



Clinical trial results: Effect of Teriparatide on Femoral Neck Fracture Healing Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2010-021395-28 |
| Trial protocol | SE ES LV FI NO LT EE DK |
| Global end of trial date | 04 December 2013 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 04 July 2016 |
| First version publication date | 02 August 2015 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | B3D-MC-GHDN |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01473589 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Alias: B3D-MC-GHDN, Trial Number: 13467 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLilly, |
| Scientific contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559, |

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 | 04 December 2013 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 December 2013 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of 6 months of treatment with teriparatide 20 microgram(μ g)/day versus placebo on the proportion of men and postmenopausal women 50 years of age with successful fracture healing 24 months after internal fixation of a low trauma femoral neck fracture

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 February 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Denmark: 2 |
| Country: Number of subjects enrolled | Lithuania: 4 |
| Country: Number of subjects enrolled | United States: 2 |
| Country: Number of subjects enrolled | Taiwan: 19 |
| Country: Number of subjects enrolled | Israel: 7 |
| Country: Number of subjects enrolled | India: 3 |
| Country: Number of subjects enrolled | Canada: 4 |
| Country: Number of subjects enrolled | Australia: 1 |
| Country: Number of subjects enrolled | Japan: 29 |
| Country: Number of subjects enrolled | New Zealand: 12 |
| Country: Number of subjects enrolled | Korea, Republic of: 18 |
| Country: Number of subjects enrolled | Spain: 15 |
| Country: Number of subjects enrolled | Latvia: 5 |
| Country: Number of subjects enrolled | Sweden: 1 |
| Worldwide total number of subjects | 122 |
| EEA total number of subjects | 27 |

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) | 44 |
| From 65 to 84 years | 58 |
| 85 years and over | 20 |

Subject disposition

Recruitment

Recruitment details:

No text entered.

Pre-assignment

Screening details:

No text entered.

Period 1

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

Arms

| | |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Teriparatide |

Arm description:

Teriparatide 20 micrograms (µg) administered once-daily by subcutaneous (SC) injection for 6 months. Participants received calcium and vitamin D supplements.

Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.

| | |
|--|---------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Teriparatide |
| Investigational medicinal product code | |
| Other name | Forteo, Forsteo, LY333334 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Teriparatide 20 micrograms (µg) administered once-daily by subcutaneous (SC) injection for 6 months. Participants received calcium and vitamin D supplements.

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

Dosage and administration details:

The supplement dose for calcium should be up to approximately 1000 milligram (mg)/day elemental calcium starting as soon as possible after screening and continuing through 12 months.

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

Dosage and administration details:

During screening, approximately 1000 International Unit (IU)/day vitamin D. The dose of vitamin D may then be increased at the discretion of the investigator.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Placebo administered once-daily by SC injection for 6 months. Participants received calcium and vitamin D supplements.

Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.

| | |
|--|------------------|
| Arm type | Placebo |
| Investigational medicinal product name | placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo administered once-daily by SC injection for 6 months. Participants received calcium and vitamin D supplements.

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

Dosage and administration details:

During screening, approximately 1000 IU/day vitamin D. The dose of vitamin D may then be increased at the discretion of the investigator.

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

Dosage and administration details:

The supplement dose for calcium should be up to approximately 1000 mg/day elemental calcium starting as soon as possible after screening and continuing through 12 months.

| Number of subjects in period 1 | Teriparatide | Placebo |
|--|--------------|---------|
| Started | 60 | 62 |
| Received at Least 1 Dose of Study Drug | 60 | 61 |
| Completed 6 Months | 51 | 54 |
| Completed 12 Months | 49 | 48 |
| Completed | 49 | 46 |
| Not completed | 11 | 16 |
| Adverse event, serious fatal | 2 | - |
| Consent withdrawn by subject | 5 | 11 |
| Physician decision | - | 1 |
| Adverse event, non-fatal | 1 | 1 |
| Lost to follow-up | 2 | 2 |
| Protocol deviation | 1 | - |
| 'Entry criteria not met ' | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Teriparatide |
|-----------------------|--------------|

Reporting group description:

Teriparatide 20 micrograms (µg) administered once-daily by subcutaneous (SC) injection for 6 months. Participants received calcium and vitamin D supplements.

Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.

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

Reporting group description:

Placebo administered once-daily by SC injection for 6 months. Participants received calcium and vitamin D supplements.

Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.

| Reporting group values | Teriparatide | Placebo | Total |
|------------------------|--------------|---------|-------|
| Number of subjects | 60 | 62 | 122 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|----------|----------|---|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 68.49 | 70.96 | |
| standard deviation | ± 11.321 | ± 12.023 | - |

| | | | |
|--------------------|----|----|----|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 43 | 44 | 87 |
| Male | 17 | 17 | 34 |
| Not recorded | 0 | 1 | 1 |

| | | | |
|---------------------|--|--|--|
| Surgical screw type | | | |
|---------------------|--|--|--|

Surgical screws used in initial surgery to repair femur neck hip fracture.

| | | | |
|--------------------|----|----|-----|
| Units: Subjects | | | |
| Cancellous Screws | 54 | 53 | 107 |
| Sliding Hip Screws | 6 | 8 | 14 |
| Not recorded | 0 | 1 | 1 |

| | | | |
|---------------------|--|--|--|
| Ethnicity (NIH/OMB) | | | |
|---------------------|--|--|--|

Full Analysis Set (FAS): All randomized participants who received at least 1 dose of study drug.

| | | | |
|-------------------------|----|----|----|
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 1 | 1 |
| Not Hispanic or Latino | 26 | 27 | 53 |
| Unknown or Not Reported | 34 | 33 | 67 |
| Not recorded | 0 | 1 | 1 |

| | | | |
|-----------------|--|--|--|
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |

| | | | |
|---|----|----|----|
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 35 | 34 | 69 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 25 | 27 | 52 |
| More than one race | 0 | 0 | 0 |

| | | | |
|-------------------------|----|----|----|
| Unknown or Not Reported | 0 | 0 | 0 |
| Not recorded | 0 | 1 | 1 |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| United States | 1 | 1 | 2 |
| Spain | 7 | 8 | 15 |
| Taiwan | 10 | 9 | 19 |
| Lithuania | 2 | 2 | 4 |
| Israel | 3 | 4 | 7 |
| India | 2 | 1 | 3 |
| Canada | 3 | 1 | 4 |
| Denmark | 1 | 1 | 2 |
| Australia | 1 | 0 | 1 |
| Latvia | 2 | 3 | 5 |
| Japan | 14 | 15 | 29 |
| New Zealand | 5 | 7 | 12 |
| Korea, Republic of | 9 | 9 | 18 |
| Sweden | 0 | 1 | 1 |

End points

End points reporting groups

| | |
|---|--------------|
| Reporting group title | Teriparatide |
| Reporting group description: Teriparatide 20 micrograms (µg) administered once-daily by subcutaneous (SC) injection for 6 months. Participants received calcium and vitamin D supplements. Baseline characteristics values based on number of subjects that received at least 1 dose of study drug. | |
| Reporting group title | Placebo |
| Reporting group description: Placebo administered once-daily by SC injection for 6 months. Participants received calcium and vitamin D supplements. Baseline characteristics values based on number of subjects that received at least 1 dose of study drug. | |

Primary: Percentage of Participants With No Revision Surgery at 12 Months After Internal Fixation of a Low-Trauma Femoral Neck Fracture

| | |
|---|--|
| End point title | Percentage of Participants With No Revision Surgery at 12 Months After Internal Fixation of a Low-Trauma Femoral Neck Fracture |
| End point description: Revision surgery (re-operation) was defined as any additional surgical intervention performed or recommended at the site of the index procedure, except those that were planned at the time of the index procedure. | |
| End point type | Primary |
| End point timeframe: 12 months | |

| End point values | Teriparatide | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 60 | 61 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 90%) | 87 (77 to 93) | 86 (76 to 92) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 for End Point 1 |
| Comparison groups | Teriparatide v Placebo |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.743 ^[1] |
| Method | K-M with Greenwood SE |
| Parameter estimate | Difference in proportion |
| Point estimate | -0.04 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 90 % |
| sides | 1-sided |
| lower limit | -0.14 |

Notes:

[1] - P-value is based on Z test statistic with Greenwood estimator for standard errors (SE) to compare two Kaplan-Meier (K-M) estimates at 12 month.

Secondary: Percentage of Participants With Radiographic Evidence of Healing

| | |
|-----------------|--|
| End point title | Percentage of Participants With Radiographic Evidence of Healing |
|-----------------|--|

End point description:

The signs of femoral neck fracture healing included disappearance of the fracture line on radiographs. If a participant had radiographic evidence of healing at the 12-month visit, that participant was considered to have radiographic evidence of healing.

Percentage was calculated as: (number of participants with radiographic evidence of healing / total number of participants analyzed) * 100.

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

End point timeframe:

Randomization, 12 months

| End point values | Teriparatide | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 60 | 61 | | |
| Units: percentage of participants | 78 | 79 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Pain Control During Ambulation

| | |
|-----------------|--|
| End point title | Percentage of Participants With Pain Control During Ambulation |
|-----------------|--|

End point description:

The worst pain numeric rating scale (NRS) was used to assess the impact of pain on a participant's life. NRS Item 3 assessed the worst musculoskeletal pain severity during the walking test. Pain was measured by an 11-point Likert scale. The following cut-points were used to categorize the NRS responses: 0 = no pain, 1 to 4 = mild pain, 5 to 6 = moderate pain, and 7 to 10 = severe pain. Participants with an NRS score of <7 were categorized as having no severe fracture-site pain with ambulation and no worsening of NRS scores >2 from baseline. Percentage was calculated as: (Number of participants with pain control during ambulation / total number of participants) * 100.

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

End point timeframe:

12 months

| End point values | Teriparatide | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 49 | | |
| Units: percentage of participants | 91 | 90 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Without Severe Fracture-Site Pain During 24 Hours Prior to Visit

| | |
|-----------------|---|
| End point title | Percentage of Participants Without Severe Fracture-Site Pain During 24 Hours Prior to Visit |
|-----------------|---|

End point description:

The worst pain NRS was used to assess the impact of pain on a participant's life. Fracture-site pain severity was assessed for pain in the 24 hours preceding a visit. Pain was measured by an 11-point Likert scale. Participants with an NRS score of <7 in the 24 hours preceding a visit and no worsening of NRS >2 from baseline were categorized as having no severe fracture-site pain. Percentage was calculated as: (number of participants with pain control during 24 hours preceding a visit / total number of participants) * 100.

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

End point timeframe:

12 months

| End point values | Teriparatide | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 51 | | |
| Units: percentage of participants | 88 | 82 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Without Severe Fracture-Site Pain During Weight Bearing

| | |
|-----------------|--|
| End point title | Percentage of Participants Without Severe Fracture-Site Pain During Weight Bearing |
|-----------------|--|

End point description:

The worst pain NRS was used to assess the impact of pain on a participant's life. Fracture-site pain severity was assessed for pain on weight bearing. Pain was measured by an 11-point Likert scale. Participants with an NRS score of <7 during weight bearing and no worsening of NRS >2 from baseline were categorized as having no severe fracture-site pain. Percentage was calculated as: (number of participants with pain control during weight bearing / total number of participants) * 100.

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

End point timeframe:

12 months

| End point values | Teriparatide | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 50 | | |
| Units: percentage of participants | 89 | 88 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Functional Evidence of Healing

| | |
|-----------------|--|
| End point title | Percentage of Participants With Functional Evidence of Healing |
|-----------------|--|

End point description:

Functional healing was defined as ability to walk with a gait speed ≥ 0.05 meters/second (m/s) with a change from baseline ≥ -0.1 m/s. The walking test involved having the participant walk a distance of 7 meters (m) at a self-selected, comfortable pace. A 4-m portion of the test was timed to determine the participant's gait speed in m/s.

Percentage was calculated as: (number of participants with functional evidence of healing / total number of participants analyzed) * 100.

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

End point timeframe:

12 Months

| End point values | Teriparatide | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 48 | 50 | | |
| Units: percentage of participants | 85 | 74 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Able to Ambulate

| | |
|-----------------|---|
| End point title | Percentage of Participants Able to Ambulate |
|-----------------|---|

End point description:

Ability to ambulate was defined as ambulatory with convalescent aid or without convalescent aid. Percentage was calculated as: (number of participants able to ambulate / number of total participants analyzed) * 100.

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

End point timeframe:

12 months

| End point values | Teriparatide | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 48 | 50 | | |
| Units: percentage of participants | 98 | 98 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Regain Their Prefracture Ambulatory Status

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Regain Their Prefracture Ambulatory Status |
|-----------------|---|

End point description:

Prefracture ambulatory status was defined as either ambulatory with or without a walking aid. A participant was considered to have regained their prefracture ambulatory status if the participant's postsurgery ambulatory status was returned to or was improved from their pre-surgery ambulatory status. Percentage was calculated as = (number of participants who regained their ambulatory status / total number analyzed) * 100.

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

End point timeframe:

12 months

| End point values | Teriparatide | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 58 | | |
| Units: percentage of participants | 73 | 57 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months in Worst Fracture-Site Pain

| | |
|-----------------|---|
| End point title | Mean Change From Baseline to 6 Months in Worst Fracture-Site Pain |
|-----------------|---|

End point description:

The worst pain NRS was used to assess the impact of pain on a participant's life. Participants with an NRS score of <7 were categorized as having no severe fracture-site pain. Least Squares (LS) means was calculated using analysis of covariance (ANCOVA) and adjusted for baseline, treatment group, region, fracture type, and fixation type.

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

End point timeframe:

Baseline, 6 Months

| End point values | Teriparatide | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 50 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| During ambulation | 0.2 (± 0.37) | 0.2 (± 0.36) | | |
| During 24 hours preceding visit | -0.3 (± 0.45) | -0.8 (± 0.42) | | |
| On weight bearing | 0.7 (± 0.39) | 0.8 (± 0.36) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months in Gait Speed

| | |
|-----------------|---|
| End point title | Mean Change From Baseline to 6 Months in Gait Speed |
|-----------------|---|

End point description:

The walking test involved having the participant walk a distance of 7 m at a self-selected, comfortable pace. A 4-m portion of the test was timed to determine the participant's gait speed in m/s. LS means was calculated using ANCOVA and adjusted for baseline, treatment group, region, fracture type, and fixation type.

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

End point timeframe:

Baseline, 6 Months

| End point values | Teriparatide | Placebo | | |
|-------------------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 47 | | |
| Units: m/s | | | | |
| least squares mean (standard error) | -0.672 (± 2.128) | 1.524 (± 2.018) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Revision Surgery

| | |
|-----------------|--------------------------|
| End point title | Time to Revision Surgery |
|-----------------|--------------------------|

End point description:

Time to revision surgery was defined as the time from initial hip fracture surgery to revision surgery, or recommendation for revision surgery if recommended but not performed. Time to revision surgery was censored at the date of the last contact.

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

End point timeframe:

Baseline, Revision surgery

| End point values | Teriparatide | Placebo | | |
|-------------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 60 | 59 | | |
| Units: days | | | | |
| median (full range (min-max)) | 358.5 (15 to 430) | 350 (12 to 412) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months on Short Form-12 (SF-12) Physical (PCS) and Mental Component Summary (MCS) Scores

| | |
|-----------------|---|
| End point title | Mean Change From Baseline to 6 Months on Short Form-12 (SF-12) Physical (PCS) and Mental Component Summary (MCS) Scores |
|-----------------|---|

End point description:

SF-12 is a self-reported questionnaire covering a mental component score (MCS) and a physical component score (PCS), each scoring from a 0 to 100 (worst to best) scale. LS mean was calculated using ANCOVA and adjusted for baseline, treatment group, region, fracture type, fixation type, visit, and visit-by-treatment interaction.

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

End point timeframe:

Baseline, 6 Months

| End point values | Teriparatide | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 58 | 59 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| PCS Month 6 (n = 49, 49) | -3.73 (± 1.2) | -4.75 (± 1.2) | | |
| MCS Month 6 (n = 49, 49) | -0.58 (± 2.1) | -0.49 (± 2.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months on Western Ontario McMaster Osteoarthritis Index (WOMAC)

| | |
|-----------------|--|
| End point title | Mean Change From Baseline to 6 Months on Western Ontario McMaster Osteoarthritis Index (WOMAC) |
|-----------------|--|

End point description:

WOMAC is: a self-reported questionnaire that consisted of 24 questions covering 3 health domains: Pain (5 items: during walking, using stairs, in bed, sitting or lying, and standing), Stiffness (2 items: after first waking and later in the day), and Physical Function. Each domain was scored by summing the individual items and transforming the scores into a 0 to 100 (best to worst) scale. LS mean was calculated using ANCOVA and adjusted for baseline, treatment group, region, fracture type, fixation type, visit, and visit-by-treatment interaction.

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

End point timeframe:

Baseline, 6 Months

| End point values | Teriparatide | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 58 | 59 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Physical Function Score - Month 6 (n=48, 51) | 12.9 (± 4.36) | 12.8 (± 4.25) | | |
| Pain Score - Month 6 (n = 51, 51) | 8.2 (± 3.76) | 10.3 (± 3.68) | | |
| Stiffness Score - Month 6 (n = 51, 51) | 13.1 (± 3.78) | 11.8 (± 3.75) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months on European Quality of Life Questionnaire (EQ-5D) Health State Score

| | |
|-----------------|--|
| End point title | Mean Change From Baseline to 6 Months on European Quality of Life Questionnaire (EQ-5D) Health State Score |
|-----------------|--|

End point description:

The EQ-5D is a 5-item, self-reported, generic, multidimensional, health-related, quality-of-life instrument with 5 items. Overall health state score was also self-reported using a visual analogue scale (VAS) marked on a scale scored from 0 (worse imaginable health state) to 100 (best imaginable health state). LS mean was calculated using ANCOVA and adjusted for baseline, treatment group, and region.

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

End point timeframe:

Baseline, 6 Months

| End point values | Teriparatide | Placebo | | |
|---|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 51 | | |
| Units: units on a scale | | | | |
| least squares mean (standard deviation) | 7.4 (\pm 4.02) | 7.6 (\pm 3.87) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

B3D-MC-GHDN

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Screening |
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Reporting group description: -

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| Reporting group title | Placebo Acute |
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Reporting group description: -

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| Reporting group title | Teriparatide 20 mcg Acute |
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Reporting group description: -

| | |
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| Reporting group title | Placebo Follow-up |
|-----------------------|-------------------|

Reporting group description: -

| | |
|-----------------------|-------------------------------|
| Reporting group title | Teriparatide 20 mcg Follow-up |
|-----------------------|-------------------------------|

Reporting group description: -

| Serious adverse events | Screening | Placebo Acute | Teriparatide 20 mcg Acute |
|---|-----------------|----------------|---------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 5 / 61 (8.20%) | 2 / 60 (3.33%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| transitional cell carcinoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| fall | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| femoral neck fracture alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| femur fracture alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| subdural haematoma alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| wound alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| bradyarrhythmia alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| supraventricular tachycardia alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| syncope | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| transient ischaemic attack | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| gastritis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| hepatitis toxic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| confusional state | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| haematuria | | | |
| alternative dictionary used: | | | |

| | | | |
|---|-----------------|----------------|----------------|
| MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| bursitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| fracture nonunion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| osteonecrosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| liver abscess | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pneumonia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Placebo Follow-up | Teriparatide 20 mcg Follow-up | |
|---|-------------------|-------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 2 / 49 (4.08%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| transitional cell carcinoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| fall | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| femoral neck fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| femur fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| subdural haematoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| wound | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| bradyarrhythmia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| supraventricular tachycardia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| syncope | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| transient ischaemic attack | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| gastritis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| hepatitis toxic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| confusional state | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| haematuria | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| bursitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| fracture nonunion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| osteonecrosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| liver abscess | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pneumonia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Screening | Placebo Acute | Teriparatide 20 mcg Acute |
|--|-------------------|------------------|---------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 39 / 122 (31.97%) | 34 / 61 (55.74%) | 31 / 60 (51.67%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| seborrhoeic keratosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| haematoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| hypertension | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| thrombosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Surgical and medical procedures | | | |
| cataract operation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| cholecystectomy | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| sebaceous cyst excision | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 2 / 61 (3.28%) | 2 / 60 (3.33%) |
| occurrences (all) | 1 | 2 | 2 |
| device breakage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| facial pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| gait disturbance | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| oedema peripheral | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 1 / 61 (1.64%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 1 | 1 |
| pyrexia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| sense of oppression | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| thirst | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| atrophic vulvovaginitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed ^[1] | 0 / 88 (0.00%) | 0 / 44 (0.00%) | 0 / 43 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| prostatitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed ^[2] | 0 / 34 (0.00%) | 0 / 17 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| vaginal haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed ^[3] | 0 / 88 (0.00%) | 1 / 44 (2.27%) | 0 / 43 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| bronchiectasis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| bronchitis chronic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| cough | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| oropharyngeal pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| respiratory failure | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| upper respiratory tract inflammation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| anxiety | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| behavioural and psychiatric symptoms of dementia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| depression | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| disorientation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| insomnia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 122 (1.64%) | 2 / 61 (3.28%) | 3 / 60 (5.00%) |
| occurrences (all) | 2 | 2 | 3 |
| mental status changes | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Investigations | | | |
| blood alkaline phosphatase increased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| blood pressure increased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| liver function test abnormal | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| weight decreased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 122 (1.64%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| bone contusion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| chest injury | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| contusion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 4 |
| excoriation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| fall | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| femur fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| humerus fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| incision site complication | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| joint injury | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| laceration | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| spinal compression fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| tooth fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| acute myocardial infarction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| aortic valve incompetence | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| arrhythmia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

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|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| palpitations | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| sinus tachycardia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| carotid arteriosclerosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| carpal tunnel syndrome | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| dizziness | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 3 / 61 (4.92%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 3 | 1 |
| headache | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 1 / 61 (1.64%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 1 | 1 |
| hypoesthesia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 2 / 60 (3.33%) |
| occurrences (all) | 0 | 0 | 2 |
| neuralgia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

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|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| paraesthesia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| parkinson's disease | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| presyncope | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| syncope | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| tremor | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| vascular dementia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| vertebral artery stenosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear and labyrinth disorders | | | |
| vertigo | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 1 / 60 (1.67%) 1 |
| Eye disorders | | | |
| cataract alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 1 / 61 (1.64%) 1 | 0 / 60 (0.00%) 0 |
| conjunctival haemorrhage alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 1 / 61 (1.64%) 1 | 0 / 60 (0.00%) 0 |
| conjunctivitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 1 / 61 (1.64%) 1 | 0 / 60 (0.00%) 0 |
| dacryostenosis acquired alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 1 / 60 (1.67%) 1 |
| glaucoma alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 1 / 61 (1.64%) 1 | 0 / 60 (0.00%) 0 |
| macular degeneration alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 1 / 61 (1.64%) 1 | 0 / 60 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| abdominal pain lower alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 1 / 60 (1.67%) 1 |
| abdominal pain upper alternative dictionary used: MedDRA 16.1 | | | |

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|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| constipation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 8 / 122 (6.56%) | 1 / 61 (1.64%) | 3 / 60 (5.00%) |
| occurrences (all) | 8 | 1 | 3 |
| dental caries | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 1 | 1 |
| diverticulum intestinal | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| faecal incontinence | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| faecaloma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 0 | 1 |
| gastritis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| gastritis atrophic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|-----------------|----------------|----------------|
| gastritis erosive | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| gastrointestinal disorder | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| gastrooesophageal reflux disease | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| gingival swelling | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| haemorrhoids | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| hiatus hernia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| nausea | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 122 (1.64%) | 0 / 61 (0.00%) | 2 / 60 (3.33%) |
| occurrences (all) | 2 | 0 | 2 |
| periodontal inflammation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| stomatitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

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|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| toothache | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| vomiting | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| cholelithiasis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| actinic keratosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| alopecia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| asteatosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| dermatitis contact | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| drug eruption | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

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|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| dyshidrotic eczema | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| erythema | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| hypertrophic scar | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| ingrowing nail | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| pruritus | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| rash | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 1 | 1 |
| skin ulcer | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| pollakiuria | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

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|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 1 / 61 (1.64%) 1 | 0 / 60 (0.00%) 0 |
| urinary retention alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 1 / 60 (1.67%) 1 |
| Endocrine disorders hyperparathyroidism secondary alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 1 / 122 (0.82%) 1 | 0 / 61 (0.00%) 0 | 0 / 60 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 1 / 122 (0.82%) 1 | 3 / 61 (4.92%) 3 | 3 / 60 (5.00%) 3 |
| back pain alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 6 / 61 (9.84%) 6 | 3 / 60 (5.00%) 3 |
| chondropathy alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 1 / 60 (1.67%) 1 |
| coccydynia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 0 / 60 (0.00%) 0 |
| flank pain alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 1 / 61 (1.64%) 1 | 0 / 60 (0.00%) 0 |
| muscular weakness alternative dictionary used: MedDRA 16.1 | | | |

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|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| musculoskeletal pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 122 (1.64%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 2 | 0 | 1 |
| myalgia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 1 / 61 (1.64%) | 2 / 60 (3.33%) |
| occurrences (all) | 1 | 1 | 2 |
| neck pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| osteoarthritis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 4 / 61 (6.56%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 4 | 1 |
| osteonecrosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| osteoporosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 3 / 60 (5.00%) |
| occurrences (all) | 0 | 1 | 3 |
| pain in extremity | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| spinal column stenosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|----------------------|---------------------|---------------------|
| spinal osteoarthritis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 1 / 61 (1.64%) 1 | 0 / 60 (0.00%) 0 |
| tenosynovitis stenosans alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 0 / 60 (0.00%) 0 |
| trigger finger alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 1 / 61 (1.64%) 1 | 1 / 60 (1.67%) 1 |
| Infections and infestations adenoiditis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 0 / 60 (0.00%) 0 |
| bronchitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 0 / 60 (0.00%) 0 |
| cellulitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 122 (0.00%) 0 | 0 / 61 (0.00%) 0 | 1 / 60 (1.67%) 1 |
| cervicitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed ^[4] occurrences (all) | 0 / 88 (0.00%) 0 | 0 / 44 (0.00%) 0 | 0 / 43 (0.00%) 0 |
| chronic hepatitis c alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 1 / 122 (0.82%) 1 | 0 / 61 (0.00%) 0 | 0 / 60 (0.00%) 0 |
| diverticulitis alternative dictionary used: MedDRA 16.1 | | | |

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|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ear infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| eye infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| gastroenteritis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| helicobacter infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| influenza | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| laryngitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| nail infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 3 / 61 (4.92%) | 4 / 60 (6.67%) |
| occurrences (all) | 0 | 4 | 5 |

| | | | |
|---|-----------------|----------------|----------------|
| oral candidiasis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| oral herpes | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| parotitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| pharyngitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| rhinitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| skin infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| tinea pedis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| tonsillitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 122 (0.82%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 2 / 61 (3.28%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| wound infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| wound infection staphylococcal | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 0 | 1 |
| folate deficiency | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| hypercalcaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 1 / 61 (1.64%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| hyperlipidaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| hypoglycaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 122 (0.82%) | 0 / 61 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 0 | 1 |
| malnutrition | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 122 (1.64%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| vitamin d deficiency | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 122 (2.46%) | 0 / 61 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |

| Non-serious adverse events | Placebo Follow-up | Teriparatide 20 mcg Follow-up | |
|---|-------------------|-------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 53 (33.96%) | 16 / 49 (32.65%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| seborrhoeic keratosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |
| haematoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| hypertension | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| thrombosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Surgical and medical procedures | | | |
| cataract operation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|--------------------------------|--------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>cholecystectomy</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>sebaceous cyst excision</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>General disorders and administration site conditions</p> <p>asthenia</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>device breakage</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>facial pain</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>gait disturbance</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>oedema peripheral</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>pain</p> <p>alternative dictionary used: MedDRA 16.1</p> | | | |

| | | | |
|--|---|---|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pyrexia</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>sense of oppression</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>thirst</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> <p>1 / 53 (1.89%)</p> <p>1</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>Reproductive system and breast disorders</p> <p>atrophic vulvovaginitis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed^[1]</p> <p>occurrences (all)</p> <p>prostatitis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed^[2]</p> <p>occurrences (all)</p> <p>vaginal haemorrhage</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed^[3]</p> <p>occurrences (all)</p> | <p>1 / 39 (2.56%)</p> <p>1</p> <p>0 / 14 (0.00%)</p> <p>0</p> <p>0 / 39 (0.00%)</p> <p>0</p> | <p>0 / 39 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 39 (0.00%)</p> <p>0</p> | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>bronchiectasis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>bronchitis chronic</p> <p>alternative dictionary used: MedDRA 16.1</p> | <p>1 / 53 (1.89%)</p> <p>2</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| cough | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| oropharyngeal pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| respiratory failure | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| upper respiratory tract inflammation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| anxiety | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| behavioural and psychiatric symptoms of dementia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| depression | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| disorientation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>insomnia</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>mental status changes</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>Investigations</p> <p>blood alkaline phosphatase increased</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>blood pressure increased</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>liver function test abnormal</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>weight decreased</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>1 / 53 (1.89%)</p> <p>1</p> | <p>0 / 49 (0.00%)</p> <p>0</p> <p>1 / 49 (2.04%)</p> <p>1</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>Injury, poisoning and procedural complications</p> <p>bone contusion</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>chest injury</p> <p>alternative dictionary used: MedDRA 16.1</p> | <p>1 / 53 (1.89%)</p> <p>1</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |

| | | |
|---|----------------|----------------|
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| contusion | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 |
| excoriation | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| fall | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| femur fracture | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| humerus fracture | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| incision site complication | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| joint injury | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| laceration | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |

| | | | |
|---|---------------------|---------------------|--|
| spinal compression fracture alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| tooth fracture alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 1 / 49 (2.04%) 1 | |
| Cardiac disorders acute myocardial infarction alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| aortic valve incompetence alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| arrhythmia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| palpitations alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| sinus tachycardia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| Nervous system disorders carotid arteriosclerosis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| carpal tunnel syndrome | | | |

| | | | |
|---|----------------|----------------|--|
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) | |
| occurrences (all) | 0 | 1 | |
| dizziness | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 1 / 49 (2.04%) | |
| occurrences (all) | 1 | 1 | |
| headache | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| hypoaesthesia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| neuralgia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) | |
| occurrences (all) | 0 | 1 | |
| paraesthesia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| parkinson's disease | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| presyncope | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| syncope | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>tremor</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>vascular dementia</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>vertebral artery stenosis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 53 (1.89%)</p> <p>1</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>1 / 53 (1.89%)</p> <p>1</p> <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>Ear and labyrinth disorders</p> <p>vertigo</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>Eye disorders</p> <p>cataract</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>conjunctival haemorrhage</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>conjunctivitis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dacryostenosis acquired</p> <p>alternative dictionary used: MedDRA 16.1</p> | <p>1 / 53 (1.89%)</p> <p>1</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>1 / 53 (1.89%)</p> <p>1</p> | <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| glaucoma alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| macular degeneration alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| Gastrointestinal disorders abdominal pain lower alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| abdominal pain upper alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| constipation alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 1 / 49 (2.04%) 1 | |
| dental caries alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| diarrhoea alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 1 / 53 (1.89%) 1 | 0 / 49 (0.00%) 0 | |
| diverticulum intestinal alternative dictionary used: MedDRA 16.1 | | | |

| | | |
|---|----------------|----------------|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| faecal incontinence | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| faecaloma | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| gastritis | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| gastritis atrophic | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| gastritis erosive | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| gastrointestinal disorder | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| gastrooesophageal reflux disease | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| gingival swelling | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |

| | | | |
|--|---------------------|---------------------|--|
| haemorrhoids alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 1 / 49 (2.04%) 1 | |
| hiatus hernia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 1 / 49 (2.04%) 1 | |
| nausea alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 1 / 49 (2.04%) 1 | |
| periodontal inflammation alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 1 / 49 (2.04%) 1 | |
| stomatitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 1 / 49 (2.04%) 1 | |
| toothache alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| vomiting alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 1 / 49 (2.04%) 1 | |
| Hepatobiliary disorders cholelithiasis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 53 (0.00%) 0 | 0 / 49 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders | | | |

| | | |
|---|----------------|----------------|
| actinic keratosis | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 |
| alopecia | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| asteatosis | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| dermatitis contact | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| drug eruption | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| dyshidrotic eczema | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| erythema | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| hypertrophic scar | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| ingrowing nail | | |
| alternative dictionary used: MedDRA 16.1 | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 53 (1.89%)</p> <p>1</p> <p>0 / 49 (0.00%)</p> <p>0</p> | | | |
| <p>pruritus</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 53 (1.89%)</p> <p>1</p> <p>0 / 49 (0.00%)</p> <p>0</p> | | | |
| <p>rash</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> | | | |
| <p>skin ulcer</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>1 / 49 (2.04%)</p> <p>1</p> | | | |
| <p>Renal and urinary disorders</p> <p>pollakiuria</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>urinary retention</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> | | | |
| <p>Endocrine disorders</p> <p>hyperparathyroidism secondary</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> | | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 53 (0.00%)</p> <p>0</p> <p>3 / 49 (6.12%)</p> <p>3</p> <p>back pain</p> <p>alternative dictionary used: MedDRA 16.1</p> | | | |

| | | |
|---|----------------|----------------|
| subjects affected / exposed | 2 / 53 (3.77%) | 0 / 49 (0.00%) |
| occurrences (all) | 2 | 0 |
| chondropathy | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| coccydynia | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 |
| flank pain | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| muscular weakness | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| musculoskeletal pain | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| myalgia | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| neck pain | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 |
| osteoarthritis | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |

| | | | |
|---|--------------------------------|--------------------------------|--|
| <p>osteonecrosis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>2 / 49 (4.08%)</p> <p>2</p> | |
| <p>osteoporosis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>pain in extremity</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 53 (1.89%)</p> <p>1</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>spinal column stenosis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>spinal osteoarthritis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>tenosynovitis stenosans</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>1 / 49 (2.04%)</p> <p>1</p> | |
| <p>trigger finger</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>0 / 49 (0.00%)</p> <p>0</p> | |
| <p>Infections and infestations</p> <p>adenoiditis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>bronchitis</p> <p>alternative dictionary used: MedDRA 16.1</p> | <p>0 / 53 (0.00%)</p> <p>0</p> | <p>1 / 49 (2.04%)</p> <p>1</p> | |

| | | |
|---|----------------|----------------|
| subjects affected / exposed | 0 / 53 (0.00%) | 2 / 49 (4.08%) |
| occurrences (all) | 0 | 2 |
| cellulitis | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| cervicitis | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed ^[4] | 1 / 39 (2.56%) | 0 / 39 (0.00%) |
| occurrences (all) | 1 | 0 |
| chronic hepatitis c | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| diverticulitis | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| ear infection | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| eye infection | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| gastroenteritis | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 |
| helicobacter infection | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |

| | | | |
|---|----------------|----------------|--|
| influenza | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| laryngitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| nail infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) | |
| occurrences (all) | 0 | 1 | |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| oral candidiasis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| oral herpes | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| parotitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| pharyngitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| rhinitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| skin infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) | |
| occurrences (all) | 0 | 1 | |
| tinea pedis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| tonsillitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 49 (2.04%) | |
| occurrences (all) | 0 | 1 | |
| wound infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| wound infection staphylococcal | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolism and nutrition disorders | | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| folate deficiency | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| hypercalcaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| hyperlipidaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| hypoglycaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 49 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| malnutrition | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| vitamin d deficiency | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 49 (0.00%) | |
| occurrences (all) | 0 | 0 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 13 December 2012 | The sponsor decided to end enrolment prematurely. The decision to stop enrolment was due to operational challenges and enrolment feasibility with regard to completing the study in a timely manner and not based on any safety or efficacy concerns in the trial. All active patients who were enrolled were offered to continue, and complete the study to 12 months. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported