



## Clinical trial results:

### Translational therapy in patients with Osteogenesis imperfecta - a pilot trial on treatment with the RANKL-antibody Denosumab

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2012-002887-29  |
| Trial protocol           | DE              |
| Global end of trial date | 26 January 2015 |

#### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)                                    |
| This version publication date     | 06 January 2021                                 |
| First version publication date    | 06 January 2021                                 |
| Summary attachment (see zip file) | OI-AK_summary (OI-AK_Ergebnisbericht_EUCTR.pdf) |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | Uni-Koeln-1574 |
|-----------------------|----------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | University of Cologne  |
| Sponsor organisation address | Albertus-Magnus-Platz, Cologne, Germany, 50923   |
| Public contact               | Klinisches Studienzentrum Pädiatrie, Children's Hospital of the University of Cologne, +49 2214784361, joerg.semmler@uk-koeln.de |
| Scientific contact           | Klinisches Studienzentrum Pädiatrie, Children's Hospital of the University of Cologne, +49 2214784361, joerg.semmler@uk-koeln.de |

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                       | 26 January 2015 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 26 January 2015 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

Pilot study to assess the safety and efficacy of a therapy with the RANKL-antibody Denosumab in children 5-10 years of age with mutation in COL1A1 or COL1A2 leading to a defect in collagen production (Osteogenesis imperfecta). Efficacy will be assessed by DXA measurements at the lumbar spine (BMD).

Protection of trial subjects:

The trial was conducted according to Good Clinical Practice guidelines, the applicable local laws, and in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

The competent authorities approved the trial as required by national regulations.

Regulatory authorities were notified of the trial and amendments as required by national regulations.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 01 January 2013 |
| 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 | Germany: 10 |
| Worldwide total number of subjects   | 10          |
| EEA total number of subjects         | 10          |

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)                     | 10 |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |

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

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

11 patients were screened into the trial (The screening period was defined as week -12 until week 0 (baseline). Patients who met all in- and exclusion criteria were enrolled (n=10) and received the investigational medicinal product

### Period 1

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

### Arms

|  |                        |
|--|------------------------|
| Arm title                              | Denosumab              |
| Arm description: -                     |                        |
| Arm type                               | Experimental           |
| Investigational medicinal product name | Denosumab              |
| Investigational medicinal product code |                        |
| Other name                             | Prolia                 |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

1mg/kg body weight in 3-monthly intervals

| Number of subjects in period 1 | Denosumab |
|--------------------------------|-----------|
| Started                        | 10        |
| Completed                      | 10        |

## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

| Reporting group values  | Overall trial      | Total |  |
|---|--------------------|-------|--|
| Number of subjects  | 10                 | 10    |  |
| Age categorical<br>Units: Subjects  |                    |       |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>full range (min-max) | 7<br>5.02 to 10.96 | -     |  |
| Gender categorical<br>Units: Subjects                                     |                    |       |  |
| Female  | 3                  | 3     |  |
| Male  | 7                  | 7     |  |

## End points

### End points reporting groups

|                                   |                      |
|-----------------------------------|----------------------|
| Reporting group title             | Denosumab            |
| Reporting group description:      | -                    |
| Subject analysis set title        | baseline-BMD (g/cm2) |
| Subject analysis set type         | Intention-to-treat   |
| Subject analysis set description: | xxx                  |
| Subject analysis set title        | 48h-BMD (g/cm2)      |
| Subject analysis set type         | Intention-to-treat   |
| Subject analysis set description: | xxx                  |

### Primary: Changes in bone mineral density (BMD)

|                        |  |
|------------------------|--|
| End point title        | Changes in bone mineral density (BMD)  |
| End point description: | Changes of bone mineral density (BMD [g/cm2]) in study week 48 of the lumbar vertebrae L2-L4 after 36 weeks of treatment with denosumab compared to baseline |
| End point type         | Primary  |
| End point timeframe:   | 48 weeks   |

| End point values                          | Denosumab          | baseline-BMD (g/cm2)      | 48h-BMD (g/cm2)           |  |
|---|--------------------|---------------------------|---------------------------|--|
| Subject group type                        | Reporting group    | Subject analysis set      | Subject analysis set      |  |
| Number of subjects analysed               | 10                 | 10                        | 10                        |  |
| Units: g/cm <sup>2</sup>                  |                    |                           |                           |  |
| arithmetic mean (confidence interval 95%) | 0.1 (0.06 to 0.15) | 0.5070 (0.3912 to 0.6228) | 0.6118 (0.4696 to 0.7540) |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | xx                                     |
| Statistical analysis description:       | Add text from CSR                      |
| Comparison groups                       | 48h-BMD (g/cm2) v baseline-BMD (g/cm2) |
| Number of subjects included in analysis | 20                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other <sup>[1]</sup>                   |
| P-value                                 | < 0.05 <sup>[2]</sup>                  |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Mean difference (final values)         |
| Point estimate                          | 96                                     |

|                      |                    |
|----------------------|--------------------|
| Confidence interval  |                    |
| level                | 95 %               |
| sides                | 2-sided            |
| lower limit          | 90                 |
| upper limit          | 99                 |
| Variability estimate | Standard deviation |
| Dispersion value     | 1                  |

Notes:

[1] - not mandatory

[2] - xx

### Primary: Changes in bone mineral density (BMD): Z-score

|   |   |
|---|---|
| End point title   | Changes in bone mineral density (BMD): Z-score <sup>[3]</sup> |
| End point description:<br>BMD lumbar vertebrae L2-L4 Z-score. Z-score: Age-dependent standard deviation |   |
| End point type  | Primary   |
| End point timeframe:<br>48 weeks after baseline   |   |

Notes:

[3] - 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: For the statistical analysis of the primary endpoint, please refer to the attached summary report.

|   |                       |  |  |  |
|---|-----------------------|--|--|--|
| <b>End point values</b>                   | Denosumab             |  |  |  |
| Subject group type                        | Reporting group       |  |  |  |
| Number of subjects analysed               | 10                    |  |  |  |
| Units: standard deviation score           |                       |  |  |  |
| arithmetic mean (confidence interval 95%) | 0.96 (0.597 to 1.323) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Osteoclastic activity-DPD

|   |                           |
|---|---------------------------|
| End point title   | Osteoclastic activity-DPD |
| End point description:<br>DPD: Deoxypyridinolin             |                           |
| End point type  | Secondary                 |
| End point timeframe:<br>Week 0 (baseline) and week 48 weeks |                           |

| End point values                     | Denosumab          |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| Subject group type                   | Reporting group    |  |  |  |
| Number of subjects analysed          | 10                 |  |  |  |
| Units: µg/g                          |                    |  |  |  |
| arithmetic mean (standard deviation) |                    |  |  |  |
| baseline                             | 189.700 (± 71.294) |  |  |  |
| week 48                              | 237.600 (± 95.539) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mobility of patients-Walking

|                               |                              |
|-------------------------------|------------------------------|
| End point title               | Mobility of patients-Walking |
| End point description:        |                              |
| Mobility of patients: Walking | 1 and 6 minute walking test  |
| End point type                | Secondary                    |
| End point timeframe:          |                              |
| change                        | from baseline to 48h         |

| End point values                          | Denosumab               |  |  |  |
|---|-------------------------|--|--|--|
| Subject group type                        | Reporting group         |  |  |  |
| Number of subjects analysed               | 7 <sup>[4]</sup>        |  |  |  |
| Units: meters                             |                         |  |  |  |
| arithmetic mean (confidence interval 95%) |                         |  |  |  |
| 1 minute walking                          | 11 (-3.633 to 25.63)    |  |  |  |
| 6 minutes walking                         | 48.7 (18.561 to 78.773) |  |  |  |

Notes:

[4] - 7 for 1 minute and 6 for 6 minutes

## Statistical analyses

No statistical analyses for this end point

## Secondary: Morphometry of spine-anterior-posterior index

|   |   |
|---|---|
| End point title                               | Morphometry of spine-anterior-posterior index |
| End point description:                        |   |
| Morphometry of spine anterior-posterior index |   |
| End point type                                | Secondary                                     |
| End point timeframe:                          |   |
| baseline and 48 weeks                         |   |

|                                      |                       |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| <b>End point values</b>              | Denosumab             |  |  |  |
| Subject group type                   | Reporting group       |  |  |  |
| Number of subjects analysed          | 8                     |  |  |  |
| Units: (1-ah/ph)*100                 |                       |  |  |  |
| arithmetic mean (standard deviation) |                       |  |  |  |
| Baseline                             | -16.18 ( $\pm$ 41.46) |  |  |  |
| Week 48                              | -4.475 ( $\pm$ 14.67) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Morphometry of spine-concavity index

|                        |                                      |
|------------------------|--------------------------------------|
| End point title        | Morphometry of spine-concavity index |
| End point description: | Morphometry of spine-concavity index |
| End point type         | Secondary                            |
| End point timeframe:   | baseline and week 48                 |

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| <b>End point values</b>              | Denosumab            |  |  |  |
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 8                    |  |  |  |
| Units: (1-mh/ah)*100                 |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Baseline                             | 5.436 ( $\pm$ 25.7)  |  |  |  |
| Week 48                              | 7.332 ( $\pm$ 23.96) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mobility of patients-GMFM88

|                        |                                    |
|------------------------|------------------------------------|
| End point title        | Mobility of patients-GMFM88        |
| End point description: | GMFM= Gross Motor Function Measure |
| End point type         | Secondary                          |

End point timeframe:  
changes from baseline to 48 hours

|   |                        |  |  |  |
|---|------------------------|--|--|--|
| <b>End point values</b>                   | Denosumab              |  |  |  |
| Subject group type                        | Reporting group        |  |  |  |
| Number of subjects analysed               | 9                      |  |  |  |
| Units: percent                            |                        |  |  |  |
| arithmetic mean (confidence interval 95%) | 2.722 (0.8253 to 6.27) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Changes of bone mineral density (BMD)-total without head

|  |  |
|--|--|
| End point title  | Changes of bone mineral density (BMD)-total without head |
| End point description:   |  |
| End point type   | Secondary  |
| End point timeframe:<br>change in value between week 48 and baseline |  |

|   |                          |  |  |  |
|---|--------------------------|--|--|--|
| <b>End point values</b>                   | Denosumab                |  |  |  |
| Subject group type                        | Reporting group          |  |  |  |
| Number of subjects analysed               | 9                        |  |  |  |
| Units: g/cm <sup>2</sup>                  |                          |  |  |  |
| arithmetic mean (confidence interval 95%) | 0.049 (-0.0005 to 0.099) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Changes of bone mineral density (BMD)-total without head

|   |  |
|---|--|
| End point title   | Changes of bone mineral density (BMD)-total without head |
| End point description:  |  |
| End point type  | Secondary  |
| End point timeframe:<br>change in value 48 weeks after baseline |  |

|   |                           |  |  |  |
|---|---------------------------|--|--|--|
| <b>End point values</b>                   | Denosumab                 |  |  |  |
| Subject group type                        | Reporting group           |  |  |  |
| Number of subjects analysed               | 9                         |  |  |  |
| Units: Z-score                            |                           |  |  |  |
| arithmetic mean (confidence interval 95%) | 0.566 (0.30738 to 0.8259) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: BMC total body without head

|   |                             |
|---|-----------------------------|
| End point title                         | BMC total body without head |
| End point description:                  |                             |
| BMC: bone mineral content               |                             |
| End point type                          | Secondary                   |
| End point timeframe:                    |                             |
| change in value 48 weeks after baseline |                             |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| <b>End point values</b>                   | Denosumab       |  |  |  |
| Subject group type                        | Reporting group |  |  |  |
| Number of subjects analysed               | 10              |  |  |  |
| Units: gram(s)                            |                 |  |  |  |
| arithmetic mean (confidence interval 95%) | 85 (36 to 134)  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Osteoclastic activity-Calcium

|                                |                               |
|--------------------------------|-------------------------------|
| End point title                | Osteoclastic activity-Calcium |
| End point description:         |                               |
| End point type                 | Secondary                     |
| End point timeframe:           |                               |
| baseline (week 0) and 48 weeks |                               |

|                                      |                 |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| <b>End point values</b>              | Denosumab       |  |  |  |
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 10              |  |  |  |
| Units: mmol/l                        |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| baseline                             | 2.440 (± 0.080) |  |  |  |
| week 48                              | 2.568 (± 0.124) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events were reported from inclusion of patients into the study (signature of informed consent).

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

|                       |           |
|-----------------------|-----------|
| Reporting group title | Denosumab |
|-----------------------|-----------|

Reporting group description: -

| Serious adverse events                            | Denosumab       |  |  |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events |                 |  |  |
| subjects affected / exposed                       | 1 / 10 (10.00%) |  |  |
| number of deaths (all causes)                     | 0               |  |  |
| number of deaths resulting from adverse events    | 0               |  |  |
| Surgical and medical procedures                   |                 |  |  |
| Interne Fixatur einer Fraktur                     |                 |  |  |
| subjects affected / exposed                       | 1 / 10 (10.00%) |  |  |
| occurrences causally related to treatment / all   | 0 / 2           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |

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

| Non-serious adverse events                            | Denosumab   |  |  |
|---|---|--|--|
| Total subjects affected by non-serious adverse events |   |  |  |
| subjects affected / exposed                           | 10 / 10 (100.00%)                                 |  |  |
| Investigations  |   |  |  |
| Kalzium im Blut erniedrigt                            | Additional description: Calcium ionised decreased |  |  |
| subjects affected / exposed                           | 1 / 10 (10.00%)                                   |  |  |
| occurrences (all)                                     | 2   |  |  |
| Injury, poisoning and procedural complications        |   |  |  |
| Fraktur des Schluesselbeins                           | Additional description: Clavicle fracture         |  |  |
| subjects affected / exposed                           | 1 / 10 (10.00%)                                   |  |  |
| occurrences (all)                                     | 2   |  |  |
| Obeschenkelfraktur                                    |   |  |  |

|   |  |  |  |
|---|--|--|--|
| subjects affected / exposed<br>occurrences (all)        | 3 / 10 (30.00%)<br>4                   |  |  |
| Sturz   | Additional description: fall           |  |  |
| subjects affected / exposed<br>occurrences (all)        | 1 / 10 (10.00%)<br>1                   |  |  |
| Tibiafraktur  | Additional description: Tibia fracture |  |  |
| subjects affected / exposed<br>occurrences (all)        | 1 / 10 (10.00%)<br>1                   |  |  |
| Surgical and medical procedures                         |  |  |  |
| Operation am Penis                                      |  |  |  |
| subjects affected / exposed<br>occurrences (all)        | 1 / 10 (10.00%)<br>1                   |  |  |
| Husten  |  |  |  |
| subjects affected / exposed<br>occurrences (all)        | 2 / 10 (20.00%)<br>2                   |  |  |
| Nervous system disorders                                |  |  |  |
| Erniedrigter Muskeltonus                                |  |  |  |
| subjects affected / exposed<br>occurrences (all)        | 1 / 10 (10.00%)<br>1                   |  |  |
| General disorders and administration<br>site conditions |  |  |  |
| Fieber  |  |  |  |
| subjects affected / exposed<br>occurrences (all)        | 4 / 10 (40.00%)<br>4                   |  |  |
| Blood and lymphatic system disorders                    |  |  |  |
| Lymphadenopathie  |  |  |  |
| subjects affected / exposed<br>occurrences (all)        | 1 / 10 (10.00%)<br>1                   |  |  |
| Gastrointestinal disorders                              |  |  |  |
| Abdominalschmerz  |  |  |  |
| subjects affected / exposed<br>occurrences (all)        | 2 / 10 (20.00%)<br>2                   |  |  |
| Diarrhoe  |  |  |  |
| subjects affected / exposed<br>occurrences (all)        | 1 / 10 (10.00%)<br>1                   |  |  |
| Erbrechen   |  |  |  |

|  |   |  |  |
|--|---|--|--|
| subjects affected / exposed                        | 3 / 10 (30.00%)                         |  |  |
| occurrences (all)                                  | 5                                       |  |  |
| Funktionsstörung des<br>Gastrointestinaltrakts     |   |  |  |
| subjects affected / exposed                        | 1 / 10 (10.00%)                         |  |  |
| occurrences (all)                                  | 1                                       |  |  |
| Gaumenerkrankung                                   |   |  |  |
| subjects affected / exposed                        | 1 / 10 (10.00%)                         |  |  |
| occurrences (all)                                  | 1                                       |  |  |
| Respiratory, thoracic and mediastinal<br>disorders |   |  |  |
| Nasenverstopfung                                   |   |  |  |
| subjects affected / exposed                        | 2 / 10 (20.00%)                         |  |  |
| occurrences (all)                                  | 2                                       |  |  |
| Schmerzen im Oropharynx                            |   |  |  |
| subjects affected / exposed                        | 1 / 10 (10.00%)                         |  |  |
| occurrences (all)                                  | 1                                       |  |  |
| Symptom einer allergischen<br>Erkrankung           |   |  |  |
| subjects affected / exposed                        | 1 / 10 (10.00%)                         |  |  |
| occurrences (all)                                  | 1                                       |  |  |
| Skin and subcutaneous tissue disorders             |   |  |  |
| Ausschlag mit Juckreiz                             |   |  |  |
| subjects affected / exposed                        | 1 / 10 (10.00%)                         |  |  |
| occurrences (all)                                  | 1                                       |  |  |
| Musculoskeletal and connective tissue<br>disorders |   |  |  |
| Arthralgie   |   |  |  |
| subjects affected / exposed                        | 3 / 10 (30.00%)                         |  |  |
| occurrences (all)                                  | 7                                       |  |  |
| Brustschmerzen die<br>Skelettmuskulatur betreffend |   |  |  |
| subjects affected / exposed                        | 1 / 10 (10.00%)                         |  |  |
| occurrences (all)                                  | 1                                       |  |  |
| Gelenkschwellung                                   |   |  |  |
| subjects affected / exposed                        | 1 / 10 (10.00%)                         |  |  |
| occurrences (all)                                  | 1                                       |  |  |
| Gliederbeschwerden                                 | Additional description: Limb discomfort |  |  |

|                               |                                       |  |  |
|-------------------------------|---------------------------------------|--|--|
| subjects affected / exposed   | 1 / 10 (10.00%)                       |  |  |
| occurrences (all)             | 1                                     |  |  |
| Muskelspasmen                 | Additional description: Muscle spasms |  |  |
| subjects affected / exposed   | 1 / 10 (10.00%)                       |  |  |
| occurrences (all)             | 1                                     |  |  |
| Rückenschmerzen               | Additional description: Back pain     |  |  |
| subjects affected / exposed   | 1 / 10 (10.00%)                       |  |  |
| occurrences (all)             | 1                                     |  |  |
| Schmerz in einer Extremität   |                                       |  |  |
| subjects affected / exposed   | 3 / 10 (30.00%)                       |  |  |
| occurrences (all)             | 4                                     |  |  |
| Wachstumsschmerzen            | Additional description: Growing pains |  |  |
| subjects affected / exposed   | 1 / 10 (10.00%)                       |  |  |
| occurrences (all)             | 1                                     |  |  |
| Infections and infestations   |                                       |  |  |
| Gastroenteritis               |                                       |  |  |
| subjects affected / exposed   | 1 / 10 (10.00%)                       |  |  |
| occurrences (all)             | 1                                     |  |  |
| Hand-Fuß-Mund Krankheit       |                                       |  |  |
| subjects affected / exposed   | 1 / 10 (10.00%)                       |  |  |
| occurrences (all)             | 1                                     |  |  |
| Infektion                     |                                       |  |  |
| subjects affected / exposed   | 2 / 10 (20.00%)                       |  |  |
| occurrences (all)             | 2                                     |  |  |
| Infektion der oberen Atemwege |                                       |  |  |
| subjects affected / exposed   | 3 / 10 (30.00%)                       |  |  |
| occurrences (all)             | 5                                     |  |  |
| Nasopharyngitis               |                                       |  |  |
| subjects affected / exposed   | 2 / 10 (20.00%)                       |  |  |
| occurrences (all)             | 3                                     |  |  |
| Streptokokken-Infektion       |                                       |  |  |
| subjects affected / exposed   | 1 / 10 (10.00%)                       |  |  |
| occurrences (all)             | 2                                     |  |  |
| Virusinfektion                |                                       |  |  |
| subjects affected / exposed   | 1 / 10 (10.00%)                       |  |  |
| occurrences (all)             | 1                                     |  |  |

|                                    |  |  |  |
|------------------------------------|--|--|--|
| Metabolism and nutrition disorders |  |  |  |
| Appetit vermindert                 | Additional description: Decreased appetite |  |  |
| subjects affected / exposed        | 1 / 10 (10.00%)                            |  |  |
| occurrences (all)                  | 1  |  |  |

## 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