

**Clinical trial results:****A Randomized, Double-blind, Placebo-Controlled, Comparative Multicenter Phase 3 Study to Evaluate the Safety and Efficacy of BA058 (Abaloparatide) for Injection for Prevention of Fracture in Ambulatory Postmenopausal Women With Severe Osteoporosis and at Risk of Fracture****Summary**

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2010-022576-30  |
| Trial protocol           | EE LT DK CZ PL  |
| Global end of trial date | 07 October 2014 |

**Results information**

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 23 May 2020  |
| First version publication date | 23 May 2020  |

**Trial information****Trial identification**

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | BA058-05-003 |
|-----------------------|--------------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01343004 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Radius Health, Inc.  |
| Sponsor organisation address | 950 Winter Street, Waltham, MA, United States, 02451   |
| Public contact               | Associate Director, Clinical Operations, Radius Health, Inc., +1 6175514077, ncantacesso@radiuspharm.com |
| Scientific contact           | VP, Oncology Clinical Development, Radius Health, Inc., +1 6175514086, mconlan@radiuspharm.com           |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 10 December 2014 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 07 October 2014  |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 07 October 2014  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to determine the safety and efficacy of abaloparatide-subcutaneous (SC) 80 microgram ( $\mu\text{g}$ ) when compared to placebo for prevention of new vertebral fracture in otherwise healthy ambulatory postmenopausal women at risk of osteoporotic fracture.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki in its revised edition (Seoul, 2008), the guidelines for current Good Clinical Practice (GCP) International Conference on Harmonization (ICH) (CPMP/ICH/135/95), the US Food and Drug Administration (FDA) Code of Federal Regulations (CFR) (21 CFR Parts 50, 54, 56 and 312), Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (ANMAT) regulations (Argentinean Investigators only), and all other applicable local regulatory and ethical requirements.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 15 March 2011 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | Argentina: 45       |
| Country: Number of subjects enrolled | Brazil: 616         |
| Country: Number of subjects enrolled | Czech Republic: 456 |
| Country: Number of subjects enrolled | Denmark: 396        |
| Country: Number of subjects enrolled | Estonia: 97         |
| Country: Number of subjects enrolled | Hong Kong: 387      |
| Country: Number of subjects enrolled | Lithuania: 84       |
| Country: Number of subjects enrolled | Poland: 199         |
| Country: Number of subjects enrolled | United States: 39   |
| Country: Number of subjects enrolled | Romania: 144        |
| Worldwide total number of subjects   | 2463                |
| EEA total number of subjects         | 1376                |

Notes:

| <b>Subjects enrolled per age group</b>    |      |
|---|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 0    |
| Adults (18-64 years)                      | 464  |
| From 65 to 84 years                       | 1997 |
| 85 years and over                         | 2    |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 5268 patients were screened and 2463 patients were enrolled in the study.

### Period 1

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

### Arms

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

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

Arm description:

Placebo identical in appearance to BA058 study drug Placebo: Placebo 0 mcg subcutaneous daily

|  |                                     |
|--|-------------------------------------|
| Arm type                               | Placebo                             |
| Investigational medicinal product name | Placebo                             |
| Investigational medicinal product code |                                     |
| Other name                             |                                     |
| Pharmaceutical forms                   | Solution for injection in cartridge |
| Routes of administration               | Subcutaneous use                    |

Dosage and administration details:

Placebo identical in appearance to BA058 study drug.

Placebo 0 mcg subcutaneous daily

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | BA058 80 mcg (abaloparatide) |
|------------------|------------------------------|

Arm description:

BA058 80 mcg: BA058 80 mcg subcutaneous daily

|  |                                     |
|--|-------------------------------------|
| Arm type                               | Experimental                        |
| Investigational medicinal product name | BA058 80 mcg (abaloparatide)        |
| Investigational medicinal product code |                                     |
| Other name                             | abaloparatide, Abaloparatide-SC     |
| Pharmaceutical forms                   | Solution for injection in cartridge |
| Routes of administration               | Subcutaneous use                    |

Dosage and administration details:

BA058 80 mcg subcutaneous daily

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

Arm description:

Blinded until after randomization, then open-label teriparatide: teriparatide 20 mcg subcutaneous daily

|  |                                     |
|--|-------------------------------------|
| Arm type                               | Active comparator                   |
| Investigational medicinal product name | teriparatide                        |
| Investigational medicinal product code |                                     |
| Other name                             | Forteo,<br>Forsteo                  |
| Pharmaceutical forms                   | Solution for injection in cartridge |
| Routes of administration               | Subcutaneous use                    |

Dosage and administration details:

Blinded until after randomization, then open-label.

Teriparatide 20 mcg subcutaneous daily

| <b>Number of subjects in period 1</b>                 | Placebo | BA058 80 mcg<br>(abaloparatide) | Teriparatide |
|---|---------|---------------------------------|--------------|
| Started   | 821     | 824                             | 818          |
| Completed   | 637     | 606                             | 658          |
| Not completed   | 184     | 218                             | 160          |
| Significant deterioration from<br>baseline of BMD     | 12      | 1                               | 1            |
| Adverse event, serious fatal                          | 5       | 3                               | 3            |
| Serious Intercurrent Illness                          | -       | 4                               | 5            |
| Hypersensitivity:<br>aloparatide/placebo/teriparatide | 1       | -                               | -            |
| Patient died during the study                         | 5       | 3                               | 2            |
| Other than Specified                                  | 6       | 5                               | 3            |
| Hypercalcemia or Hypercalciuria                       | -       | 1                               | 1            |
| Refusal of Treatment                                  | 33      | 31                              | 19           |
| Administrative Reasons                                | -       | 1                               | -            |
| Consent withdrawn by subject                          | 48      | 47                              | 45           |
| Adverse event, non-fatal                              | 48      | 86                              | 50           |
| Non-compliance  | 10      | 6                               | 9            |
| Treatment related SAE                                 | -       | -                               | 2            |
| Lost to follow-up                                     | 5       | 15                              | 10           |
| Protocol deviation                                    | 4       | 4                               | 5            |
| Inability to Complete Study<br>Procedures             | 7       | 11                              | 5            |

## Baseline characteristics

### Reporting groups

|   |                              |
|---|------------------------------|
| Reporting group title   | Placebo                      |
| Reporting group description:  |                              |
| Placebo identical in appearance to BA058 study drug Placebo: Placebo 0 mcg subcutaneous daily           |                              |
| Reporting group title   | BA058 80 mcg (abaloparatide) |
| Reporting group description:  |                              |
| BA058 80 mcg: BA058 80 mcg subcutaneous daily   |                              |
| Reporting group title   | Teriparatide                 |
| Reporting group description:  |                              |
| Blinded until after randomization, then open-label teriparatide: teriparatide 20 mcg subcutaneous daily |                              |

| Reporting group values | Placebo | BA058 80 mcg (abaloparatide) | Teriparatide |
|------------------------|---------|------------------------------|--------------|
| Number of subjects     | 821     | 824                          | 818          |
| Age categorical        |         |                              |              |
| Units: Subjects        |         |                              |              |
| <65 years              | 161     | 152                          | 151          |
| 65 to <75 years        | 512     | 517                          | 503          |
| >=75 years             | 148     | 155                          | 164          |
| Age Continuous         |         |                              |              |
| Units: years           |         |                              |              |
| arithmetic mean        | 68.7    | 68.9                         | 68.8         |
| standard deviation     | ± 6.5   | ± 6.5                        | ± 6.6        |
| Gender, Male/Female    |         |                              |              |
| Units:                 |         |                              |              |
| Female                 | 821     | 824                          | 818          |
| Male                   | 0       | 0                            | 0            |

| Reporting group values | Total |  |  |
|------------------------|-------|--|--|
| Number of subjects     | 2463  |  |  |
| Age categorical        |       |  |  |
| Units: Subjects        |       |  |  |
| <65 years              | 464   |  |  |
| 65 to <75 years        | 1532  |  |  |
| >=75 years             | 467   |  |  |
| Age Continuous         |       |  |  |
| Units: years           |       |  |  |
| arithmetic mean        |       |  |  |
| standard deviation     | -     |  |  |
| Gender, Male/Female    |       |  |  |
| Units:                 |       |  |  |
| Female                 | 2463  |  |  |
| Male                   | 0     |  |  |

## End points

### End points reporting groups

|   |                              |
|---|------------------------------|
| Reporting group title   | Placebo                      |
| Reporting group description:  |                              |
| Placebo identical in appearance to BA058 study drug Placebo: Placebo 0 mcg subcutaneous daily           |                              |
| Reporting group title   | BA058 80 mcg (abaloparatide) |
| Reporting group description:  |                              |
| BA058 80 mcg: BA058 80 mcg subcutaneous daily   |                              |
| Reporting group title   | Teriparatide                 |
| Reporting group description:  |                              |
| Blinded until after randomization, then open-label teriparatide: teriparatide 20 mcg subcutaneous daily |                              |

### Primary: Number of Participants with New Vertebral Fractures at 18 Months

|   |  |
|---|--|
| End point title   | Number of Participants with New Vertebral Fractures at 18 Months |
| End point description:  |  |
| Modified intent-to-treat (MITT) population included all patients with pre-treatment and end-of-treatment evaluable radiologic assessment (spine X-ray). |  |
| End point type  | Primary  |
| End point timeframe:  |  |
| 18 months   |  |

| End point values            | Placebo         | BA058 80 mcg (abaloparatide) | Teriparatide    |  |
|-----------------------------|-----------------|------------------------------|-----------------|--|
| Subject group type          | Reporting group | Reporting group              | Reporting group |  |
| Number of subjects analysed | 711             | 690                          | 717             |  |
| Units: participants         | 30              | 4                            | 6               |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | Placebo versus BA058 80 mcg (Abaloparatide) |
| Comparison groups                       | Placebo v BA058 80 mcg (abaloparatide)      |
| Number of subjects included in analysis | 1401  |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           |   |
| P-value                                 | < 0.0001                                    |
| Method                                  | Fisher exact                                |

|                            |                             |
|----------------------------|-----------------------------|
| Statistical analysis title | Placebo versus Teriparatide |
| Comparison groups          | Placebo v Teriparatide      |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 1428          |
| Analysis specification                  | Pre-specified |
| Analysis type                           |               |
| P-value                                 | < 0.0001      |
| Method                                  | Fisher exact  |

### Secondary: Percent Change in Bone Mineral Density (BMD) of Lumbar Spine from Baseline to 18 Months

|                 |   |
|-----------------|---|
| End point title | Percent Change in Bone Mineral Density (BMD) of Lumbar Spine from Baseline to 18 Months |
|-----------------|---|

End point description:

Intent-to-treat population included all patients who were randomized into the study by assigning the randomized study medication kit on Day 1. Baseline BMD data were missing for some patients; the method of last observation carried forward (LOCF) was used to impute missing data.

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

End point timeframe:

Baseline and 18 months

| End point values                     | Placebo         | BA058 80 mcg (abaloparatide) | Teriparatide    |  |
|--------------------------------------|-----------------|------------------------------|-----------------|--|
| Subject group type                   | Reporting group | Reporting group              | Reporting group |  |
| Number of subjects analysed          | 821             | 823                          | 818             |  |
| Units: percent change from baseline  |                 |                              |                 |  |
| arithmetic mean (standard deviation) | 0.48 (± 3.82)   | 9.20 (± 7.54)                | 9.12 (± 6.28)   |  |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Placebo versus BA058 80 mcg (Abaloparatide) |
| Comparison groups                       | Placebo v BA058 80 mcg (abaloparatide)      |
| Number of subjects included in analysis | 1644  |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           |   |
| P-value                                 | < 0.0001                                    |
| Method                                  | ANCOVA                                      |

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | BA058 80 mcg (Abaloparatide) versus Teriparatide |
| Comparison groups                 | BA058 80 mcg (abaloparatide) v Teriparatide      |



|   |               |
|---|---------------|
| Number of subjects included in analysis | 1641          |
| Analysis specification                  | Pre-specified |
| Analysis type                           |               |
| P-value                                 | = 0.8155      |
| Method                                  | ANCOVA        |

|   |                             |
|---|-----------------------------|
| <b>Statistical analysis title</b>       | Placebo versus Teriparatide |
| Comparison groups                       | Placebo v Teriparatide      |
| Number of subjects included in analysis | 1639                        |
| Analysis specification                  | Pre-specified               |
| Analysis type                           |                             |
| P-value                                 | < 0.0001                    |
| Method                                  | ANCOVA                      |

### Secondary: Percent Change in Bone Mineral Density (BMD) of Total Hip from Baseline to Month 18

|  |   |
|--|---|
| End point title  | Percent Change in Bone Mineral Density (BMD) of Total Hip from Baseline to Month 18 |
| End point description:<br>Intent-to-treat population included all patients who were randomized into the study by assigning the randomized study medication kit on Day 1. Baseline BMD data were missing for some patients; the method of LOCF was used to impute missing data. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Baseline and 18 months   |   |

| End point values                     | Placebo         | BA058 80 mcg (abaloparatide) | Teriparatide    |  |
|--------------------------------------|-----------------|------------------------------|-----------------|--|
| Subject group type                   | Reporting group | Reporting group              | Reporting group |  |
| Number of subjects analysed          | 820             | 822                          | 818             |  |
| Units: percent change                |                 |                              |                 |  |
| arithmetic mean (standard deviation) | -0.08 (± 2.77)  | 3.44 (± 3.51)                | 2.81 (± 3.33)   |  |

### Statistical analyses

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Placebo versus BA058 80 mcg (Abaloparatide) |
| Comparison groups                 | Placebo v BA058 80 mcg (abaloparatide)      |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 1642          |
| Analysis specification                  | Pre-specified |
| Analysis type                           |               |
| P-value                                 | < 0.0001      |
| Method                                  | ANCOVA        |

|   |                             |
|---|-----------------------------|
| <b>Statistical analysis title</b>       | Placebo versus Teriparatide |
| Comparison groups                       | Placebo v Teriparatide      |
| Number of subjects included in analysis | 1638                        |
| Analysis specification                  | Pre-specified               |
| Analysis type                           |                             |
| P-value                                 | < 0.0001                    |
| Method                                  | ANCOVA                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | BA058 80 mcg (Abaloparatide) versus Teriparatide |
| Comparison groups                       | BA058 80 mcg (abaloparatide) v Teriparatide      |
| Number of subjects included in analysis | 1640   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           |  |
| P-value                                 | < 0.0001   |
| Method                                  | ANCOVA   |

## Secondary: Percent Change in Bone Mineral Density (BMD) of Femoral Neck from Baseline to Month 18

|                 |  |
|-----------------|--|
| End point title | Percent Change in Bone Mineral Density (BMD) of Femoral Neck from Baseline to Month 18 |
|-----------------|--|

End point description:

Intent-to-treat population included all patients who were randomized into the study by assigning the randomized study medication kit on Day 1. Baseline BMD data were missing for some patients; the method of LOCF was used to impute missing data.

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

End point timeframe:

Baseline and 18 months

| End point values                     | Placebo         | BA058 80 mcg (abaloparatide) | Teriparatide    |  |
|--------------------------------------|-----------------|------------------------------|-----------------|--|
| Subject group type                   | Reporting group | Reporting group              | Reporting group |  |
| Number of subjects analysed          | 820             | 822                          | 818             |  |
| Units: percent change                |                 |                              |                 |  |
| arithmetic mean (standard deviation) | -0.44 (± 3.57)  | 2.90 (± 4.21)                | 2.26 (± 3.57)   |  |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Placebo versus BA058 80 mcg (Abaloparatide) |
| Comparison groups                       | Placebo v BA058 80 mcg (abaloparatide)      |
| Number of subjects included in analysis | 1642  |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           |   |
| P-value                                 | < 0.0001                                    |
| Method                                  | ANCOVA                                      |

|   |                             |
|---|-----------------------------|
| <b>Statistical analysis title</b>       | Placebo versus Teriparatide |
| Comparison groups                       | Placebo v Teriparatide      |
| Number of subjects included in analysis | 1638                        |
| Analysis specification                  | Pre-specified               |
| Analysis type                           |                             |
| P-value                                 | < 0.0001                    |
| Method                                  | ANCOVA                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | BA058 80 mcg (Abaloparatide) versus Teriparatide |
| Comparison groups                       | BA058 80 mcg (abaloparatide) v Teriparatide      |
| Number of subjects included in analysis | 1640   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           |  |
| P-value                                 | = 0.0004   |
| Method                                  | ANCOVA   |

### Secondary: Number of Participants with Non-vertebral Fractures at 18 Months

|  |  |
|--|--|
| End point title  | Number of Participants with Non-vertebral Fractures at 18 Months |
| End point description:<br>Intent-to-treat population included all patients who were randomized into the study by assigning the randomized study medication kit on Day 1. |  |
| End point type   | Secondary  |
| End point timeframe:<br>18 months  |  |

| <b>End point values</b>     | Placebo         | BA058 80 mcg (abaloparatide) | Teriparatide    |  |
|-----------------------------|-----------------|------------------------------|-----------------|--|
| Subject group type          | Reporting group | Reporting group              | Reporting group |  |
| Number of subjects analysed | 821             | 824                          | 818             |  |
| Units: Participants         | 33              | 18                           | 24              |  |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Placebo versus BA058 80 mcg (Abaloparatide) |
| Comparison groups                       | Placebo v BA058 80 mcg (abaloparatide)      |
| Number of subjects included in analysis | 1645  |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           |   |
| P-value                                 | = 0.0318                                    |
| Method                                  | Chi-squared                                 |

|   |                             |
|---|-----------------------------|
| <b>Statistical analysis title</b>       | Placebo versus Teriparatide |
| Comparison groups                       | Placebo v Teriparatide      |
| Number of subjects included in analysis | 1639                        |
| Analysis specification                  | Pre-specified               |
| Analysis type                           |                             |
| P-value                                 | = 0.2304                    |
| Method                                  | Chi-squared                 |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | BA058 80 mcg (Abaloparatide) versus Teriparatide |
| Comparison groups                       | BA058 80 mcg (abaloparatide) v Teriparatide      |
| Number of subjects included in analysis | 1642   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           |  |
| P-value                                 | = 0.3361   |
| Method                                  | Chi-squared                                      |

### Secondary: Number of Treatment-Emergent Adverse Events Associated with Hypercalcemia at 18 Months

|                 |  |
|-----------------|--|
| End point title | Number of Treatment-Emergent Adverse Events Associated with Hypercalcemia at 18 Months |
|-----------------|--|

End point description:

Safety population included all patients who received 1 or more doses of study medication.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| 18 months            |           |

| <b>End point values</b>     | Placebo         | BA058 80 mcg<br>(abaloparatide) | Teriparatide    |  |
|-----------------------------|-----------------|---------------------------------|-----------------|--|
| Subject group type          | Reporting group | Reporting group                 | Reporting group |  |
| Number of subjects analysed | 820             | 822                             | 818             |  |
| Units: Hypercalcemic events | 5               | 15                              | 34              |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to 18 months

Adverse event reporting additional description:

Individual number of occurrences (events) are not available for this study. Therefore, the number of subjects exposed per preferred term are reported in the field for the number of occurrences (events).

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

### Dictionary used

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

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

### Reporting groups

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

Reporting group description:

Placebo identical in appearance to BA058 study drug Placebo: Placebo 0 mcg subcutaneous daily

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

Reporting group description:

Blinded until after randomization, then open-label teriparatide: teriparatide 20 mcg subcutaneous daily

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | BA058 80 mcg (abaloparatide) |
|-----------------------|------------------------------|

Reporting group description:

BA058 80 mcg: BA058 80 mcg subcutaneous daily

| Serious adverse events  | Placebo           | Teriparatide      | BA058 80 mcg (abaloparatide) |
|---|-------------------|-------------------|------------------------------|
| Total subjects affected by serious adverse events                   |                   |                   |                              |
| subjects affected / exposed   | 90 / 820 (10.98%) | 82 / 818 (10.02%) | 80 / 822 (9.73%)             |
| number of deaths (all causes)                                       | 5                 | 3                 | 3                            |
| number of deaths resulting from adverse events                      | 5                 | 3                 | 3                            |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                   |                              |
| Breast cancer   |                   |                   |                              |
| subjects affected / exposed   | 1 / 820 (0.12%)   | 6 / 818 (0.73%)   | 3 / 822 (0.36%)              |
| occurrences causally related to treatment / all                     | 0 / 1             | 0 / 6             | 0 / 3                        |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             | 0 / 0                        |
| Adenocarcinoma of colon   |                   |                   |                              |
| subjects affected / exposed   | 0 / 820 (0.00%)   | 0 / 818 (0.00%)   | 2 / 822 (0.24%)              |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 0             | 0 / 2                        |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             | 0 / 0                        |
| Breast cancer stage II  |                   |                   |                              |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Melanocytic naevus                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pancreatic neoplasm                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Adenocarcinoma gastric                          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Angiolipoma                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Benign neoplasm of thyroid gland                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Bile duct adenocarcinoma                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Breast neoplasm                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Chronic leukaemia                               |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastric neoplasm                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal carcinoma                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| Invasive ductal breast carcinoma                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Lung adenocarcinoma                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Lung neoplasm malignant                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Malignant melanoma                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Metastatic malignant melanoma                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Metastatic squamous cell carcinoma              |                 |                 |                 |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Myeloproliferative disorder                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Uterine cancer                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Pancreatic carcinoma                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 2 / 818 (0.24%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| Vascular disorders                              |                 |                 |                 |
| Intermittent claudication                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Aortic dissection                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| Essential hypertension                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Hypertension                                    |                 |                 |                 |
| subjects affected / exposed                     | 2 / 820 (0.24%) | 2 / 818 (0.24%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 1 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypertensive crisis                             |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Surgical and medical procedures                 |                 |                 |                 |
| Cholecystectomy                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Colporrhaphy                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Coronary angioplasty                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hip arthroplasty                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Joint arthroplasty                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Knee arthroplasty                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Osteosynthesis                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Rectocele repair                                |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Removal of internal fixation                         |                 |                 |                 |
| subjects affected / exposed                          | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Toe operation  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| General disorders and administration site conditions |                 |                 |                 |
| Chest pain   |                 |                 |                 |
| subjects affected / exposed                          | 2 / 820 (0.24%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Pyrexia  |                 |                 |                 |
| subjects affected / exposed                          | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Chest discomfort                                     |                 |                 |                 |
| subjects affected / exposed                          | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| General physical health deterioration                |                 |                 |                 |
| subjects affected / exposed                          | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1           | 0 / 0           |
| Sudden death   |                 |                 |                 |
| subjects affected / exposed                          | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           | 0 / 0           |
| Reproductive system and breast disorders             |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Ovarian cyst                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Postmenopausal haemorrhage                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Uterine prolapse                                |                 |                 |                 |
| subjects affected / exposed                     | 2 / 820 (0.24%) | 1 / 818 (0.12%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cervical dysplasia                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cystocele                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 3 / 818 (0.37%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Uterine polyp                                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Bronchiectasis                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| Dyspnoea  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Pulmonary embolism                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Sinus polyp                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Allergic bronchitis                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Pulmonary mass                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Investigations                                  |                 |                 |                 |
| Weight decreased                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Blood glucose increased                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Body temperature increased                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Bronchoscopy                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Liver function test abnormal                    |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Injury, poisoning and procedural complications  |                 |                 |                 |
| Cranio-cerebral injury                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Fibula fracture                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Humerus fracture                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Incisional hernia                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Joint dislocation                               |                 |                 |                 |
| subjects affected / exposed                     | 2 / 820 (0.24%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ligament rupture                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Patella fracture                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Postoperative hernia                            |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Spinal compression fracture                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 2 / 818 (0.24%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Upper limb fracture                             |                 |                 |                 |
| subjects affected / exposed                     | 2 / 820 (0.24%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ankle fracture                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Contusion                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Extradural haematoma                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Femur fracture                                  |                 |                 |                 |
| subjects affected / exposed                     | 3 / 820 (0.37%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Fracture displacement                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hand fracture                                   |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Lower limb fracture                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Lumbar vertebral fracture                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Meniscus injury                                 |                 |                 |                 |
| subjects affected / exposed                     | 3 / 820 (0.37%) | 2 / 818 (0.24%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pelvic fracture                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Radius fracture                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Tibia fracture                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ulna fracture                                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Wrist fracture                                  |                 |                 |                 |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 820 (0.00%) | 2 / 818 (0.24%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders                               |                 |                 |                 |
| Myocardial ischaemia                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| Supraventricular tachycardia                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Atrioventricular block                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardio-respiratory arrest                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| Palpitations                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Acute coronary syndrome                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Acute myocardial infarction                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Angina pectoris                                 |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Angina unstable                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Atrial fibrillation                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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 failure congestive                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiomyopathy                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Coronary artery stenosis                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Mitral valve stenosis                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Sinus bradycardia                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Myocardial infarction                           |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 2 / 820 (0.24%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Transient ischaemic attack                      |                 |                 |                 |
| subjects affected / exposed                     | 2 / 820 (0.24%) | 2 / 818 (0.24%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Depressed level of consciousness                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hydrocephalus                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Intracranial aneurysm                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Radicular syndrome                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Sciatica  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Subarchnoid haemorrhage                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope   |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Tension headache                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Carpal tunnel syndrome                          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebrovascular accident                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Dizziness                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 2 / 818 (0.24%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ischaemic stroke                                |                 |                 |                 |
| subjects affected / exposed                     | 3 / 820 (0.37%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Lacunar infarction                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Loss of consciousness                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| VIIth nerve paralysis                           |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Blood and lymphatic system disorders            |                 |                 |                 |
| Anaemia   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ear and labyrinth disorders                     |                 |                 |                 |
| Vertigo   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vestibular disorder                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Eye disorders                                   |                 |                 |                 |
| Malculopathy                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Retinal artery occlusion                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cataract  |                 |                 |                 |
| subjects affected / exposed                     | 2 / 820 (0.24%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Gastric Ulcer                                   |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Abdominal pain                                  |                 |                 |                 |
| subjects affected / exposed                     | 3 / 820 (0.37%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Colitis   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Constipation                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Duodenal ulcer                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Haemorrhoids                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Intestinal obstruction                          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| Pancreatitis acute                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vomiting  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Change of bowel habit                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Diverticulum                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Enterocoele                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastric haemorrhage                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Gastritis                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Gastrointestinal haemorrhage                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Inguinal hernia                                 |                 |                 |                 |
| subjects affected / exposed                     | 2 / 820 (0.24%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Large intestine polyp                           |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 2 / 820 (0.24%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Hepatobiliary disorders</b>                  |                 |                 |                 |
| Cholelithiasis                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 3 / 822 (0.36%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cholangitis                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Bile duct stenosis                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Biliary dyskinesia                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cholecystitis acute                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Skin and subcutaneous tissue disorders</b>   |                 |                 |                 |
| Dermatitis allergic                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Drug eruption                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypersensitivity vasculitis                     |                 |                 |                 |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Hydronephrosis                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Calculus urinary                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Goitre  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 2 / 818 (0.24%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Thyroid cyst                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Osteoarthritis                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 3 / 818 (0.37%) | 3 / 822 (0.36%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 3           | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Back pain                                       |                 |                 |                 |
| subjects affected / exposed                     | 3 / 820 (0.37%) | 1 / 818 (0.12%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Foot deformity                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Spinal column stenosis                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Spinal pain                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Arthralgia                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Arthritis reactive                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Lumbar spine stenosis                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Spinal osteoarthritis                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Spondylolisthesis                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| Sepsis  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| Urinary tract infection                         |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Appendicitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Bronchiolitis                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Bronchitis                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Bronchopneumonia                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Influenza                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumonia                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Bacterial infection                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Dengue fever                                    |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Gastroenteritis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Helicobacter infection                          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Localised infection                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Nasopharyngitis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Paronychia                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pyelonephritis acute                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory tract infection                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 820 (0.12%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Viral infection                                 |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 820 (0.12%) | 0 / 818 (0.00%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Metabolism and nutrition disorders</b>       |                 |                 |                 |
| Hypoglycaemia                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 2 / 822 (0.24%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hyperglycaemia                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 0 / 818 (0.00%) | 1 / 822 (0.12%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gout  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (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           |
| Hypercalcaemia                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 820 (0.00%) | 1 / 818 (0.12%) | 0 / 822 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

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

| <b>Non-serious adverse events</b>                            | Placebo            | Teriparatide       | BA058 80 mcg (abaloparatide) |
|--|--------------------|--------------------|------------------------------|
| <b>Total subjects affected by non-serious adverse events</b> |                    |                    |                              |
| subjects affected / exposed                                  | 447 / 820 (54.51%) | 456 / 818 (55.75%) | 492 / 822 (59.85%)           |
| <b>Vascular disorders</b>                                    |                    |                    |                              |
| Hypertension   |                    |                    |                              |
| subjects affected / exposed                                  | 52 / 820 (6.34%)   | 41 / 818 (5.01%)   | 59 / 822 (7.18%)             |
| occurrences (all)  | 52                 | 41                 | 59                           |
| <b>Cardiac disorders</b>                                     |                    |                    |                              |
| Palpitations   |                    |                    |                              |
| subjects affected / exposed                                  | 3 / 820 (0.37%)    | 13 / 818 (1.59%)   | 42 / 822 (5.11%)             |
| occurrences (all)  | 3                  | 13                 | 42                           |
| <b>Nervous system disorders</b>                              |                    |                    |                              |

|   |                        |                           |                         |
|---|------------------------|---------------------------|-------------------------|
| Dizziness<br>subjects affected / exposed<br>occurrences (all)         | 50 / 820 (6.10%)<br>50 | 59 / 818 (7.21%)<br>59    | 82 / 822 (9.98%)<br>82  |
| Headache<br>subjects affected / exposed<br>occurrences (all)          | 49 / 820 (5.98%)<br>49 | 51 / 818 (6.23%)<br>51    | 62 / 822 (7.54%)<br>62  |
| Gastrointestinal disorders  |                        |                           |                         |
| Constipation<br>subjects affected / exposed<br>occurrences (all)      | 42 / 820 (5.12%)<br>42 | 34 / 818 (4.16%)<br>34    | 36 / 822 (4.38%)<br>36  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)            | 25 / 820 (3.05%)<br>25 | 42 / 818 (5.13%)<br>42    | 68 / 822 (8.27%)<br>68  |
| Renal and urinary disorders   |                        |                           |                         |
| Hypercalciuria<br>subjects affected / exposed<br>occurrences (all)    | 74 / 820 (9.02%)<br>74 | 102 / 818 (12.47%)<br>102 | 93 / 822 (11.31%)<br>93 |
| Musculoskeletal and connective tissue disorders                       |                        |                           |                         |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)        | 80 / 820 (9.76%)<br>80 | 70 / 818 (8.56%)<br>70    | 71 / 822 (8.64%)<br>71  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)         | 81 / 820 (9.88%)<br>81 | 58 / 818 (7.09%)<br>58    | 69 / 822 (8.39%)<br>69  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all) | 49 / 820 (5.98%)<br>49 | 42 / 818 (5.13%)<br>42    | 40 / 822 (4.87%)<br>40  |
| Infections and infestations   |                        |                           |                         |
| Influenza<br>subjects affected / exposed<br>occurrences (all)         | 39 / 820 (4.76%)<br>39 | 34 / 818 (4.16%)<br>34    | 52 / 822 (6.33%)<br>52  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)   | 66 / 820 (8.05%)<br>66 | 52 / 818 (6.36%)<br>52    | 48 / 822 (5.84%)<br>48  |
| Upper respiratory tract infection                                     |                        |                           |                         |

|                             |                  |                  |                  |
|-----------------------------|------------------|------------------|------------------|
| subjects affected / exposed | 63 / 820 (7.68%) | 73 / 818 (8.92%) | 68 / 822 (8.27%) |
| occurrences (all)           | 63               | 73               | 68               |
| Urinary tract infection     |                  |                  |                  |
| subjects affected / exposed | 38 / 820 (4.63%) | 41 / 818 (5.01%) | 43 / 822 (5.23%) |
| occurrences (all)           | 38               | 41               | 43               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 21 October 2011 | <p>The protocol was amended to:</p> <ul style="list-style-type: none"><li>• modify the "Inclusion Criteria" section of the synopsis to clarify that patients who had participated in a clinical study of any novel unapproved medication in the past 12 months would be excluded from participation in BA058-005-03 unless they had received placebo.</li><li>• to allow patients who might have been considered for the study but were ineligible because of recent or current use of thiazides to be considered for enrollment after activation of this amendment</li><li>• increase the time allowed for screening procedures to facilitate sample transport and reporting, and repeat samples, and</li><li>• provide clarification on a number of questions arising from participating sites.</li></ul> <p>These modifications did not impact the conduct of the study, but rather clarified certain aspects of the study conduct, such as</p> <ul style="list-style-type: none"><li>– to clarify the timing of post-dose assessment of serum calcium levels,</li><li>– to allow retesting of serum 25 hydroxy vitamin D and PTH levels after vitamin D supplementation</li><li>– to clarify that albumin-corrected calcium will be used for assessment of serum calcium, both in safety and PD assessments, and</li><li>– to clarify that ionized calcium levels can be considered in assessing eligibility.</li></ul> |
| 05 July 2012    | <p>The following modifications were made to the protocol:</p> <ul style="list-style-type: none"><li>• Pre- and post-study renal CT scans in patients in selected centers was added; the previous version of the protocol required only post-study renal CT scans.</li><li>• A bone biopsy was added for teriparatide patients; the previous version of the protocol required bone biopsies for patients in the abaloparatide and placebo arms.</li><li>• A modification of the description of the Extension Study (Protocol BA058-05-005 [NCT01657162]) was made. The revised Study BA058-05-005 offered patients receiving abaloparatide/placebo treatment an additional six months of osteoporosis care, including recommended treatment with alendronate, as appropriate. The previous version of the Extension Study called for an additional six months of abaloparatide followed by 24 months of treatment with a bisphosphonate.</li><li>• A paragraph was added to describe the results of an ongoing rat carcinogenicity study with abaloparatide.</li><li>• A requirement was added that subjects who experience a clinical fracture during the study and elect to continue to participate would need to provide re-consent prior to continuing in the study.</li></ul>   |
| 31 March 2014   | <p>The following modifications were made to the protocol:</p> <ul style="list-style-type: none"><li>• The name of BA058 was changed to abaloparatide throughout the document.</li><li>• A new Sponsor Medical Monitor/Study Safety Officer was added.</li><li>• Clarifications were made to more accurately describe the sequence of procedures in the protocol.</li><li>• Modifications were made to more clearly define how incident vertebral and nonvertebral fractures were diagnosed.</li><li>• Modifications were made to clarify that the hypercalcemia algorithm is based on pre- not post-dose serum calcium.</li><li>• Modifications were made to clarify the patient populations to be analyzed.</li><li>• Clarification of the definition of a protocol violation was added to align the protocol with Radius' Protocol Deviation/Violation Procedure Manual (Version 3.0, 1 October 2012).</li><li>• Clarification of the definition of a protocol deviation was added to align the protocol with Radius' Protocol Deviation/Violation Procedure Manual (Version 3.0, 1 October 2012).</li></ul>  |

Notes:



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## **Interruptions (globally)**

Were there any global interruptions to the trial? No

## **Limitations and caveats**

None reported