



## Clinical trial results:

**An open, multicenter, randomized, controlled trial to evaluate the correlation between spontaneous catch-up growth, clinical response to Saizen® (recombinant human growth hormone, r-hGH) and gene expression profiling in children small for gestational age (SGA)**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-001681-25 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 10 July 2009   |

### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 23 May 2016    |
| First version publication date | 05 August 2015 |

### Trial information

#### Trial identification

|                       |       |
|-----------------------|-------|
| Sponsor protocol code | 23681 |
|-----------------------|-------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01067352 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Merck KGaA  |
| Sponsor organisation address | Frankfurter Strasse 250, Darmstadt, Germany, 64293                                  |
| Public contact               | Communication Centre Merck KGaA, Merck KGaA, +49 6151725200, service@merckgroup.com |
| Scientific contact           | Communication Centre Merck KGaA, Merck KGaA, +49 6151725200, service@merckgroup.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 1901/2006 apply to this trial? | Yes |

Notes:

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**Results analysis stage**

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|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 10 July 2009 |
| Is this the analysis of the primary completion data? | No           |

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|                                  |              |
|----------------------------------|--------------|
| Global end of trial reached?     | Yes          |
| Global end of trial date         | 10 July 2009 |
| Was the trial ended prematurely? | No           |

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Notes:

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**General information about the trial**

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Main objective of the trial:

The primary objective of this study was to evaluate the correlation between gene expression and catch-up growth (either spontaneous or drug-induced after one year of treatment) in SGA children.

A secondary objective was to evaluate the percentage of patients who were not treated, but who showed a spontaneous catch-up growth during two years of observation.

Safety objectives included the safety and tolerability of Saizen (recombinant human growth hormone, r-hGH) in SGA children.

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Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

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Background therapy: -

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Evidence for comparator: -

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|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 20 February 2004 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Italy: 25 |
| Worldwide total number of subjects   | 25        |
| EEA total number of subjects         | 25        |

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Notes:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| 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)                     | 25 |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |

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

## Subject disposition

### Recruitment

Recruitment details:

Subjects were recruited in 12 study centers in Italy from 20 Feb 2004 to 10 Jul 2009.

### Pre-assignment

Screening details:

in total, 25 subject enrolled in this study

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (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> | Group A, less than third percentile (Saizen) |
|------------------|--|

Arm description:

Subjects with less than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received Saizen (recombinant human growth hormone, r-hGH) subcutaneously (s.c) at the daily dose of 0.035 milligram(mg)/kilogram(kg) for 2 years.

|  |  |
|--|--|
| Arm type                               | Experimental                             |
| Investigational medicinal product name | Recombinant human growth hormone (r-hGH) |
| Investigational medicinal product code |  |
| Other name                             | Saizen                                   |
| Pharmaceutical forms                   | Powder for solution for injection        |
| Routes of administration               | Subcutaneous use                         |

Dosage and administration details:

Recombinant human GH were administered subcutaneously at the daily dose of 0.067 mg/kg of body weight to Group A1.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Group A2, less than third percentile (No treatment) |
|------------------|---|

Arm description:

Subjects with less than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received no drug treatment for 2 years.

|   |                 |
|---|-----------------|
| Arm type  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

|                  |  |
|------------------|--|
| <b>Arm title</b> | Group B, more than third percentile (No treatment) |
|------------------|--|

Arm description:

Subjects with more than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received no drug treatment for 2 years.

|   |                 |
|---|-----------------|
| Arm type  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

| <b>Number of subjects in period 1</b> | Group A, less than third percentile (Saizen) | Group A2, less than third percentile (No treatment) | Group B, more than third percentile (No treatment) |
|---------------------------------------|--|---|--|
| Started                               | 9  | 6   | 10   |
| Completed                             | 8  | 3   | 9  |
| Not completed                         | 1  | 3   | 1  |
| Consent withdrawn by subject          | 1  | 2   | 1  |
| Physician decision                    | -  | 1   | -  |

## Baseline characteristics

### Reporting groups

|   |   |
|---|---|
| Reporting group title   | Group A, less than third percentile (Saizen)        |
| Reporting group description:<br>Subjects with less than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received Saizen (recombinant human growth hormone, r-hGH) subcutaneously (s.c) at the daily dose of 0.035 milligram(mg)/kilogram(kg) for 2 years. |   |
| Reporting group title   | Group A2, less than third percentile (No treatment) |
| Reporting group description:<br>Subjects with less than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received no drug treatment for 2 years.   |   |
| Reporting group title   | Group B, more than third percentile (No treatment)  |
| Reporting group description:<br>Subjects with more than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received no drug treatment for 2 years.   |   |

| Reporting group values             | Group A, less than third percentile (Saizen) | Group A2, less than third percentile (No treatment) | Group B, more than third percentile (No treatment) |
|------------------------------------|--|---|--|
| Number of subjects                 | 9  | 6   | 10   |
| Age categorical<br>Units: Subjects |  |   |  |

|   |              |            |              |
|---|--------------|------------|--------------|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 5.7<br>± 1.2 | 5<br>± 0.7 | 5.2<br>± 0.4 |
| Gender, Male/Female<br>Units: participants                              |              |            |              |
| Female  | 4            | 4          | 5            |
| Male  | 5            | 2          | 5            |

| Reporting group values             | Total |  |  |
|------------------------------------|-------|--|--|
| Number of subjects                 | 25    |  |  |
| Age categorical<br>Units: Subjects |       |  |  |

|   |    |  |  |
|---|----|--|--|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -  |  |  |
| Gender, Male/Female<br>Units: participants                              |    |  |  |
| Female  | 13 |  |  |
| Male  | 12 |  |  |

## End points

### End points reporting groups

|   |   |
|---|---|
| Reporting group title   | Group A, less than third percentile (Saizen)        |
| Reporting group description:<br>Subjects with less than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received Saizen (recombinant human growth hormone, r-hGH) subcutaneously (s.c) at the daily dose of 0.035 milligram(mg)/kilogram(kg) for 2 years. |   |
| Reporting group title   | Group A2, less than third percentile (No treatment) |
| Reporting group description:<br>Subjects with less than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received no drug treatment for 2 years.   |   |
| Reporting group title   | Group B, more than third percentile (No treatment)  |
| Reporting group description:<br>Subjects with more than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received no drug treatment for 2 years.   |   |

### Primary: Correlation between gene expression profiling and catch-up growth in small for gestational age (SGA) children

|   |  |
|---|--|
| End point title   | Correlation between gene expression profiling and catch-up growth in small for gestational age (SGA) children <sup>[1]</sup> |
| End point description:<br>Gene expression profiling:analysis of ribonucleic acid (RNA) extracted from body tissue or fluids using Clontech Atlas Human Array to study level of activation of genes in tissue analyzed. Analysis was performed to identify possible correlation between catch-up growth (either spontaneous or drug-induced after Week 48) and therapeutic response to rhGH. Spontaneous catch up growth:shown by SGA subjects having length more than third percentile at Week 96 without any treatment;drug induced growth was by SGA subjects having length more than third percentile at Week 96 with drug treatment. Gene expression profiling was not performed due to RNA degradation in nearly all of the blood samples and hence no comparison between gene expression and growth was made. |  |
| End point type  | Primary  |
| End point timeframe:<br>Baseline and Week 48  |  |

#### 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: Gene expression profiling was not performed due to RNA degradation in nearly all of the blood samples and hence no comparison between gene expression and growth was made.

| End point values                     | Group A, less than third percentile (Saizen) | Group A2, less than third percentile (No treatment) | Group B, more than third percentile (No treatment) |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                              | Reporting group                                     | Reporting group                                    |  |
| Number of subjects analysed          | 0 <sup>[2]</sup>                             | 0 <sup>[3]</sup>                                    | 0 <sup>[4]</sup>                                   |  |
| Units: correlation factor            |  |   |  |  |
| arithmetic mean (standard deviation) | ()   | ()  | ()   |  |

#### Notes:

[2] - Comparison between gene expression and growth could not be done as gene profiling could not be done.

[3] - Comparison between gene expression and growth could not be done as gene profiling could not be done.

[4] - Comparison between gene expression and growth could not be done as gene profiling could not be

done.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of untreated subjects who showed a spontaneous catch-up growth

|   |   |
|---|---|
| End point title   | Percentage of untreated subjects who showed a spontaneous catch-up growth |
| End point description:<br>Spontaneous catch up growth was the growth shown by SGA subjects having length more than third percentile at Week 96 without any study drug treatment. Data was not analyzed due to small number of evaluable participants. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Baseline through Week 96  |   |

| End point values              | Group A, less than third percentile (Saizen) | Group A2, less than third percentile (No treatment) | Group B, more than third percentile (No treatment) |  |
|-------------------------------|--|---|--|--|
| Subject group type            | Reporting group                              | Reporting group                                     | Reporting group                                    |  |
| Number of subjects analysed   | 0 <sup>[5]</sup>                             | 0 <sup>[6]</sup>                                    | 0 <sup>[7]</sup>                                   |  |
| Units: Percentage of subjects |  |   |  |  |
| number (not applicable)       |  |   |  |  |

Notes:

[5] - Data was not analyzed due to small number of evaluable subjects.

[6] - Data was not analyzed due to small number of evaluable subjects.

[7] - Data was not analyzed due to small number of evaluable subjects.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with adverse events (AEs), serious adverse events (SAEs) and AEs leading to study drug discontinuation

|  |   |
|--|---|
| End point title  | Number of subjects with adverse events (AEs), serious adverse events (SAEs) and AEs leading to study drug discontinuation |
| End point description:<br>AEs: any new untoward medical occurrences/worsening of pre-existing medical condition, whether or not related to study drug , SAE: any AE that resulted in death; was life threatening; resulted in persistent/significant disability/incapacity; resulted in/prolonged an existing in-patient hospitalization; was a congenital anomaly/birth defect; or was an overdose. Subjects who discontinued from the study due to AE were also recorded. This endpoint was assessed in safety analysis population which included all randomized subjectss with at least 1 post-baseline assessment. |   |
| End point type   | Secondary   |



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End point timeframe:  
Baseline through Week 96

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| <b>End point values</b>     | Group A, less than third percentile (Saizen) | Group A2, less than third percentile (No treatment) | Group B, more than third percentile (No treatment) |  |
|-----------------------------|--|---|--|--|
| Subject group type          | Reporting group                              | Reporting group                                     | Reporting group                                    |  |
| Number of subjects analysed | 8  | 4   | 10   |  |
| Units: subjects             |  |   |  |  |
| number (not applicable)     |  |   |  |  |
| AEs                         | 6  | 4   | 9  |  |
| SAEs                        | 0  | 0   | 0  |  |
| Discontinuation due to AEs  | 0  | 0   | 0  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs were collected on an ongoing basis from day of written informed consent. All new AEs were recorded until the post-treatment safety, on Day 30 post-drug administration.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |            |
|--------------------|------------|
| Dictionary version | MedDRA (U) |
|--------------------|------------|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Group A, less than third percentile (Saizen) |
|-----------------------|--|

Reporting group description:

Subjects with less than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received Saizen (recombinant human growth hormone, r-hGH) subcutaneously (s.c) at the daily dose of 0.035 milligram(mg)/kilogram(kg) for 2 years.

|                       |   |
|-----------------------|---|
| Reporting group title | Group A2, less than third percentile (No treatment) |
|-----------------------|---|

Reporting group description:

Subjects with less than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received no drug treatment for 2 years.

|                       |  |
|-----------------------|--|
| Reporting group title | Group B, more than third percentile (No treatment) |
|-----------------------|--|

Reporting group description:

Subjects with more than third percentile for height (according to the Tanner reference table) at the age of 4-6 years received no drug treatment for 2 years.

| Serious adverse events                            | Group A, less than third percentile (Saizen) | Group A2, less than third percentile (No treatment) | Group B, more than third percentile (No treatment) |
|---|--|---|--|
| Total subjects affected by serious adverse events |  |   |  |
| subjects affected / exposed                       | 0 / 8 (0.00%)                                | 0 / 4 (0.00%)                                       | 0 / 10 (0.00%)                                     |
| number of deaths (all causes)                     | 0  | 0   | 0  |
| number of deaths resulting from adverse events    |  |   |  |

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

| Non-serious adverse events                            | Group A, less than third percentile (Saizen) | Group A2, less than third percentile (No treatment) | Group B, more than third percentile (No treatment) |
|---|--|---|--|
| Total subjects affected by non-serious adverse events |  |   |  |
| subjects affected / exposed                           | 6 / 8 (75.00%)                               | 4 / 4 (100.00%)                                     | 9 / 10 (90.00%)                                    |
| General disorders and administration site conditions  |  |   |  |
| Cyst  |  |   |  |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0               |
| Pyrexia   |                |                |                 |
| subjects affected / exposed                     | 6 / 8 (75.00%) | 2 / 4 (50.00%) | 4 / 10 (40.00%) |
| occurrences (all)                               | 15             | 6              | 6               |
| Immune system disorders                         |                |                |                 |
| Milk allergy                                    |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Respiratory, thoracic and mediastinal disorders |                |                |                 |
| Adenoidal hypertrophy                           |                |                |                 |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0               |
| Cough   |                |                |                 |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)                               | 4              | 0              | 2               |
| Oropharyngeal pain                              |                |                |                 |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0               |
| Rhinitis allergic                               |                |                |                 |
| subjects affected / exposed                     | 2 / 8 (25.00%) | 0 / 4 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 2              | 0              | 0               |
| Investigations                                  |                |                |                 |
| Blood alkaline phosphatase increased            |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Blood cholesterol increased                     |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Lipoprotein (a) abnormal                        |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Blood insulin decreased                         |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0              | 0              | 1               |
| Injury, poisoning and procedural complications  |                |                |                 |

|   |                     |                     |                      |
|---|---------------------|---------------------|----------------------|
| Road traffic accident<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 8 (12.50%)<br>1 | 0 / 4 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Blood and lymphatic system disorders<br>Iron deficiency anaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 8 (12.50%)<br>1 | 0 / 4 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Microcytic anaemia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 8 (12.50%)<br>2 | 0 / 4 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Eye disorders<br>Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 8 (12.50%)<br>1 | 0 / 4 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 8 (12.50%)<br>1 | 0 / 4 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Stomatitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 8 (12.50%)<br>1 | 0 / 4 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 1 / 4 (25.00%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 10 (10.00%)<br>2 |
| Skin and subcutaneous tissue disorders<br>Alopecia  |                     |                     |                      |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                        | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                  | 1              | 0              | 0               |
| Acute generalised exanthematous<br>pustulosis      |                |                |                 |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                  | 0              | 0              | 1               |
| Pruritus   |                |                |                 |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                  | 0              | 0              | 1               |
| Renal and urinary disorders                        |                |                |                 |
| Proteinuria  |                |                |                 |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                  | 0              | 0              | 2               |
| Musculoskeletal and connective tissue<br>disorders |                |                |                 |
| Neck pain  |                |                |                 |
| subjects affected / exposed                        | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                  | 1              | 0              | 0               |
| Infections and infestations                        |                |                |                 |
| Ear infection                                      |                |                |                 |
| subjects affected / exposed                        | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                  | 3              | 0              | 1               |
| Bronchitis   |                |                |                 |
| subjects affected / exposed                        | 2 / 8 (25.00%) | 1 / 4 (25.00%) | 3 / 10 (30.00%) |
| occurrences (all)                                  | 2              | 1              | 4               |
| Pharyngitis  |                |                |                 |
| subjects affected / exposed                        | 1 / 8 (12.50%) | 2 / 4 (50.00%) | 2 / 10 (20.00%) |
| occurrences (all)                                  | 4              | 2              | 2               |
| Rhinitis   |                |                |                 |
| subjects affected / exposed                        | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                  | 1              | 0              | 1               |
| Gastroenteritis                                    |                |                |                 |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                                  | 0              | 2              | 0               |
| Tonsillitis  |                |                |                 |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 1 / 10 (10.00%) |
| occurrences (all)                                  | 0              | 2              | 1               |
| Varicella  |                |                |                 |

|                                    |               |                |                 |
|------------------------------------|---------------|----------------|-----------------|
| subjects affected / exposed        | 0 / 8 (0.00%) | 2 / 4 (50.00%) | 2 / 10 (20.00%) |
| occurrences (all)                  | 0             | 2              | 2               |
| Enterocolitis infectious           |               |                |                 |
| subjects affected / exposed        | 0 / 8 (0.00%) | 0 / 4 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 0             | 0              | 1               |
| Influenza                          |               |                |                 |
| subjects affected / exposed        | 0 / 8 (0.00%) | 0 / 4 (0.00%)  | 3 / 10 (30.00%) |
| occurrences (all)                  | 0             | 0              | 3               |
| Laryngitis                         |               |                |                 |
| subjects affected / exposed        | 0 / 8 (0.00%) | 0 / 4 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 0             | 0              | 1               |
| Metabolism and nutrition disorders |               |                |                 |
| Hypercholesterolaemia              |               |                |                 |
| subjects affected / exposed        | 0 / 8 (0.00%) | 0 / 4 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 0             | 0              | 2               |

## 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

|   |
|---|
| The primary and secondary efficacy objectives were not met because of poor subject enrollment and no quality RNA samples obtained to evaluate (RNA degradation in nearly all of the blood samples). |
|---|

Notes: