 applications by application of a cocaine 5% nasal spray. To ensure effective local anesthesia, an interval of 15 minutes was maintained between the application of the cocaine and the blinded nasal spray.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 01 March 2015 |
| 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 | Belgium: 80 |
| Worldwide total number of subjects   | 80          |
| EEA total number of subjects         | 80          |

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)                 | 0  |
| Adults (18-64 years)                      | 80 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited in Belgium from 2015 till 2018.

### Pre-assignment

Screening details:

Main inclusion criteria:

- Idiopathic rhinitis (IR) patients with at least 1 persistent (> 12w) rhinological symptoms (nasal discharge, sneezing, nasal congestion) for an average of at least 1 h per day,
- IR patients with a total nasal symptoms score (TNS) of 5 or more on a visual analogue scale (VAS).
- Age > 18 and < 60 years.

### Period 1

|                              |                                 |
|------------------------------|---------------------------------|
| Period 1 title               | Overall period (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>             | 0,1mM Capsaicin / Placebo |

Arm description: -

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Capsaicin         |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Nasal spray       |
| Routes of administration               | Intranasal use    |

Dosage and administration details:

Patient is treated with 0,1mM capsaicin, 5 applications on 1 day at 1-hour intervals.  
per application: 2 puffs in each nostril, 0.4mL/puff.  
4 weeks thereafter, the patient is treated daily with placebo

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Placebo / 0,01mM Capsaicin |
|------------------|----------------------------|

Arm description: -

|  |                |
|--|----------------|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Capsaicin      |
| Investigational medicinal product code |                |
| Other name                             |                |
| Pharmaceutical forms                   | Nasal spray    |
| Routes of administration               | Intranasal use |

Dosage and administration details:

Patient is treated with placebo, 5 applications on 1 day at 1-hour intervals.  
per application: 2 puffs in each nostril, 0.4mL/puff.  
4 weeks thereafter, the patient is treated daily with 0,01mM Capsaicin

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | Placebo / 0,001mM Capsaicin |
|------------------|-----------------------------|

Arm description: -

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                |
|--|----------------|
| Investigational medicinal product name | Capsaicin      |
| Investigational medicinal product code |                |
| Other name                             |                |
| Pharmaceutical forms                   | Nasal spray    |
| Routes of administration               | Intranasal use |

Dosage and administration details:

Patient is treated with placebo, 5 applications on 1 day at 1-hour intervals.

per application: 2 puffs in each nostril, 0.4mL/puff.

4 weeks thereafter, the patient is treated daily with 0,001mM Capsaicin

|  |                   |
|--|-------------------|
| <b>Arm title</b>                       | Placebo / Placebo |
| Arm description: -                     |                   |
| Arm type                               | Placebo           |
| Investigational medicinal product name | Placebo           |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Nasal spray       |
| Routes of administration               | Intranasal use    |

Dosage and administration details:

Patient is treated with placebo, 5 applications on 1 day at 1-hour intervals.

per application: 2 puffs in each nostril, 0.4mL/puff.

4 weeks thereafter, the patient is treated daily with placebo

| <b>Number of subjects in period 1</b> | 0,1mM Capsaicin / Placebo | Placebo / 0,01mM Capsaicin | Placebo / 0,001mM Capsaicin |
|---------------------------------------|---------------------------|----------------------------|-----------------------------|
| Started                               | 20                        | 20                         | 20                          |
| Completed                             | 16                        | 16                         | 18                          |
| Not completed                         | 4                         | 4                          | 2                           |
| Lost to follow-up                     | 2                         | 3                          | 2                           |
| Protocol deviation                    | 2                         | 1                          | -                           |
| Lack of efficacy                      | -                         | -                          | -                           |

| <b>Number of subjects in period 1</b> | Placebo / Placebo |
|---------------------------------------|-------------------|
| Started                               | 20                |
| Completed                             | 18                |
| Not completed                         | 2                 |
| Lost to follow-up                     | 1                 |
| Protocol deviation                    | -                 |
| Lack of efficacy                      | 1                 |

## Baseline characteristics

### Reporting groups

|                                |                             |
|--------------------------------|-----------------------------|
| Reporting group title          | 0,1mM Capsaicin / Placebo   |
| Reporting group description: - |                             |
| Reporting group title          | Placebo / 0,01mM Capsaicin  |
| Reporting group description: - |                             |
| Reporting group title          | Placebo / 0,001mM Capsaicin |
| Reporting group description: - |                             |
| Reporting group title          | Placebo / Placebo           |
| Reporting group description: - |                             |

| Reporting group values  | 0,1mM Capsaicin / Placebo | Placebo / 0,01mM Capsaicin | Placebo / 0,001mM Capsaicin |
|---|---------------------------|----------------------------|-----------------------------|
| Number of subjects  | 20                        | 20                         | 20                          |
| Age categorical<br>Units: Subjects  |                           |                            |                             |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                           |                            |                             |
| Age continuous<br>Units: years  |                           |                            |                             |
| arithmetic mean<br>standard deviation   | 50<br>± 14                | 45<br>± 10                 | 48<br>± 14                  |
| Gender categorical<br>Units: Subjects   |                           |                            |                             |
| Female  | 11                        | 9                          | 10                          |
| Male  | 9                         | 11                         | 10                          |

| Reporting group values   | Placebo / Placebo | Total                           |  |
|--|-------------------|---------------------------------|--|
| Number of subjects   | 20                | 80                              |  |
| Age categorical<br>Units: Subjects   |                   |                                 |  |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years |                   | 0<br>0<br>0<br>0<br>0<br>0<br>0 |  |

|                   |  |   |  |
|-------------------|--|---|--|
| 85 years and over |  | 0 |  |
|-------------------|--|---|--|

|                    |      |    |  |
|--------------------|------|----|--|
| Age continuous     |      |    |  |
| Units: years       |      |    |  |
| arithmetic mean    | 45   |    |  |
| standard deviation | ± 15 | -  |  |
| Gender categorical |      |    |  |
| Units: Subjects    |      |    |  |
| Female             | 11   | 41 |  |
| Male               | 9    | 39 |  |

## End points

### End points reporting groups

|                                |                             |
|--------------------------------|-----------------------------|
| Reporting group title          | 0,1mM Capsaicin / Placebo   |
| Reporting group description: - |                             |
| Reporting group title          | Placebo / 0,01mM Capsaicin  |
| Reporting group description: - |                             |
| Reporting group title          | Placebo / 0,001mM Capsaicin |
| Reporting group description: - |                             |
| Reporting group title          | Placebo / Placebo           |
| Reporting group description: - |                             |

### Primary: VAS major nasal symptom at week 4

|                        |  |
|------------------------|--|
| End point title        | VAS major nasal symptom at week 4  |
| End point description: | Comparison of VAS for major nasal symptom at week 4 in all treatments modalities. The region of equivalence of the compared treatment modalities is defined as a difference in VAS of less than 1. |
| End point type         | Primary  |
| End point timeframe:   |  |
| Week 4 after treatment |  |

| End point values                     | 0,1mM Capsaicin / Placebo | Placebo / 0,01mM | Placebo / 0,001mM | Placebo / Placebo |
|--------------------------------------|---------------------------|------------------|-------------------|-------------------|
| Subject group type                   | Reporting group           | Reporting group  | Reporting group   | Reporting group   |
| Number of subjects analysed          | 16                        | 16               | 18                | 18                |
| Units: VAS score                     |                           |                  |                   |                   |
| arithmetic mean (standard deviation) | 3.66 (± 2.78)             | 4.29 (± 2.92)    | 4.49 (± 2.93)     | 5.6 (± 1.67)      |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title  | Comparison of VAS values between different groups  |
| Statistical analysis description:   |  |
| The VAS major nasal symptom was compared at 4 weeks post treatment between the different treatment groups |  |
| Comparison groups   | 0,1mM Capsaicin / Placebo v Placebo / 0,01mM Capsaicin v Placebo / 0,001mM Capsaicin v Placebo / Placebo |
| Number of subjects included in analysis   | 68   |
| Analysis specification  | Pre-specified  |
| Analysis type   | equivalence  |
| P-value   | ≤ 0.05   |
| Method  | ANOVA  |





## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From signing informed consent till end of study

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

### Reporting groups

|                       |                           |
|-----------------------|---------------------------|
| Reporting group title | 0,1mM Capsaicin / Placebo |
|-----------------------|---------------------------|

Reporting group description: -

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Placebo / 0,01mM Capsaicin |
|-----------------------|----------------------------|

Reporting group description: -

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Placebo / 0,001mM Capsaicin |
|-----------------------|-----------------------------|

Reporting group description: -

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

Reporting group description: -

| Serious adverse events                            | 0,1mM Capsaicin / Placebo | Placebo / 0,01mM Capsaicin | Placebo / 0,001mM Capsaicin |
|---|---------------------------|----------------------------|-----------------------------|
| Total subjects affected by serious adverse events |                           |                            |                             |
| subjects affected / exposed                       | 0 / 16 (0.00%)            | 0 / 16 (0.00%)             | 0 / 18 (0.00%)              |
| number of deaths (all causes)                     | 0                         | 0                          | 0                           |
| number of deaths resulting from adverse events    | 0                         | 0                          | 0                           |

| Serious adverse events                            | Placebo / Placebo |  |  |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events |                   |  |  |
| subjects affected / exposed                       | 0 / 18 (0.00%)    |  |  |
| number of deaths (all causes)                     | 0                 |  |  |
| number of deaths resulting from adverse events    | 0                 |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | 0,1mM Capsaicin / Placebo | Placebo / 0,01mM Capsaicin | Placebo / 0,001mM Capsaicin |
|---|---------------------------|----------------------------|-----------------------------|
| Total subjects affected by non-serious adverse events |                           |                            |                             |
| subjects affected / exposed                           | 10 / 16 (62.50%)          | 8 / 16 (50.00%)            | 14 / 18 (77.78%)            |
| Surgical and medical procedures                       |                           |                            |                             |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Eyelid operation<br>subjects affected / exposed<br>occurrences (all)       | 1 / 16 (6.25%)<br>1 | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 |
| Nervous system disorders   |                     |                     |                     |
| Head discomfort<br>subjects affected / exposed<br>occurrences (all)        | 0 / 16 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 |
| Headache<br>subjects affected / exposed<br>occurrences (all)               | 0 / 16 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Loss of consciousness<br>subjects affected / exposed<br>occurrences (all)  | 0 / 16 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 |
| General disorders and administration<br>site conditions                    |                     |                     |                     |
| Influenza like illness<br>subjects affected / exposed<br>occurrences (all) | 0 / 16 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>1 |
| Malaise<br>subjects affected / exposed<br>occurrences (all)                | 0 / 16 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 16 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1 | 0 / 18 (0.00%)<br>0 |
| Ear and labyrinth disorders  |                     |                     |                     |
| Ear discomfort<br>subjects affected / exposed<br>occurrences (all)         | 0 / 16 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 |
| Immune system disorders  |                     |                     |                     |
| Mite allergy<br>subjects affected / exposed<br>occurrences (all)           | 1 / 16 (6.25%)<br>1 | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 |
| Eye disorders  |                     |                     |                     |
| Eye irritation<br>subjects affected / exposed<br>occurrences (all)         | 0 / 16 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Eye pruritus   |                     |                     |                     |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 16 (6.25%)<br>1 | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 |
| Gastrointestinal disorders                       |                     |                     |                     |
| Abdominal pain upper                             |                     |                     |                     |
| subjects affected / exposed                      | 1 / 16 (6.25%)      | 0 / 16 (0.00%)      | 1 / 18 (5.56%)      |
| occurrences (all)                                | 1                   | 0                   | 1                   |
| Food poisoning                                   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 0 / 16 (0.00%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Respiratory, thoracic and mediastinal disorders  |                     |                     |                     |
| Cough  |                     |                     |                     |
| subjects affected / exposed                      | 1 / 16 (6.25%)      | 2 / 16 (12.50%)     | 0 / 18 (0.00%)      |
| occurrences (all)                                | 1                   | 2                   | 0                   |
| Epistaxis  |                     |                     |                     |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 0 / 16 (0.00%)      | 1 / 18 (5.56%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Nasal congestion                                 |                     |                     |                     |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 3 / 16 (18.75%)     | 1 / 18 (5.56%)      |
| occurrences (all)                                | 0                   | 3                   | 1                   |
| Nasal crusting                                   |                     |                     |                     |
| subjects affected / exposed                      | 1 / 16 (6.25%)      | 0 / 16 (0.00%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Nasal discomfort                                 |                     |                     |                     |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 0 / 16 (0.00%)      | 1 / 18 (5.56%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Oropharyngeal pain                               |                     |                     |                     |
| subjects affected / exposed                      | 1 / 16 (6.25%)      | 0 / 16 (0.00%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Rhinorrhoea                                      |                     |                     |                     |
| subjects affected / exposed                      | 2 / 16 (12.50%)     | 2 / 16 (12.50%)     | 1 / 18 (5.56%)      |
| occurrences (all)                                | 2                   | 2                   | 1                   |
| Sneezing   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 1 / 16 (6.25%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Throat clearing                                  |                     |                     |                     |

|   |                      |                     |                      |
|---|----------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                | 0 / 16 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  |
| Upper-airway cough syndrome<br>subjects affected / exposed<br>occurrences (all) | 0 / 16 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  |
| Musculoskeletal and connective tissue disorders                                 |                      |                     |                      |
| Arthritis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 16 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 16 (12.50%)<br>2 | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)           | 0 / 16 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1 | 0 / 18 (0.00%)<br>0  |
| Infections and infestations   |                      |                     |                      |
| Cystitis<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 16 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1 | 0 / 18 (0.00%)<br>0  |
| Ear infection<br>subjects affected / exposed<br>occurrences (all)               | 0 / 16 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  |
| Eye infection<br>subjects affected / exposed<br>occurrences (all)               | 0 / 16 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  |
| Gastroenteritis viral<br>subjects affected / exposed<br>occurrences (all)       | 0 / 16 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  |
| Gastrointestinal infection<br>subjects affected / exposed<br>occurrences (all)  | 0 / 16 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 16 (6.25%)<br>1  | 1 / 16 (6.25%)<br>1 | 3 / 18 (16.67%)<br>3 |
| Laryngitis  |                      |                     |                      |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 16 (6.25%)  | 1 / 16 (6.25%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 1               | 2               | 0               |
| Nasopharyngitis             |                 |                 |                 |
| subjects affected / exposed | 7 / 16 (43.75%) | 5 / 16 (31.25%) | 8 / 18 (44.44%) |
| occurrences (all)           | 11              | 9               | 9               |
| Pneumonia                   |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 16 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Respiratory tract infection |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 16 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Rhinitis                    |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 16 (6.25%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Sinusitis                   |                 |                 |                 |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 16 (0.00%)  | 3 / 18 (16.67%) |
| occurrences (all)           | 2               | 0               | 5               |
| Tonsillitis                 |                 |                 |                 |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 16 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 1               | 1               | 0               |

|   |                   |  |  |
|---|-------------------|--|--|
| <b>Non-serious adverse events</b>                     | Placebo / Placebo |  |  |
| Total subjects affected by non-serious adverse events |                   |  |  |
| subjects affected / exposed                           | 12 / 18 (66.67%)  |  |  |
| Surgical and medical procedures                       |                   |  |  |
| Eyelid operation                                      |                   |  |  |
| subjects affected / exposed                           | 0 / 18 (0.00%)    |  |  |
| occurrences (all)                                     | 0                 |  |  |
| Nervous system disorders                              |                   |  |  |
| Head discomfort                                       |                   |  |  |
| subjects affected / exposed                           | 1 / 18 (5.56%)    |  |  |
| occurrences (all)                                     | 1                 |  |  |
| Headache  |                   |  |  |
| subjects affected / exposed                           | 1 / 18 (5.56%)    |  |  |
| occurrences (all)                                     | 2                 |  |  |
| Loss of consciousness                                 |                   |  |  |

|   |                     |  |  |
|---|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all)        | 1 / 18 (5.56%)<br>1 |  |  |
| General disorders and administration<br>site conditions |                     |  |  |
| Influenza like illness                                  |                     |  |  |
| subjects affected / exposed                             | 1 / 18 (5.56%)      |  |  |
| occurrences (all)                                       | 1                   |  |  |
| Malaise   |                     |  |  |
| subjects affected / exposed                             | 0 / 18 (0.00%)      |  |  |
| occurrences (all)                                       | 0                   |  |  |
| Pyrexia   |                     |  |  |
| subjects affected / exposed                             | 0 / 18 (0.00%)      |  |  |
| occurrences (all)                                       | 0                   |  |  |
| Ear and labyrinth disorders                             |                     |  |  |
| Ear discomfort  |                     |  |  |
| subjects affected / exposed                             | 1 / 18 (5.56%)      |  |  |
| occurrences (all)                                       | 1                   |  |  |
| Immune system disorders                                 |                     |  |  |
| Mite allergy  |                     |  |  |
| subjects affected / exposed                             | 0 / 18 (0.00%)      |  |  |
| occurrences (all)                                       | 0                   |  |  |
| Eye disorders   |                     |  |  |
| Eye irritation  |                     |  |  |
| subjects affected / exposed                             | 0 / 18 (0.00%)      |  |  |
| occurrences (all)                                       | 0                   |  |  |
| Eye pruritus  |                     |  |  |
| subjects affected / exposed                             | 0 / 18 (0.00%)      |  |  |
| occurrences (all)                                       | 0                   |  |  |
| Gastrointestinal disorders                              |                     |  |  |
| Abdominal pain upper                                    |                     |  |  |
| subjects affected / exposed                             | 0 / 18 (0.00%)      |  |  |
| occurrences (all)                                       | 0                   |  |  |
| Food poisoning  |                     |  |  |
| subjects affected / exposed                             | 1 / 18 (5.56%)      |  |  |
| occurrences (all)                                       | 1                   |  |  |
| Respiratory, thoracic and mediastinal<br>disorders      |                     |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Cough   |                |  |  |
| subjects affected / exposed                     | 1 / 18 (5.56%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Epistaxis                                       |                |  |  |
| subjects affected / exposed                     | 1 / 18 (5.56%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Nasal congestion                                |                |  |  |
| subjects affected / exposed                     | 1 / 18 (5.56%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Nasal crusting                                  |                |  |  |
| subjects affected / exposed                     | 0 / 18 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Nasal discomfort                                |                |  |  |
| subjects affected / exposed                     | 1 / 18 (5.56%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Oropharyngeal pain                              |                |  |  |
| subjects affected / exposed                     | 1 / 18 (5.56%) |  |  |
| occurrences (all)                               | 2              |  |  |
| Rhinorrhoea                                     |                |  |  |
| subjects affected / exposed                     | 0 / 18 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Sneezing  |                |  |  |
| subjects affected / exposed                     | 0 / 18 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Throat clearing                                 |                |  |  |
| subjects affected / exposed                     | 0 / 18 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Upper-airway cough syndrome                     |                |  |  |
| subjects affected / exposed                     | 0 / 18 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Arthritis                                       |                |  |  |
| subjects affected / exposed                     | 1 / 18 (5.56%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Back pain                                       |                |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 18 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Pain in extremity           |                 |  |  |
| subjects affected / exposed | 0 / 18 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Infections and infestations |                 |  |  |
| Cystitis                    |                 |  |  |
| subjects affected / exposed | 0 / 18 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Ear infection               |                 |  |  |
| subjects affected / exposed | 0 / 18 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Eye infection               |                 |  |  |
| subjects affected / exposed | 0 / 18 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Gastroenteritis viral       |                 |  |  |
| subjects affected / exposed | 1 / 18 (5.56%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Gastrointestinal infection  |                 |  |  |
| subjects affected / exposed | 0 / 18 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Influenza                   |                 |  |  |
| subjects affected / exposed | 1 / 18 (5.56%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Laryngitis                  |                 |  |  |
| subjects affected / exposed | 1 / 18 (5.56%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Nasopharyngitis             |                 |  |  |
| subjects affected / exposed | 6 / 18 (33.33%) |  |  |
| occurrences (all)           | 9               |  |  |
| Pneumonia                   |                 |  |  |
| subjects affected / exposed | 0 / 18 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Respiratory tract infection |                 |  |  |
| subjects affected / exposed | 0 / 18 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |



|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| Rhinitis                    |                 |  |  |
| subjects affected / exposed | 1 / 18 (5.56%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Sinusitis                   |                 |  |  |
| subjects affected / exposed | 2 / 18 (11.11%) |  |  |
| occurrences (all)           | 2               |  |  |
| Tonsillitis                 |                 |  |  |
| subjects affected / exposed | 0 / 18 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported