

**Clinical trial results:**

**A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety, Tolerability, and Efficacy of MK-0822 in the Treatment of Postmenopausal Women With Osteoporosis; A 12-Month Extension to: A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety, Tolerability, and Efficacy of MK-0822 (Cathepsin-K Inhibitor) in the Treatment of Postmenopausal Women With Osteoporosis; A 24-Month Extension to: A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety, Tolerability, and Efficacy of Odanacatib (MK-0822) in the Treatment of Postmenopausal Women With Osteoporosis; and A 5-Year Open-Label Extension to: A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety, Tolerability, and Efficacy of Odanacatib (MK-0822) in the Treatment of Postmenopausal Women With Osteoporosis**

**Summary**

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2005-001511-22  |
| Trial protocol           | SE DK GB        |
| Global end of trial date | 20 January 2016 |

**Results information**

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1               |
| This version publication date  | 04 February 2017 |
| First version publication date | 04 February 2017 |

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

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 0822-004 |
|-----------------------|----------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00112437 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |                                                                                              |
|------------------------------|----------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Merck Sharp & Dohme Corp.                                                                    |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033                               |
| Public contact               | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |

Notes:

**Paediatric regulatory details**

|                                       |    |
|---------------------------------------|----|
| Is trial part of an agreed paediatric | No |
|---------------------------------------|----|

|                                                                      |    |
|----------------------------------------------------------------------|----|
| investigation plan (PIP)                                             |    |
| 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                       | 20 January 2016 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         |                 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 20 January 2016 |
| Was the trial ended prematurely?                     | No              |
| Notes:                                               |                 |

## General information about the trial

Main objective of the trial:

The primary objectives of the study were: 1) To estimate the change from baseline (randomization in Protocol 004-02) in bone mineral density (BMD) at the lumbar spine at Years 8 and 10 with 50 mg of odanacatib once weekly in postmenopausal osteoporotic women previously treated for up to 5 years with odanacatib once weekly (in Protocols 004-02, 004-11, and 004-22); and 2) To assess the safety of treatment with odanacatib 50 mg once weekly for up to 10 years.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 24 June 2005 |
| 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 | Australia: 15   |
| Country: Number of subjects enrolled | Austria: 24     |
| Country: Number of subjects enrolled | Chile: 15       |
| Country: Number of subjects enrolled | Colombia: 22    |
| Country: Number of subjects enrolled | Denmark: 24     |
| Country: Number of subjects enrolled | France: 18      |
| Country: Number of subjects enrolled | Mexico: 19      |
| Country: Number of subjects enrolled | New Zealand: 28 |
| Country: Number of subjects enrolled | Norway: 30      |
| Country: Number of subjects enrolled | Peru: 20        |
| Country: Number of subjects enrolled | Sweden: 20      |

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Switzerland: 17    |
| Country: Number of subjects enrolled | United Kingdom: 15 |
| Country: Number of subjects enrolled | United States: 132 |
| Worldwide total number of subjects   | 399                |
| EEA total number of subjects         | 131                |

Notes:

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### Subjects enrolled per age group

|                                           |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 223 |
| From 65 to 84 years                       | 174 |
| 85 years and over                         | 2   |

## Subject disposition

### Recruitment

Recruitment details:

Approximately 375 participants were recruited from June 2005 to December 2005. Investigators used one or more of the following recruitment methods: Investigator Patient/Subject Database or Medical Records, Investigator's Local Recruitment/Advertising, Other Health Professional and, Physician Referral (Primary/Specialist/Family Doctor).

### Pre-assignment

Screening details:

Participants entered screening followed by a 3-week placebo run-in. All took vitamin D3, 5600 IU once weekly, those with average daily calcium intakes <1000 mg took calcium 500 mg/day as calcium carbonate. Participants were excluded from active treatment based on predetermined exclusion criteria (BMD and laboratory results).

### Period 1

|                              |                              |
|------------------------------|------------------------------|
| Period 1 title               | YEAR 1 (12-Month Base Study) |
| Is this the baseline period? | Yes                          |
| Allocation method            | Randomised - controlled      |
| Blinding used                | Double blind                 |
| Roles blinded                | Subject, Investigator        |

### Arms

|                              |              |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes          |
| <b>Arm title</b>             | Placebo-Base |

Arm description:

One placebo tablet once a week

|                                        |          |
|----------------------------------------|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

One placebo tablet once a week

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | Odanacatib 3 mg-Base |
|------------------|----------------------|

Arm description:

One odanacatib 3 mg tablet once a week

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Odanacatib   |
| Investigational medicinal product code | MK-0822      |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

One 3 mg tablet once a week

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Odanacatib 10 mg-Base |
|------------------|-----------------------|

Arm description:

One odanacatib 10 mg tablet once a week

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

|                                         |                       |
|-----------------------------------------|-----------------------|
| Investigational medicinal product name  | Odanacatib            |
| Investigational medicinal product code  | MK-0822               |
| Other name                              |                       |
| Pharmaceutical forms                    | Tablet                |
| Routes of administration                | Oral use              |
| Dosage and administration details:      |                       |
| One 10 mg tablet once a week            |                       |
| <b>Arm title</b>                        | Odanacatib 25 mg-Base |
| Arm description:                        |                       |
| One odanacatib 25 mg tablet once a week |                       |
| Arm type                                | Experimental          |
| Investigational medicinal product name  | Odanacatib            |
| Investigational medicinal product code  | MK-0822               |
| Other name                              |                       |
| Pharmaceutical forms                    | Tablet                |
| Routes of administration                | Oral use              |
| Dosage and administration details:      |                       |
| One 25 mg tablet once a week            |                       |
| <b>Arm title</b>                        | Odanacatib 50 mg-Base |
| Arm description:                        |                       |
| One odanacatib 50 mg tablet once a week |                       |
| Arm type                                | Experimental          |
| Investigational medicinal product name  | Odanacatib            |
| Investigational medicinal product code  | MK-0822               |
| Other name                              |                       |
| Pharmaceutical forms                    | Tablet                |
| Routes of administration                | Oral use              |
| Dosage and administration details:      |                       |
| One 50 mg tablet once a week            |                       |

| <b>Number of subjects in period 1</b>    | Placebo-Base | Odanacatib 3 mg-Base | Odanacatib 10 mg-Base |
|------------------------------------------|--------------|----------------------|-----------------------|
| Started                                  | 83           | 82                   | 77                    |
| Completed                                | 68           | 64                   | 65                    |
| Not completed                            | 15           | 18                   | 12                    |
| Consent withdrawn by subject             | 5            | 5                    | 2                     |
| Adverse event, non-fatal                 | 9            | 10                   | 6                     |
| DXA was lower by more than 8%            | -            | -                    | -                     |
| Lost to follow-up                        | -            | 1                    | -                     |
| Moved                                    | -            | 1                    | 1                     |
| patient was unsure that they needed drug | -            | -                    | -                     |
| Protocol deviation                       | 1            | -                    | 3                     |
| Lack of efficacy                         | -            | 1                    | -                     |

| <b>Number of subjects in period 1</b> | Odanacatib 25 mg-Base | Odanacatib 50 mg-Base |
|---------------------------------------|-----------------------|-----------------------|
|---------------------------------------|-----------------------|-----------------------|

|                                          |    |    |
|------------------------------------------|----|----|
| Started                                  | 79 | 78 |
| Completed                                | 71 | 66 |
| Not completed                            | 8  | 12 |
| Consent withdrawn by subject             | 1  | 7  |
| Adverse event, non-fatal                 | 4  | 3  |
| DXA was lower by more than 8%            | -  | 1  |
| Lost to follow-up                        | -  | -  |
| Moved                                    | -  | -  |
| patient was unsure that they needed drug | 2  | -  |
| Protocol deviation                       | 1  | 1  |
| Lack of efficacy                         | -  | -  |

## Period 2

|                              |                             |
|------------------------------|-----------------------------|
| Period 2 title               | YEAR 2 (12-Month Extension) |
| Is this the baseline period? | No                          |
| Allocation method            | Randomised - controlled     |
| Blinding used                | Double blind                |
| Roles blinded                | Subject, Investigator       |

## Arms

|                              |               |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes           |
| <b>Arm title</b>             | Placebo-Ext 1 |

Arm description:

One placebo tablet once a week

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Placebo      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

One placebo tablet once a week

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Odanacatib 3 mg-Ext 1 |
|------------------|-----------------------|

Arm description:

One odanacatib 3 mg tablet once a week

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Odanacatib   |
| Investigational medicinal product code | MK-0822      |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

One 3 mg tablet once a week

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | Odanacatib 10 mg-Ext 1 |
|------------------|------------------------|

|                                         |                        |
|-----------------------------------------|------------------------|
| Arm description:                        |                        |
| One odanacatib 10 mg tablet once a week |                        |
| Arm type                                | Experimental           |
| Investigational medicinal product name  | Odanacatib             |
| Investigational medicinal product code  | MK-0822                |
| Other name                              |                        |
| Pharmaceutical forms                    | Tablet                 |
| Routes of administration                | Oral use               |
| Dosage and administration details:      |                        |
| One 10 mg tablet once a week            |                        |
| <b>Arm title</b>                        | Odanacatib 25 mg-Ext 1 |
| Arm description:                        |                        |
| One odanacatib 25 mg tablet once a week |                        |
| Arm type                                | Experimental           |
| Investigational medicinal product name  | Odanacatib             |
| Investigational medicinal product code  | MK-0822                |
| Other name                              |                        |
| Pharmaceutical forms                    | Tablet                 |
| Routes of administration                | Oral use               |
| Dosage and administration details:      |                        |
| One 25 mg tablet once a week            |                        |
| <b>Arm title</b>                        | Odanacatib 50 mg-Ext 1 |
| Arm description:                        |                        |
| One odanacatib 50 mg tablet once a week |                        |
| Arm type                                | Experimental           |
| Investigational medicinal product name  | Odanacatib             |
| Investigational medicinal product code  | MK-0822                |
| Other name                              |                        |
| Pharmaceutical forms                    | Tablet                 |
| Routes of administration                | Oral use               |
| Dosage and administration details:      |                        |
| One 50 mg tablet once a week            |                        |

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Placebo-Ext 1 | Odanacatib 3 mg-Ext 1 | Odanacatib 10 mg-Ext 1 |
|-----------------------------------------------------|---------------|-----------------------|------------------------|
| Started                                             | 63            | 62                    | 63                     |
| Completed                                           | 60            | 53                    | 55                     |
| Not completed                                       | 3             | 9                     | 8                      |
| Consent withdrawn by subject                        | 1             | 1                     | 2                      |
| Adverse event, non-fatal                            | 1             | 2                     | 6                      |
| Patient stopped taking medication                   | -             | -                     | -                      |
| patient was out of windows                          | -             | -                     | -                      |
| Lost to follow-up                                   | -             | -                     | -                      |
| Moved                                               | -             | -                     | -                      |
| Lack of efficacy                                    | 1             | 6                     | -                      |

|                    |   |   |   |
|--------------------|---|---|---|
| Protocol deviation | - | - | - |
|--------------------|---|---|---|

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Odanacatib 25 mg-Ext 1 | Odanacatib 50 mg-Ext 1 |
|-----------------------------------------------------|------------------------|------------------------|
| Started                                             | 69                     | 63                     |
| Completed                                           | 62                     | 50                     |
| Not completed                                       | 7                      | 13                     |
| Consent withdrawn by subject                        | 4                      | 1                      |
| Adverse event, non-fatal                            | 1                      | 7                      |
| Patient stopped taking medication                   | -                      | 1                      |
| patient was out of windows                          | -                      | 1                      |
| Lost to follow-up                                   | 1                      | -                      |
| Moved                                               | -                      | 1                      |
| Lack of efficacy                                    | -                      | 2                      |
| Protocol deviation                                  | 1                      | -                      |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the preceding period entered this extension.

### Period 3

|                              |                             |
|------------------------------|-----------------------------|
| Period 3 title               | YEAR 3 (12-Month Extension) |
| Is this the baseline period? | No                          |
| Allocation method            | Randomised - controlled     |
| Blinding used                | Double blind                |
| Roles blinded                | Subject, Investigator       |

### Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| <b>Arm title</b>             | Placebo/Placebo-Ext 2 |

Arm description:

During this 12-month extension (Year 3), participants in this treatment group took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one placebo tablet once a week for 2 years.

|                                        |          |
|----------------------------------------|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

One placebo tablet once a week

|                  |                                |
|------------------|--------------------------------|
| <b>Arm title</b> | Placebo/Odanacatib 50 mg-Ext 2 |
|------------------|--------------------------------|

Arm description:

During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one placebo tablet once a week for 2 years.

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

|                                                                                                                                                                                                                                              |                                         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Investigational medicinal product name                                                                                                                                                                                                       | Odanacatib                              |
| Investigational medicinal product code                                                                                                                                                                                                       | MK-0822                                 |
| Other name                                                                                                                                                                                                                                   |                                         |
| Pharmaceutical forms                                                                                                                                                                                                                         | Tablet                                  |
| Routes of administration                                                                                                                                                                                                                     | Oral use                                |
| Dosage and administration details:                                                                                                                                                                                                           |                                         |
| One 50 mg tablet once a week                                                                                                                                                                                                                 |                                         |
| <b>Arm title</b>                                                                                                                                                                                                                             | Odanacatib 3 mg/Placebo-Ext 2           |
| Arm description:                                                                                                                                                                                                                             |                                         |
| During this 12-month extension (Year 3), participants took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one 3 mg tablet of odanacatib once a week for 2 years.             |                                         |
| Arm type                                                                                                                                                                                                                                     | Experimental                            |
| Investigational medicinal product name                                                                                                                                                                                                       | Placebo                                 |
| Investigational medicinal product code                                                                                                                                                                                                       |                                         |
| Other name                                                                                                                                                                                                                                   |                                         |
| Pharmaceutical forms                                                                                                                                                                                                                         | Tablet                                  |
| Routes of administration                                                                                                                                                                                                                     | Oral use                                |
| Dosage and administration details:                                                                                                                                                                                                           |                                         |
| One placebo tablet once a week                                                                                                                                                                                                               |                                         |
| <b>Arm title</b>                                                                                                                                                                                                                             | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2  |
| Arm description:                                                                                                                                                                                                                             |                                         |
| During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one 3 mg tablet of odanacatib once a week for 2 years. |                                         |
| Arm type                                                                                                                                                                                                                                     | Experimental                            |
| Investigational medicinal product name                                                                                                                                                                                                       | Odanacatib                              |
| Investigational medicinal product code                                                                                                                                                                                                       | MK-0822                                 |
| Other name                                                                                                                                                                                                                                   |                                         |
| Pharmaceutical forms                                                                                                                                                                                                                         | Tablet                                  |
| Routes of administration                                                                                                                                                                                                                     | Oral use                                |
| Dosage and administration details:                                                                                                                                                                                                           |                                         |
| One 50 mg tablet once a week                                                                                                                                                                                                                 |                                         |
| <b>Arm title</b>                                                                                                                                                                                                                             | Odanacatib 10 mg/Placebo-Ext 2          |
| Arm description:                                                                                                                                                                                                                             |                                         |
| During this 12-month extension (Year 3), participants took one placebo tablet once a week. Before entering this extension, participants had taken one 10 mg tablet of odanacatib once a week for 2 years.                                    |                                         |
| Arm type                                                                                                                                                                                                                                     | Experimental                            |
| Investigational medicinal product name                                                                                                                                                                                                       | Placebo                                 |
| Investigational medicinal product code                                                                                                                                                                                                       |                                         |
| Other name                                                                                                                                                                                                                                   |                                         |
| Pharmaceutical forms                                                                                                                                                                                                                         | Tablet                                  |
| Routes of administration                                                                                                                                                                                                                     | Oral use                                |
| Dosage and administration details:                                                                                                                                                                                                           |                                         |
| One placebo tablet once a week                                                                                                                                                                                                               |                                         |
| <b>Arm title</b>                                                                                                                                                                                                                             | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 |
| Arm description:                                                                                                                                                                                                                             |                                         |
| During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group took one 10 mg tablet of odanacatib once a week for 2 years.     |                                         |
| Arm type                                                                                                                                                                                                                                     | Experimental                            |

|                                        |                                |
|----------------------------------------|--------------------------------|
| Investigational medicinal product name | Odanacatib                     |
| Investigational medicinal product code | MK-0822                        |
| Other name                             |                                |
| Pharmaceutical forms                   | Tablet                         |
| Routes of administration               | Oral use                       |
| Dosage and administration details:     |                                |
| One 50 mg tablet once a week           |                                |
| <b>Arm title</b>                       | Odanacatib 25 mg/Placebo-Ext 2 |

Arm description:

During this 12-month extension (Year 3), participants in this treatment group took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one 25 mg tablet of odanacatib once a week for 2 years.

|                                        |                                         |
|----------------------------------------|-----------------------------------------|
| Arm type                               | Experimental                            |
| Investigational medicinal product name | Placebo                                 |
| Investigational medicinal product code |                                         |
| Other name                             |                                         |
| Pharmaceutical forms                   | Tablet                                  |
| Routes of administration               | Oral use                                |
| Dosage and administration details:     |                                         |
| One placebo tablet once a week         |                                         |
| <b>Arm title</b>                       | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |

Arm description:

During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one 25 mg tablet of odanacatib once a week for 2 years.

|                                        |                                |
|----------------------------------------|--------------------------------|
| Arm type                               | Experimental                   |
| Investigational medicinal product name | Odanacatib                     |
| Investigational medicinal product code | MK-0822                        |
| Other name                             |                                |
| Pharmaceutical forms                   | Tablet                         |
| Routes of administration               | Oral use                       |
| Dosage and administration details:     |                                |
| One 50 mg tablet once a week           |                                |
| <b>Arm title</b>                       | Odanacatib 50 mg/Placebo-Ext 2 |

Arm description:

During this 12-month extension (Year 3), participants in this treatment group took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one 50 mg tablet of odanacatib once a week for 2 years.

|                                        |                                         |
|----------------------------------------|-----------------------------------------|
| Arm type                               | Experimental                            |
| Investigational medicinal product name | Placebo                                 |
| Investigational medicinal product code |                                         |
| Other name                             |                                         |
| Pharmaceutical forms                   | Tablet                                  |
| Routes of administration               | Oral use                                |
| Dosage and administration details:     |                                         |
| One placebo tablet once a week         |                                         |
| <b>Arm title</b>                       | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |

Arm description:

During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one 50 mg tablet of odanacatib once a week for 2 years.

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

|                                        |            |
|----------------------------------------|------------|
| Investigational medicinal product name | Odanacatib |
| Investigational medicinal product code | MK-0822    |
| Other name                             |            |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

One 50 mg tablet once a week

| <b>Number of subjects in period 3<sup>[2]</sup></b> | Placebo/Placebo-Ext 2 | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 |
|-----------------------------------------------------|-----------------------|--------------------------------|-------------------------------|
| Started                                             | 19                    | 22                             | 18                            |
| Completed                                           | 17                    | 17                             | 18                            |
| Not completed                                       | 2                     | 5                              | 0                             |
| Consent withdrawn by subject                        | -                     | 3                              | -                             |
| Adverse event, non-fatal                            | 1                     | -                              | -                             |
| Lost to follow-up                                   | -                     | -                              | -                             |
| cortisone therapy, upcoming surgery                 | 1                     | 1                              | -                             |
| Lack of efficacy                                    | -                     | 1                              | -                             |
| Protocol deviation                                  | -                     | -                              | -                             |

| <b>Number of subjects in period 3<sup>[2]</sup></b> | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 |
|-----------------------------------------------------|----------------------------------------|--------------------------------|-----------------------------------------|
| Started                                             | 17                                     | 18                             | 17                                      |
| Completed                                           | 16                                     | 17                             | 13                                      |
| Not completed                                       | 1                                      | 1                              | 4                                       |
| Consent withdrawn by subject                        | -                                      | 1                              | -                                       |
| Adverse event, non-fatal                            | -                                      | -                              | 1                                       |
| Lost to follow-up                                   | -                                      | -                              | 1                                       |
| cortisone therapy, upcoming surgery                 | -                                      | -                              | -                                       |
| Lack of efficacy                                    | 1                                      | -                              | 1                                       |
| Protocol deviation                                  | -                                      | -                              | 1                                       |

| <b>Number of subjects in period 3<sup>[2]</sup></b> | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 50 mg/Placebo-Ext 2 |
|-----------------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|
| Started                                             | 19                             | 21                                      | 18                             |
| Completed                                           | 16                             | 20                                      | 16                             |
| Not completed                                       | 3                              | 1                                       | 2                              |
| Consent withdrawn by subject                        | -                              | -                                       | -                              |
| Adverse event, non-fatal                            | 3                              | 1                                       | -                              |
| Lost to follow-up                                   | -                              | -                                       | -                              |
| cortisone therapy, upcoming surgery                 | -                              | -                                       | -                              |

|                    |   |   |   |
|--------------------|---|---|---|
| Lack of efficacy   | - | - | 2 |
| Protocol deviation | - | - | - |

| <b>Number of subjects in period 3<sup>[2]</sup></b> | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
|-----------------------------------------------------|-----------------------------------------|
| Started                                             | 20                                      |
| Completed                                           | 19                                      |
| Not completed                                       | 1                                       |
| Consent withdrawn by subject                        | -                                       |
| Adverse event, non-fatal                            | 1                                       |
| Lost to follow-up                                   | -                                       |
| cortisone therapy, upcoming surgery                 | -                                       |
| Lack of efficacy                                    | -                                       |
| Protocol deviation                                  | -                                       |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the preceding period entered this extension.

#### Period 4

|                              |                                |
|------------------------------|--------------------------------|
| Period 4 title               | YEARS 4-5 (24-Month Extension) |
| Is this the baseline period? | No                             |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Investigator, Subject          |

#### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | Placebo once weekly |

Arm description:

One placebo tablet once a week

|                                        |          |
|----------------------------------------|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

One placebo tablet once a week

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Odanacatib 50 mg once weekly |
|------------------|------------------------------|

Arm description:

One odanacatib 50 mg tablet once a week

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Odanacatib   |
| Investigational medicinal product code | MK-0822      |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

One 50 mg tablet once a week

| <b>Number of subjects in period 4<sup>[3]</sup></b> | Placebo once weekly | Odanacatib 50 mg once weekly |
|-----------------------------------------------------|---------------------|------------------------------|
| Started                                             | 41                  | 100                          |
| Completed                                           | 37                  | 92                           |
| Not completed                                       | 4                   | 8                            |
| Participant moved                                   | -                   | 1                            |
| Consent withdrawn by subject                        | 1                   | 2                            |
| Adverse event, non-fatal                            | -                   | 4                            |
| Participant discontinued for other reason           | 1                   | -                            |
| Lack of efficacy                                    | 2                   | 1                            |

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the preceding period entered this extension.

## Period 5

|                              |                                 |
|------------------------------|---------------------------------|
| Period 5 title               | YEARS 6-10 (60-Month Extension) |
| Is this the baseline period? | No                              |
| Allocation method            | Not applicable                  |
| Blinding used                | Not blinded                     |

## Arms

|                              |                                       |
|------------------------------|---------------------------------------|
| Are arms mutually exclusive? | Yes                                   |
| <b>Arm title</b>             | Group A: Odanacatib 50 mg once weekly |

Arm description:

Group A consists of a combination of participants who were treated with odanacatib 25 mg for 2 years, then odanacatib 50 mg for 8 years; and participants who were treated with odanacatib 50 mg for 10 years.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Odanacatib   |
| Investigational medicinal product code | MK-0822      |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

One 50 mg tablet once a week

|                  |                                       |
|------------------|---------------------------------------|
| <b>Arm title</b> | Group B: Odanacatib 50 mg once weekly |
|------------------|---------------------------------------|

Arm description:

Group B consists of a combination participants who were treated with placebo for 2 years, then

odanacatib 50 mg for 8 years; participants who were treated with odanacatib 3 mg for 2 years, then odanacatib 50 mg for 8 years; and participants who were treated with odanacatib 10 mg for 2 years, then odanacatib 50 mg for 8 years.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Odanacatib   |
| Investigational medicinal product code | MK-0822      |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

One 50 mg tablet once a week

|                  |                                       |
|------------------|---------------------------------------|
| <b>Arm title</b> | Group C: Odanacatib 50 mg once weekly |
|------------------|---------------------------------------|

Arm description:

Group C consists of a combination of participants who were treated with placebo for 3 years, then odanacatib 50 mg for 7 years; and participants who were treated with odanacatib 3 mg for 2 years, then placebo for 1 year, then odanacatib 50 mg for 7 years.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Odanacatib   |
| Investigational medicinal product code | MK-0822      |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

One 50 mg tablet once a week

|                  |                                       |
|------------------|---------------------------------------|
| <b>Arm title</b> | Group D: Odanacatib 50 mg once weekly |
|------------------|---------------------------------------|

Arm description:

Group D consists of a combination of participants who were treated with odanacatib 10 mg for 2 years, then placebo for 3 years, then odanacatib 50 mg for 5 years; participants who were treated with odanacatib 25 mg for 5 years, then placebo for 3 years, then odanacatib 50 mg for 5 years; and participants who were treated with odanacatib 50 mg for 2 years, then placebo for 3 years, then odanacatib 50 mg for 5 years.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Odanacatib   |
| Investigational medicinal product code | MK-0822      |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

One 50 mg tablet once a week

| <b>Number of subjects in period 5<sup>[4]</sup></b> | Group A: Odanacatib 50 mg once weekly | Group B: Odanacatib 50 mg once weekly | Group C: Odanacatib 50 mg once weekly |
|-----------------------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Started                                             | 28                                    | 34                                    | 23                                    |
| Completed                                           | 23                                    | 22                                    | 22                                    |
| Not completed                                       | 5                                     | 12                                    | 1                                     |
| Physician decision                                  | -                                     | 2                                     | -                                     |
| Adverse event, non-fatal                            | 1                                     | 2                                     | -                                     |
| Death                                               | -                                     | 2                                     | -                                     |

|                       |   |   |   |
|-----------------------|---|---|---|
| Other                 | - | - | 1 |
| Lost to follow-up     | - | - | - |
| Withdrawal by subject | 4 | 6 | - |

| <b>Number of subjects in period 5<sup>[4]</sup></b> | Group D:<br>Odanacatib 50 mg<br>once weekly |
|-----------------------------------------------------|---------------------------------------------|
| Started                                             | 32                                          |
| Completed                                           | 27                                          |
| Not completed                                       | 5                                           |
| Physician decision                                  | -                                           |
| Adverse event, non-fatal                            | 1                                           |
| Death                                               | -                                           |
| Other                                               | -                                           |
| Lost to follow-up                                   | 1                                           |
| Withdrawal by subject                               | 3                                           |

Notes:

[4] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the preceding period entered this extension.

## Baseline characteristics

### Reporting groups

|                                         |                       |
|-----------------------------------------|-----------------------|
| Reporting group title                   | Placebo-Base          |
| Reporting group description:            |                       |
| One placebo tablet once a week          |                       |
| Reporting group title                   | Odanacatib 3 mg-Base  |
| Reporting group description:            |                       |
| One odanacatib 3 mg tablet once a week  |                       |
| Reporting group title                   | Odanacatib 10 mg-Base |
| Reporting group description:            |                       |
| One odanacatib 10 mg tablet once a week |                       |
| Reporting group title                   | Odanacatib 25 mg-Base |
| Reporting group description:            |                       |
| One odanacatib 25 mg tablet once a week |                       |
| Reporting group title                   | Odanacatib 50 mg-Base |
| Reporting group description:            |                       |
| One odanacatib 50 mg tablet once a week |                       |

| Reporting group values | Placebo-Base | Odanacatib 3 mg-Base | Odanacatib 10 mg-Base |
|------------------------|--------------|----------------------|-----------------------|
| Number of subjects     | 83           | 82                   | 77                    |
| Age categorical        |              |                      |                       |
| Units: Subjects        |              |                      |                       |

|                    |       |       |      |
|--------------------|-------|-------|------|
| Age continuous     |       |       |      |
| Units: years       |       |       |      |
| arithmetic mean    | 65.9  | 63.1  | 64.5 |
| standard deviation | ± 7.8 | ± 7.3 | ± 8  |
| Gender categorical |       |       |      |
| Units: Subjects    |       |       |      |
| Female             | 83    | 82    | 77   |
| Male               | 0     | 0     | 0    |

| Reporting group values | Odanacatib 25 mg-Base | Odanacatib 50 mg-Base | Total |
|------------------------|-----------------------|-----------------------|-------|
| Number of subjects     | 79                    | 78                    | 399   |
| Age categorical        |                       |                       |       |
| Units: Subjects        |                       |                       |       |

|                    |       |       |     |
|--------------------|-------|-------|-----|
| Age continuous     |       |       |     |
| Units: years       |       |       |     |
| arithmetic mean    | 62.9  | 64.5  |     |
| standard deviation | ± 7.4 | ± 8.1 | -   |
| Gender categorical |       |       |     |
| Units: Subjects    |       |       |     |
| Female             | 79    | 78    | 399 |
| Male               | 0     | 0     | 0   |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                               |                                        |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                         | Placebo-Base                           |
| Reporting group description:<br>One placebo tablet once a week                                                                                                                                                                                                                |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 3 mg-Base                   |
| Reporting group description:<br>One odanacatib 3 mg tablet once a week                                                                                                                                                                                                        |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 10 mg-Base                  |
| Reporting group description:<br>One odanacatib 10 mg tablet once a week                                                                                                                                                                                                       |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 25 mg-Base                  |
| Reporting group description:<br>One odanacatib 25 mg tablet once a week                                                                                                                                                                                                       |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 50 mg-Base                  |
| Reporting group description:<br>One odanacatib 50 mg tablet once a week                                                                                                                                                                                                       |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Placebo-Ext 1                          |
| Reporting group description:<br>One placebo tablet once a week                                                                                                                                                                                                                |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 3 mg-Ext 1                  |
| Reporting group description:<br>One odanacatib 3 mg tablet once a week                                                                                                                                                                                                        |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 10 mg-Ext 1                 |
| Reporting group description:<br>One odanacatib 10 mg tablet once a week                                                                                                                                                                                                       |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 25 mg-Ext 1                 |
| Reporting group description:<br>One odanacatib 25 mg tablet once a week                                                                                                                                                                                                       |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 50 mg-Ext 1                 |
| Reporting group description:<br>One odanacatib 50 mg tablet once a week                                                                                                                                                                                                       |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Placebo/Placebo-Ext 2                  |
| Reporting group description:<br>During this 12-month extension (Year 3), participants in this treatment group took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one placebo tablet once a week for 2 years. |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Placebo/Odanacatib 50 mg-Ext 2         |
| Reporting group description:<br>During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one placebo tablet once a week for 2 years.             |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 3 mg/Placebo-Ext 2          |
| Reporting group description:<br>During this 12-month extension (Year 3), participants took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one 3 mg tablet of odanacatib once a week for 2 years.              |                                        |
| Reporting group title                                                                                                                                                                                                                                                         | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
| Reporting group description:<br>During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one 3 mg tablet of odanacatib once a week for 2 years.  |                                        |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                         |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Odanacatib 10 mg/Placebo-Ext 2          |
| Reporting group description:<br>During this 12-month extension (Year 3), participants took one placebo tablet once a week. Before entering this extension, participants had taken one 10 mg tablet of odanacatib once a week for 2 years.                                                                                                                                                                                                                          |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 |
| Reporting group description:<br>During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group took one 10 mg tablet of odanacatib once a week for 2 years.                                                                                                                                                                                           |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Odanacatib 25 mg/Placebo-Ext 2          |
| Reporting group description:<br>During this 12-month extension (Year 3), participants in this treatment group took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one 25 mg tablet of odanacatib once a week for 2 years.                                                                                                                                                                          |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
| Reporting group description:<br>During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one 25 mg tablet of odanacatib once a week for 2 years.                                                                                                                                                                                      |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Odanacatib 50 mg/Placebo-Ext 2          |
| Reporting group description:<br>During this 12-month extension (Year 3), participants in this treatment group took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one 50 mg tablet of odanacatib once a week for 2 years.                                                                                                                                                                          |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Reporting group description:<br>During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one 50 mg tablet of odanacatib once a week for 2 years.                                                                                                                                                                                      |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Placebo once weekly                     |
| Reporting group description:<br>One placebo tablet once a week                                                                                                                                                                                                                                                                                                                                                                                                     |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Odanacatib 50 mg once weekly            |
| Reporting group description:<br>One odanacatib 50 mg tablet once a week                                                                                                                                                                                                                                                                                                                                                                                            |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Group A: Odanacatib 50 mg once weekly   |
| Reporting group description:<br>Group A consists of a combination of participants who were treated with odanacatib 25 mg for 2 years, then odanacatib 50 mg for 8 years; and participants who were treated with odanacatib 50 mg for 10 years.                                                                                                                                                                                                                     |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Group B: Odanacatib 50 mg once weekly   |
| Reporting group description:<br>Group B consists of a combination participants who were treated with placebo for 2 years, then odanacatib 50 mg for 8 years; participants who were treated with odanacatib 3 mg for 2 years, then odanacatib 50 mg for 8 years; and participants who were treated with odanacatib 10 mg for 2 years, then odanacatib 50 mg for 8 years.                                                                                            |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Group C: Odanacatib 50 mg once weekly   |
| Reporting group description:<br>Group C consists of a combination of participants who were treated with placebo for 3 years, then odanacatib 50 mg for 7 years; and participants who were treated with odanacatib 3 mg for 2 years, then placebo for 1 year, then odanacatib 50 mg for 7 years.                                                                                                                                                                    |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Group D: Odanacatib 50 mg once weekly   |
| Reporting group description:<br>Group D consists of a combination of participants who were treated with odanacatib 10 mg for 2 years, then placebo for 3 years, then odanacatib 50 mg for 5 years; participants who were treated with odanacatib 25 mg for 5 years, then placebo for 3 years, then odanacatib 50 mg for 5 years; and participants who were treated with odanacatib 50 mg for 2 years, then placebo for 3 years, then odanacatib 50 mg for 5 years. |                                         |

**Primary: Percentage Change From Baseline in Lumbar Spine Bone Mineral Density (BMD) at 12 Months**

|                 |                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Lumbar Spine Bone Mineral Density (BMD) at 12 Months |
|-----------------|-----------------------------------------------------------------------------------------|

End point description:

Percentage change in lumbar spine BMD (relative to baseline) at 12 months.

Analysis at Month 12 used Full-Analysis-Set (FAS) Population of patients who took at least one dose of study medication and had necessary follow-up information, in their randomization treatment group, with last observation data carried forward. Seven patients had a baseline value, but no value at Month 12 for lumbar spine BMD.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and 12 months

| End point values                             | Placebo-Base         | Odanacatib 3 mg-Base | Odanacatib 10 mg-Base | Odanacatib 25 mg-Base |
|----------------------------------------------|----------------------|----------------------|-----------------------|-----------------------|
| Subject group type                           | Reporting group      | Reporting group      | Reporting group       | Reporting group       |
| Number of subjects analysed                  | 81                   | 79                   | 77                    | 78                    |
| Units: Percent Change                        |                      |                      |                       |                       |
| least squares mean (confidence interval 95%) | -0.13 (-0.8 to 0.54) | -0.62 (-1.3 to 0.05) | 1.5 (0.82 to 2.19)    | 2.65 (1.97 to 3.33)   |

| End point values                             | Odanacatib 50 mg-Base |  |  |  |
|----------------------------------------------|-----------------------|--|--|--|
| Subject group type                           | Reporting group       |  |  |  |
| Number of subjects analysed                  | 77                    |  |  |  |
| Units: Percent Change                        |                       |  |  |  |
| least squares mean (confidence interval 95%) | 3.37 (2.68 to 4.05)   |  |  |  |

**Statistical analyses**

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|

Statistical analysis description:

The primary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Lumbar Spine BMD compared to placebo over 12 months. The primary hypothesis states that odanacatib will increase Lumbar Spine BMD compared to placebo over 12 months.

|                   |                                      |
|-------------------|--------------------------------------|
| Comparison groups | Placebo-Base v Odanacatib 50 mg-Base |
|-------------------|--------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 158                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[1]</sup>       |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | 3.5                               |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 2.54                              |
| upper limit                             | 4.45                              |

Notes:

[1] - Significance for the primary endpoint was achieved through stepdown trend-test, the highest dose group was removed and the test was repeated until lack of significance was observed.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The primary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Lumbar Spine BMD compared to placebo over 12 months. The primary hypothesis states that odanacatib will increase Lumbar Spine BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 25 mg-Base |
| Number of subjects included in analysis | 159                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $\leq 0.001$ <sup>[2]</sup>          |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 2.78                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | 1.82                                 |
| upper limit                             | 3.73                                 |

Notes:

[2] - Significance for the primary endpoint was achieved through stepdown trend-test, the highest dose group was removed and the test was repeated until lack of significance was observed.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The primary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Lumbar Spine BMD compared to placebo over 12 months. The primary hypothesis states that odanacatib will increase Lumbar Spine BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis | 158                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $= 0.003$ <sup>[3]</sup>             |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 1.63                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.68    |
| upper limit         | 2.59    |

Notes:

[3] - Significance for the primary endpoint was achieved through stepdown trend-test, the highest dose group was removed and the test was repeated until lack of significance was observed.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The primary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Lumbar Spine BMD compared to placebo over 12 months. The primary hypothesis states that odanacatib will increase Lumbar Spine BMD compared to placebo over 12 months.

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis | 160                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | other                               |
| P-value                                 | = 0.343 <sup>[4]</sup>              |
| Method                                  | ANCOVA                              |
| Parameter estimate                      | Difference in Least Squares Means   |
| Point estimate                          | -0.49                               |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -1.44                               |
| upper limit                             | 0.46                                |

Notes:

[4] - Significance for the primary endpoint was achieved through stepdown trend-test, the highest dose group was removed and the test was repeated until lack of significance was observed.

### **Primary: Percentage Change From Baseline in Lumbar Spine BMD at 24 Months**

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Lumbar Spine BMD at 24 Months |
|-----------------|------------------------------------------------------------------|

End point description:

Percentage change in lumbar spine BMD (relative to baseline) at 24 months.

Analysis on lumbar spine BMD (g/cm<sup>2</sup>) at Month 24 used the FAS Population with Last Observation Carried Forward from Month 18 to 24. No data were carried forward from the core to the extension period. Only patients who took at least one dose of extension medication were included. 17 patients were excluded from FAS.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and 24 months

| End point values                             | Placebo-Ext 1         | Odanacatib 3 mg-Ext 1 | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|-----------------------|-----------------------|------------------------|------------------------|
| Subject group type                           | Reporting group       | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 62                    | 58                    | 60                     | 65                     |
| Units: Percent Change                        |                       |                       |                        |                        |
| least squares mean (confidence interval 95%) | -0.19 (-1.13 to 0.75) | -1.03 (-2 to -0.07)   | 3.2 (2.25 to 4.15)     | 4.26 (3.35 to 5.18)    |

| End point values                             | Odanacatib 50 mg-Ext 1 |  |  |  |
|----------------------------------------------|------------------------|--|--|--|
| Subject group type                           | Reporting group        |  |  |  |
| Number of subjects analysed                  | 58                     |  |  |  |
| Units: Percent Change                        |                        |  |  |  |
| least squares mean (confidence interval 95%) | 5.48 (4.52 to 6.44)    |  |  |  |

## Statistical analyses

| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|
|----------------------------|-----------------------------------|

Statistical analysis description:

The primary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Lumbar Spine BMD compared to placebo over 24 months. The primary hypothesis states that odanacatib will increase Lumbar Spine BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
| Number of subjects included in analysis | 120                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[5]</sup>            |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 5.67                                   |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 4.32                                   |
| upper limit                             | 7.02                                   |

Notes:

[5] - Significance for the primary endpoint was achieved through stepdown trend-test, the highest dose group was removed and the test was repeated until lack of significance was observed.

| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|
|----------------------------|-----------------------------------|

Statistical analysis description:

The primary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Lumbar Spine BMD compared to placebo over 24 months. The primary hypothesis states that odanacatib will increase Lumbar Spine BMD compared to placebo over 24 months.

|                   |                                        |
|-------------------|----------------------------------------|
| Comparison groups | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
|-------------------|----------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 127                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[6]</sup>       |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | 4.45                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 3.15                              |
| upper limit                             | 5.76                              |

Notes:

[6] - Significance for the primary endpoint was achieved through stepdown trend-test, the highest dose group was removed and the test was repeated until lack of significance was observed.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The primary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Lumbar Spine BMD compared to placebo over 24 months. The primary hypothesis states that odanacatib will increase Lumbar Spine BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 122                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[7]</sup>            |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 3.39                                   |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 2.06                                   |
| upper limit                             | 4.73                                   |

Notes:

[7] - Significance for the primary endpoint was achieved through stepdown trend-test, the highest dose group was removed and the test was repeated until lack of significance was observed.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The primary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Lumbar Spine BMD compared to placebo over 24 months. The primary hypothesis states that odanacatib will increase Lumbar Spine BMD compared to placebo over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 120                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | $= 0.218$ <sup>[8]</sup>              |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | -0.84                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -2.19   |
| upper limit         | 0.51    |

Notes:

[8] - Significance for the primary endpoint was achieved through stepdown trend-test, the highest dose group was removed and the test was repeated until lack of significance was observed.

### Primary: Percentage Change From Baseline in Lumbar Spine BMD at 36 Months

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Lumbar Spine BMD at 36 Months |
|-----------------|------------------------------------------------------------------|

End point description:

Percentage change in lumbar spine BMD (relative to baseline) at 36 months.

This analysis was performed at Month 36 using the Per Protocol (PP) Population, which included participants who took at least one dose of extension study medication and had the necessary follow-up information. Missing values were not imputed. No data were carried forward from Month 30 to 36.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and 36 months

| End point values                             | Placebo/Placebo-Ext 2 | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|-----------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group       | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                    | 16                             | 17                            | 13                                     |
| Units: Percent Change                        |                       |                                |                               |                                        |
| least squares mean (confidence interval 95%) | 0.42 (-1.89 to 2.73)  | 2.95 (0.79 to 5.11)            | -1.57 (-3.67 to 0.54)         | 4.41 (2.01 to 6.82)                    |

| End point values                             | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 12                             | 10                                      | 12                             | 18                                      |
| Units: Percent Change                        |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | 2.03 (-0.47 to 4.53)           | 6.11 (3.37 to 8.85)                     | 0.32 (-2.18 to 2.82)           | 7.45 (5.41 to 9.48)                     |

| End point values                             | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 15                             | 17                                      |  |  |
| Units: Percent Change                        |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | 1.39 (-0.84 to                 | 7.85 (5.74 to                           |  |  |

|      |       |       |
|------|-------|-------|
| 95%) | 3.63) | 9.95) |
|------|-------|-------|

## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Difference in Least Squares Means                                        |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                          |
| In postmenopausal women with osteoporosis assess the time course of resolution of effect on Lumbar Spine BMD during the 12 month extension following 24 months of treatment with odanacatib once weekly. The primary objective was to assess the resolution of effect, on lumbar spine BMD, for the patients who received odanacatib 50 mg for 3 years compared to those who received odanacatib 50 mg in the 2 year base period and switched to placebo for the 3rd year extension. |                                                                          |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                                                                                                                                                              | 32                                                                       |
| Analysis specification                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Pre-specified                                                            |
| Analysis type                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | other                                                                    |
| Parameter estimate                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Difference in Least Squares Means                                        |
| Point estimate                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 6.45                                                                     |
| Confidence interval                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                          |
| level                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 95 %                                                                     |
| sides                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 2-sided                                                                  |
| lower limit                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 3.38                                                                     |
| upper limit                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 9.53                                                                     |

## Primary: Percentage Change From Baseline in Lumbar Spine BMD at 60 Months

|                 |                                                                                 |
|-----------------|---------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Lumbar Spine BMD at 60 Months <sup>[9]</sup> |
|-----------------|---------------------------------------------------------------------------------|

End point description:

Percentage change from baseline in lumbar spine BMD at 60 months.

This analysis was based on the Full-Analysis Set (FAS) population, last observation carried forward. All patients who took at least one dose of base study medication were included in the base study time points, while for the extension study time points only patients who took at least one dose of extension medication were included. Missing values were imputed using the last observation-carried-forward principle for the FAS approach.

|                        |         |
|------------------------|---------|
| End point type         | Primary |
| End point timeframe:   |         |
| Baseline and 60 months |         |

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No between-group statistical analyses were performed for the endpoint: Percentage Change From Baseline in Lumbar Spine BMD at 60 Months

| End point values                          | Placebo once weekly  | Odanacatib 50 mg once weekly |  |  |
|-------------------------------------------|----------------------|------------------------------|--|--|
| Subject group type                        | Reporting group      | Reporting group              |  |  |
| Number of subjects analysed               | 14                   | 13                           |  |  |
| Units: Percent change                     |                      |                              |  |  |
| arithmetic mean (confidence interval 95%) | -0.41 (-3.1 to 2.28) | 11.88 (7.23 to 16.54)        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage Change From Baseline in Lumbar Spine BMD at 120 Months

|                 |                                                                                   |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Lumbar Spine BMD at 120 Months <sup>[10]</sup> |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

Percentage change from baseline in lumbar spine BMD at 120 Months.

This analysis was based on the FAS population, which included all randomized participants who took at least 1 dose of extension study drug and had the necessary extension data available for this endpoint. Missing data were not imputed.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and 120 months

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No between-group statistical analyses were performed for the endpoint: Percentage Change From Baseline in Lumbar Spine BMD at 120 Months.

| End point values                          | Group A: Odanacatib 50 mg once weekly | Group B: Odanacatib 50 mg once weekly | Group C: Odanacatib 50 mg once weekly | Group D: Odanacatib 50 mg once weekly |
|-------------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type                        | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed               | 20                                    | 16                                    | 17                                    | 21                                    |
| Units: Percent change                     |                                       |                                       |                                       |                                       |
| arithmetic mean (confidence interval 95%) | 16.92 (12.28 to 21.55)                | 14.56 (11.1 to 18.02)                 | 17.18 (11.48 to 22.88)                | 7.71 (4.46 to 10.95)                  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants Who Experienced At Least One Adverse Event (AE) During Treatment Years 6-10 (60 Months)

|                 |                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Participants Who Experienced At Least One Adverse Event (AE) During Treatment Years 6-10 (60 Months) <sup>[11]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|

End point description:

Number of participants who experienced at least one adverse event (AE) during treatment years 6-10 (60 months).

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not it is considered related to the study drug.

This endpoint was based on the All Participants As Treated (APaT) population, consisting of all participants who received at least 1 administration of the trial drug during treatment years 6-10.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Years 6-10 (up to 60 months, up to 14 days after the last dose of study drug)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No between-group statistical analyses were performed for the endpoint: Number of Participants Who Experienced At Least One Adverse Event (AE) During Treatment Years 6-10 (60 Months) .

| End point values            | Group A:<br>Odanacatib 50<br>mg once<br>weekly | Group B:<br>Odanacatib 50<br>mg once<br>weekly | Group C:<br>Odanacatib 50<br>mg once<br>weekly | Group D:<br>Odanacatib 50<br>mg once<br>weekly |
|-----------------------------|------------------------------------------------|------------------------------------------------|------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group                                | Reporting group                                | Reporting group                                | Reporting group                                |
| Number of subjects analysed | 28                                             | 34                                             | 23                                             | 32                                             |
| Units: Participants         | 27                                             | 34                                             | 23                                             | 32                                             |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Who Discontinued Study Drug Due to an AE During Treatment Years 6-10 (60 Months)

|                 |                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Participants Who Discontinued Study Drug Due to an AE During Treatment Years 6-10 (60 Months) <sup>[12]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

Number of participants who discontinued study treatment drug due to an AE during treatment years 6-10 (60 months)

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not it is considered related to the study drug. This endpoint was based on the APaT population, consisting of all participants who received at least 1 administration of the trial drug during treatment years 6-10.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Years 6-10 (up to 60 months)

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No between-group statistical analyses were performed for the endpoint: Number of Participants Who Discontinued Study Drug Due to an AE During Treatment Years 6-10 (60 Months)

| End point values            | Group A:<br>Odanacatib 50<br>mg once<br>weekly | Group B:<br>Odanacatib 50<br>mg once<br>weekly | Group C:<br>Odanacatib 50<br>mg once<br>weekly | Group D:<br>Odanacatib 50<br>mg once<br>weekly |
|-----------------------------|------------------------------------------------|------------------------------------------------|------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group                                | Reporting group                                | Reporting group                                | Reporting group                                |
| Number of subjects analysed | 28                                             | 34                                             | 23                                             | 32                                             |
| Units: Participants         | 1                                              | 2                                              | 0                                              | 1                                              |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage Change From Baseline in Total Hip BMD at 12 Months

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Total Hip BMD at 12 Months |
|-----------------|---------------------------------------------------------------|

End point description:

Percentage change in total hip BMD (relative to baseline) at 12 months.

This analysis was performed at Month 12 using FAS population with Last Observation Carried Forward.

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

End point timeframe:

Baseline and 12 months

| End point values                             | Placebo-Base           | Odanacatib 3<br>mg-Base | Odanacatib 10<br>mg-Base | Odanacatib 25<br>mg-Base |
|----------------------------------------------|------------------------|-------------------------|--------------------------|--------------------------|
| Subject group type                           | Reporting group        | Reporting group         | Reporting group          | Reporting group          |
| Number of subjects analysed                  | 81                     | 79                      | 77                       | 78                       |
| Units: Percent Change                        |                        |                         |                          |                          |
| least squares mean (confidence interval 95%) | -0.61 (-1.22 to -0.01) | -1.36 (-1.97 to -0.75)  | 1.05 (0.44 to 1.67)      | 1.45 (0.84 to 2.07)      |

| End point values                             | Odanacatib 50<br>mg-Base |  |  |  |
|----------------------------------------------|--------------------------|--|--|--|
| Subject group type                           | Reporting group          |  |  |  |
| Number of subjects analysed                  | 77                       |  |  |  |
| Units: Percent Change                        |                          |  |  |  |
| least squares mean (confidence interval 95%) | 1.87 (1.25 to 2.49)      |  |  |  |

## Statistical analyses

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg

weekly, and 50 mg weekly on Total Hip BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase Total Hip BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 50 mg-Base |
| Number of subjects included in analysis | 158                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $\leq 0.001$ <sup>[13]</sup>         |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 2.49                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | 1.62                                 |
| upper limit                             | 3.35                                 |

Notes:

[13] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through a stepdown trend-test approach. Multiplicity for multiple endpoints was handled by a Hochberg procedure

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Hip BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase Total Hip BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 25 mg-Base |
| Number of subjects included in analysis | 159                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $\leq 0.001$ <sup>[14]</sup>         |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 2.06                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | 1.2                                  |
| upper limit                             | 2.93                                 |

Notes:

[14] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through a stepdown trend-test approach. Multiplicity for multiple endpoints was handled by a Hochberg procedure

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Hip BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase Total Hip BMD compared to placebo over 12 months.

|                   |                                      |
|-------------------|--------------------------------------|
| Comparison groups | Placebo-Base v Odanacatib 10 mg-Base |
|-------------------|--------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 158                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[15]</sup>      |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | 1.67                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 0.8                               |
| upper limit                             | 2.53                              |

Notes:

[15] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through a stepdown trend-test approach. Multiplicity for multiple endpoints was handled by a Hochberg procedure

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Hip BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase Total Hip BMD compared to placebo over 12 months.

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis | 160                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | other                               |
| P-value                                 | $= 0.135$ <sup>[16]</sup>           |
| Method                                  | ANCOVA                              |
| Parameter estimate                      | Difference in Least Squares Means   |
| Point estimate                          | -0.75                               |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -1.61                               |
| upper limit                             | 0.11                                |

Notes:

[16] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through a stepdown trend-test approach. Multiplicity for multiple endpoints was handled by a Hochberg procedure

### **Secondary: Percentage Change From Baseline in Femoral Neck BMD at 12 Months**

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Femoral Neck BMD at 12 Months |
|-----------------|------------------------------------------------------------------|

End point description:

Percentage change in femoral neck BMD (relative to baseline) at 12 months.

This analysis was performed at Month 12 using FAS population with Last Observation Carried Forward.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 12 months |           |

| End point values                             | Placebo-Base          | Odanacatib 3 mg-Base  | Odanacatib 10 mg-Base | Odanacatib 25 mg-Base |
|----------------------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                           | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                  | 81                    | 79                    | 77                    | 78                    |
| Units: Percentage change                     |                       |                       |                       |                       |
| least squares mean (confidence interval 95%) | -0.13 (-0.79 to 0.54) | -0.32 (-0.99 to 0.35) | 0.74 (0.05 to 1.42)   | 1.76 (1.08 to 2.44)   |

| End point values                             | Odanacatib 50 mg-Base |  |  |  |
|----------------------------------------------|-----------------------|--|--|--|
| Subject group type                           | Reporting group       |  |  |  |
| Number of subjects analysed                  | 77                    |  |  |  |
| Units: Percentage change                     |                       |  |  |  |
| least squares mean (confidence interval 95%) | 2.53 (1.85 to 3.21)   |  |  |  |

## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                                                                          | Difference in Least Squares Means    |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                   |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on femoral neck BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase femoral neck BMD compared to placebo over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                                   | Placebo-Base v Odanacatib 50 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                             | 158                                  |
| Analysis specification                                                                                                                                                                                                                                                                              | Pre-specified                        |
| Analysis type                                                                                                                                                                                                                                                                                       |                                      |
| P-value                                                                                                                                                                                                                                                                                             | $\leq 0.001$ <sup>[17]</sup>         |
| Method                                                                                                                                                                                                                                                                                              | ANCOVA                               |
| Parameter estimate                                                                                                                                                                                                                                                                                  | Difference in Least Squares Means    |
| Point estimate                                                                                                                                                                                                                                                                                      | 2.66                                 |
| Confidence interval                                                                                                                                                                                                                                                                                 |                                      |
| level                                                                                                                                                                                                                                                                                               | 95 %                                 |
| sides                                                                                                                                                                                                                                                                                               | 2-sided                              |
| lower limit                                                                                                                                                                                                                                                                                         | 1.71                                 |
| upper limit                                                                                                                                                                                                                                                                                         | 3.61                                 |

Notes:

[17] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

| Statistical analysis title                                                                                                                                                                                                                                                                          | Difference in Least Squares Means    |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                   |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on femoral neck BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase femoral neck BMD compared to placebo over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                                   | Placebo-Base v Odanacatib 25 mg-Base |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 159                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[18]</sup>      |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | 1.89                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 0.93                              |
| upper limit                             | 2.84                              |

Notes:

[18] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on femoral neck BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase femoral neck BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis | 158                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $= 0.095$ <sup>[19]</sup>            |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 0.87                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -0.09                                |
| upper limit                             | 1.82                                 |

Notes:

[19] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on femoral neck BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase femoral neck BMD compared to placebo over 12 months.

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis | 160                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | other                               |
| Method                                  | ANCOVA                              |
| Parameter estimate                      | Difference in Least Squares Means   |
| Point estimate                          | -0.19                               |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.14   |
| upper limit         | 0.75    |

### Secondary: Percentage Change From Baseline in Trochanter BMD at 12 Months

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Trochanter BMD at 12 Months |
|-----------------|----------------------------------------------------------------|

End point description:

Percentage change in trochanter BMD (relative to baseline) at 12 months.

This analysis was performed at Month 12 using FAS population with Last Observation Carried Forward.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 12 Months |           |

| End point values                             | Placebo-Base          | Odanacatib 3 mg-Base  | Odanacatib 10 mg-Base | Odanacatib 25 mg-Base |
|----------------------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                           | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                  | 81                    | 79                    | 77                    | 78                    |
| Units: Percentage change                     |                       |                       |                       |                       |
| least squares mean (confidence interval 95%) | -0.73 (-1.64 to 0.18) | -1.02 (-1.94 to -0.1) | 1.65 (0.72 to 2.58)   | 1.91 (0.99 to 2.84)   |

| End point values                             | Odanacatib 50 mg-Base |  |  |  |
|----------------------------------------------|-----------------------|--|--|--|
| Subject group type                           | Reporting group       |  |  |  |
| Number of subjects analysed                  | 77                    |  |  |  |
| Units: Percentage change                     |                       |  |  |  |
| least squares mean (confidence interval 95%) | 2.21 (1.28 to 3.14)   |  |  |  |

### Statistical analyses

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on trochanter BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase trochanter BMD compared to placebo over 12 months.

|                   |                                      |
|-------------------|--------------------------------------|
| Comparison groups | Placebo-Base v Odanacatib 50 mg-Base |
|-------------------|--------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 158                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[20]</sup>      |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | 2.94                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 1.64                              |
| upper limit                             | 4.24                              |

Notes:

[20] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on trochanter BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase trochanter BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 25 mg-Base |
| Number of subjects included in analysis | 159                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $\leq 0.001$ <sup>[21]</sup>         |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 2.65                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | 1.35                                 |
| upper limit                             | 3.94                                 |

Notes:

[21] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on trochanter BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase trochanter BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis | 158                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $\leq 0.001$ <sup>[22]</sup>         |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 2.38                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 1.08    |
| upper limit         | 3.69    |

Notes:

[22] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on trochanter BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase trochanter BMD compared to placebo over 12 months.

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis | 160                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | other                               |
| P-value                                 | = 0.731 <sup>[23]</sup>             |
| Method                                  | ANCOVA                              |
| Parameter estimate                      | Difference in Least Squares Means   |
| Point estimate                          | -0.29                               |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -1.58                               |
| upper limit                             | 1                                   |

Notes:

[23] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

## Secondary: Percentage Change From Baseline in Total Body BMD at 12 Months

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Total Body BMD at 12 Months |
|-----------------|----------------------------------------------------------------|

End point description:

Percentage change in total body BMD (relative to baseline) at 12 months.

This analysis was performed at Month 12 using the FAS population with Last Observation Carried Forward.

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

End point timeframe:

Baseline and 12 Months

| End point values                             | Placebo-Base          | Odanacatib 3 mg-Base   | Odanacatib 10 mg-Base | Odanacatib 25 mg-Base |
|----------------------------------------------|-----------------------|------------------------|-----------------------|-----------------------|
| Subject group type                           | Reporting group       | Reporting group        | Reporting group       | Reporting group       |
| Number of subjects analysed                  | 72                    | 71                     | 70                    | 75                    |
| Units: Percentage change                     |                       |                        |                       |                       |
| least squares mean (confidence interval 95%) | -0.42 (-1.16 to 0.32) | -1.89 (-2.64 to -1.14) | -1.06 (-1.81 to -0.3) | -0.51 (-1.23 to 0.22) |

|                                              |                       |  |  |  |
|----------------------------------------------|-----------------------|--|--|--|
| <b>End point values</b>                      | Odanacatib 50 mg-Base |  |  |  |
| Subject group type                           | Reporting group       |  |  |  |
| Number of subjects analysed                  | 70                    |  |  |  |
| Units: Percentage change                     |                       |  |  |  |
| least squares mean (confidence interval 95%) | -0.13 (-0.89 to 0.62) |  |  |  |

## Statistical analyses

|                                                                                                                                                                                                                                                                                                 |                                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                               | Difference in Least Squares Means    |
| Statistical analysis description:                                                                                                                                                                                                                                                               |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on total body BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase total body BMD compared to placebo over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                               | Placebo-Base v Odanacatib 50 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                         | 142                                  |
| Analysis specification                                                                                                                                                                                                                                                                          | Pre-specified                        |
| Analysis type                                                                                                                                                                                                                                                                                   | other                                |
| P-value                                                                                                                                                                                                                                                                                         | = 0.112 <sup>[24]</sup>              |
| Method                                                                                                                                                                                                                                                                                          | ANCOVA                               |
| Parameter estimate                                                                                                                                                                                                                                                                              | Difference in Least Squares Means    |
| Point estimate                                                                                                                                                                                                                                                                                  | 0.29                                 |
| Confidence interval                                                                                                                                                                                                                                                                             |                                      |
| level                                                                                                                                                                                                                                                                                           | 95 %                                 |
| sides                                                                                                                                                                                                                                                                                           | 2-sided                              |
| lower limit                                                                                                                                                                                                                                                                                     | -0.77                                |
| upper limit                                                                                                                                                                                                                                                                                     | 1.35                                 |

Notes:

[24] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                                                                                                                                                                                                                                                                                 |                                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                               | Difference in Least Squares Means    |
| Statistical analysis description:                                                                                                                                                                                                                                                               |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on total body BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase total body BMD compared to placebo over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                               | Placebo-Base v Odanacatib 25 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                         | 147                                  |
| Analysis specification                                                                                                                                                                                                                                                                          | Pre-specified                        |
| Analysis type                                                                                                                                                                                                                                                                                   | other                                |
| Method                                                                                                                                                                                                                                                                                          | ANCOVA                               |
| Parameter estimate                                                                                                                                                                                                                                                                              | Difference in Least Squares Means    |
| Point estimate                                                                                                                                                                                                                                                                                  | -0.09                                |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.13   |
| upper limit         | 0.95    |

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on total body BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase total body BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis | 142                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | -0.63                                |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -1.69                                |
| upper limit                             | 0.42                                 |

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on total body BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase total body BMD compared to placebo over 12 months.

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis | 143                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | other                               |
| Method                                  | ANCOVA                              |
| Parameter estimate                      | Difference in Least Squares Means   |
| Point estimate                          | -1.47                               |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -2.53                               |
| upper limit                             | -0.42                               |

## Secondary: Percentage Change From Baseline in Distal Forearm BMD at 12 Months

|                 |                                                                    |
|-----------------|--------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Distal Forearm BMD at 12 Months |
|-----------------|--------------------------------------------------------------------|

End point description:

Percentage change in distal forearm BMD (relative to baseline) at 12 months.

This analysis was performed at Month 12 using the FAS population with Last Observation Carried Forward.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 12 Months |           |

| End point values                             | Placebo-Base           | Odanacatib 3 mg-Base   | Odanacatib 10 mg-Base | Odanacatib 25 mg-Base |
|----------------------------------------------|------------------------|------------------------|-----------------------|-----------------------|
| Subject group type                           | Reporting group        | Reporting group        | Reporting group       | Reporting group       |
| Number of subjects analysed                  | 81                     | 79                     | 77                    | 78                    |
| Units: Percentage change                     |                        |                        |                       |                       |
| least squares mean (confidence interval 95%) | -1.27 (-1.98 to -0.57) | -2.55 (-3.26 to -1.83) | -1 (-1.73 to 0.28)    | -0.17 (-0.89 to 0.55) |

| End point values                             | Odanacatib 50 mg-Base |  |  |  |
|----------------------------------------------|-----------------------|--|--|--|
| Subject group type                           | Reporting group       |  |  |  |
| Number of subjects analysed                  | 77                    |  |  |  |
| Units: Percentage change                     |                       |  |  |  |
| least squares mean (confidence interval 95%) | -0.04 (-0.77 to 0.68) |  |  |  |

## Statistical analyses

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on distal forearm BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase distal forearm BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 50 mg-Base |
| Number of subjects included in analysis | 158                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | ≤ 0.001 <sup>[25]</sup>              |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 1.23                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | 0.22                                 |
| upper limit                             | 2.24                                 |

Notes:

[25] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on distal forearm BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase distal forearm BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 25 mg-Base |
| Number of subjects included in analysis | 159                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.005 <sup>[26]</sup>              |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 1.1                                  |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | 0.09                                 |
| upper limit                             | 2.11                                 |

Notes:

[26] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on distal forearm BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase distal forearm BMD compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis | 158                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.63 <sup>[27]</sup>               |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 0.27                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -0.74                                |
| upper limit                             | 1.29                                 |

Notes:

[27] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg

weekly, and 50 mg weekly on distal forearm BMD compared to placebo over 12 months. The secondary hypothesis states that odanacatib will increase distal forearm BMD compared to placebo over 12 months.

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis | 160                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | other                               |
| Method                                  | ANCOVA                              |
| Parameter estimate                      | Difference in Least Squares Means   |
| Point estimate                          | -1.27                               |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -2.28                               |
| upper limit                             | -0.27                               |

### Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary N-telopeptides of Type I Collagen [u-NTx]) at 12 Months

|                 |                                                                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary N-telopeptides of Type I Collagen [u-NTx]) at 12 Months |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares (LS) mean of the log-values percentage change from baseline, in biochemical marker of bone turnover (u-NTx) at 12 months.

This analysis was geometric mean percent change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 12 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP population approach did not estimate missing data.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 12 Months |           |

| End point values                             | Placebo-Base            | Odanacatib 3 mg-Base | Odanacatib 10 mg-Base     | Odanacatib 25 mg-Base    |
|----------------------------------------------|-------------------------|----------------------|---------------------------|--------------------------|
| Subject group type                           | Reporting group         | Reporting group      | Reporting group           | Reporting group          |
| Number of subjects analysed                  | 62                      | 57                   | 56                        | 63                       |
| Units: Geometric LS Mean percent change      |                         |                      |                           |                          |
| least squares mean (confidence interval 95%) | -2.37 (-14.78 to 11.85) | 8.8 (-5.5 to 25.27)  | -34.21 (-42.94 to -24.15) | -48.29 (-54.8 to -40.84) |

| End point values                        | Odanacatib 50 mg-Base |  |  |  |
|-----------------------------------------|-----------------------|--|--|--|
| Subject group type                      | Reporting group       |  |  |  |
| Number of subjects analysed             | 56                    |  |  |  |
| Units: Geometric LS Mean percent change |                       |  |  |  |

|                                              |                           |  |  |  |
|----------------------------------------------|---------------------------|--|--|--|
| least squares mean (confidence interval 95%) | -60.23 (-65.51 to -54.13) |  |  |  |
|----------------------------------------------|---------------------------|--|--|--|

## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                                                                                                                  | Difference in Least Squares Means    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                                                           |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-NTx) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-NTx) over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                                                                           | Placebo-Base v Odanacatib 50 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                     | 118                                  |
| Analysis specification                                                                                                                                                                                                                                                                                                                      | Pre-specified                        |
| Analysis type                                                                                                                                                                                                                                                                                                                               | other                                |
| P-value                                                                                                                                                                                                                                                                                                                                     | $\leq 0.001$ <sup>[28]</sup>         |
| Method                                                                                                                                                                                                                                                                                                                                      | ANCOVA                               |
| Parameter estimate                                                                                                                                                                                                                                                                                                                          | Difference in Least Squares Means    |
| Point estimate                                                                                                                                                                                                                                                                                                                              | -57.86                               |
| Confidence interval                                                                                                                                                                                                                                                                                                                         |                                      |
| level                                                                                                                                                                                                                                                                                                                                       | 95 %                                 |
| sides                                                                                                                                                                                                                                                                                                                                       | 2-sided                              |
| lower limit                                                                                                                                                                                                                                                                                                                                 | -72.33                               |
| upper limit                                                                                                                                                                                                                                                                                                                                 | -43.38                               |

Notes:

[28] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

| Statistical analysis title                                                                                                                                                                                                                                                                                                                  | Difference in Least Squares Means    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                                                           |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-NTx) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-NTx) over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                                                                           | Placebo-Base v Odanacatib 25 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                     | 125                                  |
| Analysis specification                                                                                                                                                                                                                                                                                                                      | Pre-specified                        |
| Analysis type                                                                                                                                                                                                                                                                                                                               | other                                |
| P-value                                                                                                                                                                                                                                                                                                                                     | $\leq 0.001$ <sup>[29]</sup>         |
| Method                                                                                                                                                                                                                                                                                                                                      | ANCOVA                               |
| Parameter estimate                                                                                                                                                                                                                                                                                                                          | Difference in Least Squares Means    |
| Point estimate                                                                                                                                                                                                                                                                                                                              | -45.92                               |
| Confidence interval                                                                                                                                                                                                                                                                                                                         |                                      |
| level                                                                                                                                                                                                                                                                                                                                       | 95 %                                 |
| sides                                                                                                                                                                                                                                                                                                                                       | 2-sided                              |
| lower limit                                                                                                                                                                                                                                                                                                                                 | -60.93                               |
| upper limit                                                                                                                                                                                                                                                                                                                                 | -30.91                               |

Notes:

[29] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                                                                                                                                                                                                                                                                                                                             |                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                           | Difference in Least Squares Means    |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                           |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-NTx) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-NTx) over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                                                                           | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                     | 118                                  |
| Analysis specification                                                                                                                                                                                                                                                                                                                      | Pre-specified                        |
| Analysis type                                                                                                                                                                                                                                                                                                                               | other                                |
| P-value                                                                                                                                                                                                                                                                                                                                     | $\leq 0.001$ <sup>[30]</sup>         |
| Method                                                                                                                                                                                                                                                                                                                                      | ANCOVA                               |
| Parameter estimate                                                                                                                                                                                                                                                                                                                          | Difference in Least Squares Means    |
| Point estimate                                                                                                                                                                                                                                                                                                                              | -31.84                               |
| Confidence interval                                                                                                                                                                                                                                                                                                                         |                                      |
| level                                                                                                                                                                                                                                                                                                                                       | 95 %                                 |
| sides                                                                                                                                                                                                                                                                                                                                       | 2-sided                              |
| lower limit                                                                                                                                                                                                                                                                                                                                 | -48.11                               |
| upper limit                                                                                                                                                                                                                                                                                                                                 | -15.58                               |

Notes:

[30] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                                                                                                                                                                                                                                                                                                                             |                                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                           | Difference in Least Squares Means   |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                           |                                     |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-NTx) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-NTx) over 12 months. |                                     |
| Comparison groups                                                                                                                                                                                                                                                                                                                           | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                     | 119                                 |
| Analysis specification                                                                                                                                                                                                                                                                                                                      | Pre-specified                       |
| Analysis type                                                                                                                                                                                                                                                                                                                               | other                               |
| P-value                                                                                                                                                                                                                                                                                                                                     | $= 0.249$ <sup>[31]</sup>           |
| Method                                                                                                                                                                                                                                                                                                                                      | ANCOVA                              |
| Parameter estimate                                                                                                                                                                                                                                                                                                                          | Difference in Least Squares Means   |
| Point estimate                                                                                                                                                                                                                                                                                                                              | 11.17                               |
| Confidence interval                                                                                                                                                                                                                                                                                                                         |                                     |
| level                                                                                                                                                                                                                                                                                                                                       | 95 %                                |
| sides                                                                                                                                                                                                                                                                                                                                       | 2-sided                             |
| lower limit                                                                                                                                                                                                                                                                                                                                 | -0.94                               |
| upper limit                                                                                                                                                                                                                                                                                                                                 | 43.24                               |

Notes:

[31] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

### **Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum C-telopeptides of Type 1 Collagen [s-CTx]) at 12 Months**

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of |
|-----------------|----------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares (LS) mean of the log-values percentage change from baseline in biochemical marker of bone turnover (s-CTx) at 12 Months.

This analysis was geometric mean percent change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 12 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP population approach did not estimate missing data.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 12 Months |           |

| End point values                             | Placebo-Base            | Odanacatib 3 mg-Base   | Odanacatib 10 mg-Base    | Odanacatib 25 mg-Base     |
|----------------------------------------------|-------------------------|------------------------|--------------------------|---------------------------|
| Subject group type                           | Reporting group         | Reporting group        | Reporting group          | Reporting group           |
| Number of subjects analysed                  | 62                      | 57                     | 56                       | 62                        |
| Units: Geometric LS Mean percent change      |                         |                        |                          |                           |
| least squares mean (confidence interval 95%) | -0.58 (-16.79 to 18.78) | 19.12 (-0.94 to 43.24) | -22.24 (-35.45 to -6.32) | -36.15 (-46.54 to -23.75) |

| End point values                             | Odanacatib 50 mg-Base     |  |  |  |
|----------------------------------------------|---------------------------|--|--|--|
| Subject group type                           | Reporting group           |  |  |  |
| Number of subjects analysed                  | 55                        |  |  |  |
| Units: Geometric LS Mean percent change      |                           |  |  |  |
| least squares mean (confidence interval 95%) | -56.91 (-64.31 to -47.99) |  |  |  |

## Statistical analyses

|                                                                                                                                                                                                                                                                                                                                             |                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Statistical analysis title                                                                                                                                                                                                                                                                                                                  | Difference in Least Squares Means    |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                           |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (s-CTx) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (s-CTx) over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                                                                           | Placebo-Base v Odanacatib 50 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                     | 117                                  |
| Analysis specification                                                                                                                                                                                                                                                                                                                      | Pre-specified                        |
| Analysis type                                                                                                                                                                                                                                                                                                                               | other                                |
| P-value                                                                                                                                                                                                                                                                                                                                     | ≤ 0.001 <sup>[32]</sup>              |
| Method                                                                                                                                                                                                                                                                                                                                      | ANCOVA                               |
| Parameter estimate                                                                                                                                                                                                                                                                                                                          | Difference in Least Squares Means    |
| Point estimate                                                                                                                                                                                                                                                                                                                              | -56.33                               |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -75.86  |
| upper limit         | -36.81  |

Notes:

[32] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (s-CTx) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (s-CTx) over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 25 mg-Base |
| Number of subjects included in analysis | 124                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $\leq 0.001$ <sup>[33]</sup>         |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | -35.57                               |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | -56.63  |
| upper limit | -14.51  |

Notes:

[33] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (s-CTx) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (s-CTx) over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis | 118                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $= 0.08$ <sup>[34]</sup>             |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | -21.66                               |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | -44.54  |
| upper limit | 1.23    |

Notes:

[34] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                                                                                                                                                                                                                                                                                                                             |                                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                           | Difference in Least Squares Means   |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                           |                                     |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (s-CTx) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (s-CTx) over 12 months. |                                     |
| Comparison groups                                                                                                                                                                                                                                                                                                                           | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                     | 119                                 |
| Analysis specification                                                                                                                                                                                                                                                                                                                      | Pre-specified                       |
| Analysis type                                                                                                                                                                                                                                                                                                                               | other                               |
| Method                                                                                                                                                                                                                                                                                                                                      | ANCOVA                              |
| Parameter estimate                                                                                                                                                                                                                                                                                                                          | Difference in Least Squares Means   |
| Point estimate                                                                                                                                                                                                                                                                                                                              | 19.7                                |
| Confidence interval                                                                                                                                                                                                                                                                                                                         |                                     |
| level                                                                                                                                                                                                                                                                                                                                       | 95 %                                |
| sides                                                                                                                                                                                                                                                                                                                                       | 2-sided                             |
| lower limit                                                                                                                                                                                                                                                                                                                                 | -8.48                               |
| upper limit                                                                                                                                                                                                                                                                                                                                 | 47.88                               |

### **Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary Total Deoxypyridinolines [u-DPyr]) at 12 Months**

|                 |                                                                                                                                 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary Total Deoxypyridinolines [u-DPyr]) at 12 Months |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares mean of the log-values Percentage change in biochemical marker of bone turnover (u-DPyr) (relative to baseline) at 12 months.

This analysis was geometric mean percent change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 12 using a PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP population approach did not estimate missing data.

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

End point timeframe:

Baseline and 12 months

| <b>End point values</b>                      | Placebo-Base           | Odanacatib 3 mg-Base  | Odanacatib 10 mg-Base  | Odanacatib 25 mg-Base |
|----------------------------------------------|------------------------|-----------------------|------------------------|-----------------------|
| Subject group type                           | Reporting group        | Reporting group       | Reporting group        | Reporting group       |
| Number of subjects analysed                  | 60                     | 57                    | 55                     | 63                    |
| Units: Geometric LS Mean percent change      |                        |                       |                        |                       |
| least squares mean (confidence interval 95%) | -7.25 (-19.73 to 7.18) | 20.91 (4.33 to 40.12) | -8.58 (-21.33 to 6.24) | -8.5 (-20.52 to 5.33) |

|                                              |                           |  |  |  |
|----------------------------------------------|---------------------------|--|--|--|
| <b>End point values</b>                      | Odanacatib 50 mg-Base     |  |  |  |
| Subject group type                           | Reporting group           |  |  |  |
| Number of subjects analysed                  | 55                        |  |  |  |
| Units: Geometric LS Mean percent change      |                           |  |  |  |
| least squares mean (confidence interval 95%) | -25.52 (-35.93 to -13.43) |  |  |  |

## Statistical analyses

|                                                                                                                                                                                                                                                                                                                                               |                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                             | Difference in Least Squares Means    |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                             |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-DPyr) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-DPyr) over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                                                                             | Placebo-Base v Odanacatib 50 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                       | 115                                  |
| Analysis specification                                                                                                                                                                                                                                                                                                                        | Pre-specified                        |
| Analysis type                                                                                                                                                                                                                                                                                                                                 | other                                |
| P-value                                                                                                                                                                                                                                                                                                                                       | = 0.004 <sup>[35]</sup>              |
| Method                                                                                                                                                                                                                                                                                                                                        | ANCOVA                               |
| Parameter estimate                                                                                                                                                                                                                                                                                                                            | Difference in Least Squares Means    |
| Point estimate                                                                                                                                                                                                                                                                                                                                | -18.28                               |
| Confidence interval                                                                                                                                                                                                                                                                                                                           |                                      |
| level                                                                                                                                                                                                                                                                                                                                         | 95 %                                 |
| sides                                                                                                                                                                                                                                                                                                                                         | 2-sided                              |
| lower limit                                                                                                                                                                                                                                                                                                                                   | -35.82                               |
| upper limit                                                                                                                                                                                                                                                                                                                                   | -0.74                                |

Notes:

[35] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                                                                                                                                                                                                                                                                                                                               |                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                             | Difference in Least Squares Means    |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                             |                                      |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-DPyr) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-DPyr) over 12 months. |                                      |
| Comparison groups                                                                                                                                                                                                                                                                                                                             | Placebo-Base v Odanacatib 25 mg-Base |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                       | 123                                  |
| Analysis specification                                                                                                                                                                                                                                                                                                                        | Pre-specified                        |
| Analysis type                                                                                                                                                                                                                                                                                                                                 | other                                |
| P-value                                                                                                                                                                                                                                                                                                                                       | = 0.344 <sup>[36]</sup>              |
| Method                                                                                                                                                                                                                                                                                                                                        | ANCOVA                               |
| Parameter estimate                                                                                                                                                                                                                                                                                                                            | Difference in Least Squares Means    |
| Point estimate                                                                                                                                                                                                                                                                                                                                | -1.26                                |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -19.9   |
| upper limit         | 17.39   |

Notes:

[36] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-DPyr) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-DPyr) over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis | 115                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | -1.33                                |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -20.55                               |
| upper limit                             | 17.89                                |

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-DPyr) compared to placebo over 12 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-DPyr) over 12 months.

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis | 117                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | other                               |
| Method                                  | ANCOVA                              |
| Parameter estimate                      | Difference in Least Squares Means   |
| Point estimate                          | 28.15                               |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 5.84                                |
| upper limit                             | 50.46                               |

## Secondary: Percentage Change From Baseline in Biochemical Marker of Bone

**Turnover (Serum Bone-specific Alkaline Phosphatase [s-BSAP]) at 12 Months**

|                 |                                                                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum Bone-specific Alkaline Phosphatase [s-BSAP]) at 12 Months |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares mean of the log-values percentage change from baseline, in biochemical marker of bone turnover (s-BSAP), at 12 months.

This analysis was geometric mean percent change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 12 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP population approach did not estimate missing data.

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

End point timeframe:

Baseline and 12 months

| End point values                             | Placebo-Base           | Odanacatib 3 mg-Base   | Odanacatib 10 mg-Base | Odanacatib 25 mg-Base |
|----------------------------------------------|------------------------|------------------------|-----------------------|-----------------------|
| Subject group type                           | Reporting group        | Reporting group        | Reporting group       | Reporting group       |
| Number of subjects analysed                  | 62                     | 58                     | 57                    | 64                    |
| Units: Geometric LS Mean percent change      |                        |                        |                       |                       |
| least squares mean (confidence interval 95%) | -2.77 (-10.39 to 5.49) | 42.08 (30.64 to 54.52) | 8.95 (0.1 to 18.6)    | 2.66 (-5.25 to 11.24) |

| End point values                             | Odanacatib 50 mg-Base     |  |  |  |
|----------------------------------------------|---------------------------|--|--|--|
| Subject group type                           | Reporting group           |  |  |  |
| Number of subjects analysed                  | 58                        |  |  |  |
| Units: Geometric LS Mean percent change      |                           |  |  |  |
| least squares mean (confidence interval 95%) | -18.35 (-24.93 to -11.18) |  |  |  |

**Statistical analyses**

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-BSAP) compared to placebo over 12 months.

|                   |                                      |
|-------------------|--------------------------------------|
| Comparison groups | Placebo-Base v Odanacatib 50 mg-Base |
|-------------------|--------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 120                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[37]</sup>      |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | -15.57                            |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -26.11                            |
| upper limit                             | -5.04                             |

Notes:

[37] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-BSAP) compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 25 mg-Base |
| Number of subjects included in analysis | 126                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $= 0.645$ <sup>[38]</sup>            |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 5.43                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -6.02                                |
| upper limit                             | 16.89                                |

Notes:

[38] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-BSAP) compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis | 119                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | 11.73                                |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.47   |
| upper limit         | 23.92   |

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-BSAP) compared to placebo over 12 months.

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis | 120                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | other                               |
| Method                                  | ANCOVA                              |
| Parameter estimate                      | Difference in Least Squares Means   |
| Point estimate                          | 44.85                               |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 30.55                               |
| upper limit                             | 59.16                               |

### **Secondary: Percentage Change in Biochemical Marker of Bone Turnover (Serum N-terminal Propeptide of Type 1 Collagen [s-P1NP]) at 12 Months**

|                 |                                                                                                                                 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change in Biochemical Marker of Bone Turnover (Serum N-terminal Propeptide of Type 1 Collagen [s-P1NP]) at 12 Months |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares mean of the log-values percentage change in biochemical marker of bone turnover (s-P1NP) (relative to baseline) at 12 months.

This analysis was geometric mean percent change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 12 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP population approach did not estimate missing data.

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

End point timeframe:

Baseline and 12 months

| End point values                             | Placebo-Base          | Odanacatib 3 mg-Base  | Odanacatib 10 mg-Base  | Odanacatib 25 mg-Base  |
|----------------------------------------------|-----------------------|-----------------------|------------------------|------------------------|
| Subject group type                           | Reporting group       | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 62                    | 57                    | 57                     | 63                     |
| Units: Geometric LS Mean percent change      |                       |                       |                        |                        |
| least squares mean (confidence interval 95%) | 3.91 (-8.79 to 18.38) | 50.81 (31.69 to 72.7) | 2.33 (-10.63 to 17.16) | 2.23 (-10.12 to 16.28) |

| End point values                             | Odanacatib 50 mg-Base    |  |  |  |
|----------------------------------------------|--------------------------|--|--|--|
| Subject group type                           | Reporting group          |  |  |  |
| Number of subjects analysed                  | 58                       |  |  |  |
| Units: Geometric LS Mean percent change      |                          |  |  |  |
| least squares mean (confidence interval 95%) | -31.83 (-40.4 to -22.02) |  |  |  |

## Statistical analyses

| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-P1NP) compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 50 mg-Base |
| Number of subjects included in analysis | 120                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | $\leq 0.001$ <sup>[39]</sup>         |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | -35.74                               |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -52.14                               |
| upper limit                             | -19.33                               |

Notes:

[39] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-P1NP) compared to placebo over 12 months.

|                   |                                      |
|-------------------|--------------------------------------|
| Comparison groups | Placebo-Base v Odanacatib 25 mg-Base |
|-------------------|--------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 125                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | = 0.161 <sup>[40]</sup>           |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | -1.68                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -20.58                            |
| upper limit                             | 17.23                             |

Notes:

[40] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-P1NP) compared to placebo over 12 months.

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 10 mg-Base |
| Number of subjects included in analysis | 119                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| Method                                  | ANCOVA                               |
| Parameter estimate                      | Difference in Least Squares Means    |
| Point estimate                          | -1.58                                |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -20.99                               |
| upper limit                             | 17.82                                |

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-P1NP) compared to placebo over 12 months.

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Comparison groups                       | Placebo-Base v Odanacatib 3 mg-Base |
| Number of subjects included in analysis | 119                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | other                               |
| Method                                  | ANCOVA                              |
| Parameter estimate                      | Difference in Least Squares Means   |
| Point estimate                          | 46.9                                |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 22.35   |
| upper limit         | 71.44   |

## Secondary: Percentage Change From Baseline in Total Hip BMD at 24 Months

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Total Hip BMD at 24 Months |
|-----------------|---------------------------------------------------------------|

End point description:

Percentage change in total hip BMD (relative to baseline) at 24 months.

This analysis was performed at Month 24 using FAS Population with Last Observation Carried Forward (from extension data). No data was carried forward from the core to the extension period.

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

End point timeframe:

Baseline and 24 months

| End point values                             | Placebo-Ext 1          | Odanacatib 3 mg-Ext 1 | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|------------------------|-----------------------|------------------------|------------------------|
| Subject group type                           | Reporting group        | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 61                     | 57                    | 59                     | 65                     |
| Units: Percentage change                     |                        |                       |                        |                        |
| least squares mean (confidence interval 95%) | -0.93 (-1.86 to -0.01) | -1.44 (-2.4 to -0.48) | 1.82 (0.88 to 2.76)    | 2.55 (1.66 to 3.44)    |

| End point values                             | Odanacatib 50 mg-Ext 1 |  |  |  |
|----------------------------------------------|------------------------|--|--|--|
| Subject group type                           | Reporting group        |  |  |  |
| Number of subjects analysed                  | 58                     |  |  |  |
| Units: Percentage change                     |                        |  |  |  |
| least squares mean (confidence interval 95%) | 3.16 (2.22 to 4.11)    |  |  |  |

## Statistical analyses

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Hip BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Total Hip BMD compared to placebo over 24 months.

|                   |                                        |
|-------------------|----------------------------------------|
| Comparison groups | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
|-------------------|----------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 119                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[41]</sup>      |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | 4.1                               |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 2.77                              |
| upper limit                             | 5.42                              |

Notes:

[41] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Hip BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Total Hip BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
| Number of subjects included in analysis | 126                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[42]</sup>           |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 3.48                                   |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 2.2                                    |
| upper limit                             | 4.77                                   |

Notes:

[42] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Hip BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Total Hip BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 120                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[43]</sup>           |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 2.75                                   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 1.43    |
| upper limit         | 4.07    |

Notes:

[43] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Hip BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Total Hip BMD Density compared to placebo over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 118                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | = 0.536 <sup>[44]</sup>               |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | -0.51                                 |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | -1.84   |
| upper limit | 0.83    |

Notes:

[44] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

## Secondary: Percentage Change From Baseline in Femoral Neck BMD at 24 Months

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Femoral Neck BMD at 24 Months |
|-----------------|------------------------------------------------------------------|

End point description:

Percentage change in femoral neck BMD (relative to baseline) at 24 months.

This analysis was performed at Month 24 using FAS Population with Last Observation Carried Forward (from extension data). No data was carried forward from the core to the extension period.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 24 months |           |

| End point values                             | Placebo-Ext 1         | Odanacatib 3 mg-Ext 1  | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|-----------------------|------------------------|------------------------|------------------------|
| Subject group type                           | Reporting group       | Reporting group        | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 61                    | 57                     | 59                     | 65                     |
| Units: Percentage change                     |                       |                        |                        |                        |
| least squares mean (confidence interval 95%) | -0.85 (-1.85 to 0.16) | -1.25 (-2.29 to -0.22) | 1.97 (0.95 to 2.98)    | 2.73 (1.76 to 3.69)    |

| End point values                             | Odanacatib 50 mg-Ext 1 |  |  |  |
|----------------------------------------------|------------------------|--|--|--|
| Subject group type                           | Reporting group        |  |  |  |
| Number of subjects analysed                  | 58                     |  |  |  |
| Units: Percentage change                     |                        |  |  |  |
| least squares mean (confidence interval 95%) | 3.84 (2.82 to 4.86)    |  |  |  |

## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                                                                          | Difference in Least Squares Means      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                   |                                        |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Femoral Neck BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Femoral Neck BMD compared to placebo over 24 months. |                                        |
| Comparison groups                                                                                                                                                                                                                                                                                   | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
| Number of subjects included in analysis                                                                                                                                                                                                                                                             | 119                                    |
| Analysis specification                                                                                                                                                                                                                                                                              | Pre-specified                          |
| Analysis type                                                                                                                                                                                                                                                                                       | other                                  |
| P-value                                                                                                                                                                                                                                                                                             | $\leq 0.001$ <sup>[45]</sup>           |
| Method                                                                                                                                                                                                                                                                                              | ANCOVA                                 |
| Parameter estimate                                                                                                                                                                                                                                                                                  | Difference in Least Squares Means      |
| Point estimate                                                                                                                                                                                                                                                                                      | 4.69                                   |
| Confidence interval                                                                                                                                                                                                                                                                                 |                                        |
| level                                                                                                                                                                                                                                                                                               | 95 %                                   |
| sides                                                                                                                                                                                                                                                                                               | 2-sided                                |
| lower limit                                                                                                                                                                                                                                                                                         | 3.25                                   |
| upper limit                                                                                                                                                                                                                                                                                         | 6.12                                   |

Notes:

[45] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

| Statistical analysis title                                                                                                                                                                                                                                                                          | Difference in Least Squares Means      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                   |                                        |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Femoral Neck BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Femoral Neck BMD compared to placebo over 24 months. |                                        |
| Comparison groups                                                                                                                                                                                                                                                                                   | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 126                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[46]</sup>      |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | 3.57                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 2.18                              |
| upper limit                             | 4.97                              |

Notes:

[46] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Femoral Neck BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Femoral Neck BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 120                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[47]</sup>           |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 2.82                                   |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 1.39                                   |
| upper limit                             | 4.25                                   |

Notes:

[47] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Femoral Neck BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Femoral Neck BMD compared to placebo over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 118                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | $= 0.585$ <sup>[48]</sup>             |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | -0.41                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.85   |
| upper limit         | 1.04    |

Notes:

[48] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure

## Secondary: Percentage Change From Baseline in Trochanter BMD at 24 Months

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Trochanter BMD at 24 Months |
|-----------------|----------------------------------------------------------------|

End point description:

Percentage change in trochanter BMD (relative to baseline) at 24 months.

This analysis was performed at Month 24 using FAS Population with Last Observation Carried Forward (from extension data). No data was carried forward from the core to the extension period.

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

End point timeframe:

Baseline and 24 months

| End point values                             | Placebo-Ext 1         | Odanacatib 3 mg-Ext 1 | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|-----------------------|-----------------------|------------------------|------------------------|
| Subject group type                           | Reporting group       | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 61                    | 57                    | 59                     | 65                     |
| Units: Percent Change                        |                       |                       |                        |                        |
| least squares mean (confidence interval 95%) | -0.81 (-2.15 to 0.53) | -0.85 (-2.23 to 0.53) | 3.61 (2.26 to 4.97)    | 3.75 (2.46 to 5.04)    |

| End point values                             | Odanacatib 50 mg-Ext 1 |  |  |  |
|----------------------------------------------|------------------------|--|--|--|
| Subject group type                           | Reporting group        |  |  |  |
| Number of subjects analysed                  | 58                     |  |  |  |
| Units: Percent Change                        |                        |  |  |  |
| least squares mean (confidence interval 95%) | 4.28 (2.92 to 5.65)    |  |  |  |

## Statistical analyses

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Trochanter BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Trochanter BMD compared to placebo over 24 months.

|                   |                                        |
|-------------------|----------------------------------------|
| Comparison groups | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
|-------------------|----------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 119                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[49]</sup>      |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | 5.09                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 3.18                              |
| upper limit                             | 7.01                              |

Notes:

[49] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Trochanter BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Trochanter BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
| Number of subjects included in analysis | 126                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[50]</sup>           |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 4.56                                   |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 2.7                                    |
| upper limit                             | 6.42                                   |

Notes:

[50] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Trochanter BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Trochanter BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 120                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[51]</sup>           |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Square Means       |
| Point estimate                          | 4.43                                   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 2.52    |
| upper limit         | 6.33    |

Notes:

[51] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Trochanter BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Trochanter BMD compared to placebo over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 118                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | = 0.981 <sup>[52]</sup>               |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | -0.04                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -1.97                                 |
| upper limit                             | 1.89                                  |

Notes:

[52] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

## Secondary: Percentage Change From Baseline in Total Body BMD at 24 Months

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Total Body BMD at 24 Months |
|-----------------|----------------------------------------------------------------|

End point description:

Percentage change in total body BMD (relative to baseline) at 24 months.

This analysis was performed at Month 24 using FAS Population with Last Observation Carried Forward (from extension data). No data was carried forward from the core to the extension period.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 24 months |           |

| End point values                             | Placebo-Ext 1          | Odanacatib 3 mg-Ext 1 | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|------------------------|-----------------------|------------------------|------------------------|
| Subject group type                           | Reporting group        | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 56                     | 47                    | 48                     | 58                     |
| Units: Percentage change                     |                        |                       |                        |                        |
| least squares mean (confidence interval 95%) | -1.54 (-2.42 to -0.66) | -2.7 (-3.66 to 1.74)  | -1.35 (-2.29 to -0.4)  | -0.43 (-1.29 to 0.43)  |

|                                              |                        |  |  |  |
|----------------------------------------------|------------------------|--|--|--|
| <b>End point values</b>                      | Odanacatib 50 mg-Ext 1 |  |  |  |
| Subject group type                           | Reporting group        |  |  |  |
| Number of subjects analysed                  | 51                     |  |  |  |
| Units: Percentage change                     |                        |  |  |  |
| least squares mean (confidence interval 95%) | 0.19 (-0.73 to 1.11)   |  |  |  |

## Statistical analyses

|                                                                                                                                                                                                                                                                                                 |                                        |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                               | Difference in Least Squares Means      |
| Statistical analysis description:                                                                                                                                                                                                                                                               |                                        |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Body BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Total Body BMD compared to placebo over 24 months. |                                        |
| Comparison groups                                                                                                                                                                                                                                                                               | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
| Number of subjects included in analysis                                                                                                                                                                                                                                                         | 107                                    |
| Analysis specification                                                                                                                                                                                                                                                                          | Pre-specified                          |
| Analysis type                                                                                                                                                                                                                                                                                   | other                                  |
| P-value                                                                                                                                                                                                                                                                                         | $\leq 0.001$ <sup>[53]</sup>           |
| Method                                                                                                                                                                                                                                                                                          | ANCOVA                                 |
| Parameter estimate                                                                                                                                                                                                                                                                              | Difference in Least Squares Means      |
| Point estimate                                                                                                                                                                                                                                                                                  | 1.73                                   |
| Confidence interval                                                                                                                                                                                                                                                                             |                                        |
| level                                                                                                                                                                                                                                                                                           | 95 %                                   |
| sides                                                                                                                                                                                                                                                                                           | 2-sided                                |
| lower limit                                                                                                                                                                                                                                                                                     | 0.46                                   |
| upper limit                                                                                                                                                                                                                                                                                     | 3.01                                   |

Notes:

[53] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                                                                                                                                                                                                                                                                                 |                                        |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                               | Difference in Least Squares Means      |
| Statistical analysis description:                                                                                                                                                                                                                                                               |                                        |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Body BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Total Body BMD compared to placebo over 24 months. |                                        |
| Comparison groups                                                                                                                                                                                                                                                                               | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
| Number of subjects included in analysis                                                                                                                                                                                                                                                         | 114                                    |
| Analysis specification                                                                                                                                                                                                                                                                          | Pre-specified                          |
| Analysis type                                                                                                                                                                                                                                                                                   | other                                  |
| P-value                                                                                                                                                                                                                                                                                         | $= 0.028$ <sup>[54]</sup>              |
| Method                                                                                                                                                                                                                                                                                          | ANCOVA                                 |
| Parameter estimate                                                                                                                                                                                                                                                                              | Difference in Least Squares Means      |
| Point estimate                                                                                                                                                                                                                                                                                  | 1.11                                   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.12   |
| upper limit         | 2.34    |

Notes:

[54] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Body BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Total Body BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 104                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.804 <sup>[55]</sup>                |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Square Means       |
| Point estimate                          | 0.2                                    |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -1.1                                   |
| upper limit                             | 1.49                                   |

Notes:

[55] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Total Body BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Total Body BMD compared to placebo over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 103                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | -1.15                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -2.46                                 |
| upper limit                             | 0.15                                  |

## Secondary: Percentage Change From Baseline in Distal Forearm BMD at 24 Months

|                                                                                                                                                                                              |                                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| End point title                                                                                                                                                                              | Percentage Change From Baseline in Distal Forearm BMD at 24 Months |
| End point description:                                                                                                                                                                       |                                                                    |
| Percentage change in distal forearm BMD (relative to baseline) at 24 months.                                                                                                                 |                                                                    |
| This analysis was performed at Month 24 using FAS Population with Last Observation Carried Forward (from extension data). No data was carried forward from the core to the extension period. |                                                                    |
| End point type                                                                                                                                                                               | Secondary                                                          |
| End point timeframe:                                                                                                                                                                         |                                                                    |
| Baseline and 24 months                                                                                                                                                                       |                                                                    |

| End point values                             | Placebo-Ext 1          | Odanacatib 3 mg-Ext 1 | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|------------------------|-----------------------|------------------------|------------------------|
| Subject group type                           | Reporting group        | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 61                     | 58                    | 60                     | 65                     |
| Units: Percentage change                     |                        |                       |                        |                        |
| least squares mean (confidence interval 95%) | -2.75 (-3.83 to -1.66) | -5.7 (-6.8 to -4.59)  | -1.22 (-2.31 to -0.13) | -0.65 (-1.7 to 0.39)   |

| End point values                             | Odanacatib 50 mg-Ext 1 |  |  |  |
|----------------------------------------------|------------------------|--|--|--|
| Subject group type                           | Reporting group        |  |  |  |
| Number of subjects analysed                  | 57                     |  |  |  |
| Units: Percentage change                     |                        |  |  |  |
| least squares mean (confidence interval 95%) | 0.15 (-0.97 to 1.27)   |  |  |  |

## Statistical analyses

|                                                                                                                                                                                                                                                                                                         |                                        |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Statistical analysis title                                                                                                                                                                                                                                                                              | Difference in Least Squares Means      |
| Statistical analysis description:                                                                                                                                                                                                                                                                       |                                        |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Distal Forearm BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Distal Forearm BMD compared to placebo over 24 months. |                                        |
| Comparison groups                                                                                                                                                                                                                                                                                       | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                 | 118                                    |
| Analysis specification                                                                                                                                                                                                                                                                                  | Pre-specified                          |
| Analysis type                                                                                                                                                                                                                                                                                           | other                                  |
| P-value                                                                                                                                                                                                                                                                                                 | ≤ 0.001 <sup>[56]</sup>                |
| Method                                                                                                                                                                                                                                                                                                  | ANCOVA                                 |
| Parameter estimate                                                                                                                                                                                                                                                                                      | Difference in Least Squares Means      |
| Point estimate                                                                                                                                                                                                                                                                                          | 2.9                                    |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 1.34    |
| upper limit         | 4.46    |

Notes:

[56] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Distal Forearm BMD compared to placebo over 24 months. The secondary hypothesis states that MK0822 will increase Distal Forearm BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
| Number of subjects included in analysis | 126                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[57]</sup>           |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 2.09                                   |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 0.59                                   |
| upper limit                             | 3.6                                    |

Notes:

[57] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Distal Forearm BMD compared to placebo over 24 months. The secondary hypothesis states that MK0822 will increase Distal Forearm BMD compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 121                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $= 0.094$ <sup>[58]</sup>              |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 1.53                                   |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -0.01                                  |
| upper limit                             | 3.07                                   |

Notes:

[58] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                                                                                                                                                                                                                                                                                         |                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                       | Difference in Least Squares Means     |
| Statistical analysis description:                                                                                                                                                                                                                                                                       |                                       |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on Distal Forearm BMD compared to placebo over 24 months. The secondary hypothesis states that odanacatib will increase Distal Forearm BMD compared to placebo over 24 months. |                                       |
| Comparison groups                                                                                                                                                                                                                                                                                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                 | 119                                   |
| Analysis specification                                                                                                                                                                                                                                                                                  | Pre-specified                         |
| Analysis type                                                                                                                                                                                                                                                                                           | other                                 |
| Method                                                                                                                                                                                                                                                                                                  | ANCOVA                                |
| Parameter estimate                                                                                                                                                                                                                                                                                      | Difference in Least Squares Means     |
| Point estimate                                                                                                                                                                                                                                                                                          | -2.95                                 |
| Confidence interval                                                                                                                                                                                                                                                                                     |                                       |
| level                                                                                                                                                                                                                                                                                                   | 95 %                                  |
| sides                                                                                                                                                                                                                                                                                                   | 2-sided                               |
| lower limit                                                                                                                                                                                                                                                                                             | -4.5                                  |
| upper limit                                                                                                                                                                                                                                                                                             | -1.4                                  |

### Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary N-telopeptides of Type I Collagen [u-NTx]) at 24 Months

|                 |                                                                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary N-telopeptides of Type I Collagen [u-NTx]) at 24 Months |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares mean of the log-values percentage change from baseline, in biochemical marker of bone turnover (u- NTx) (relative to baseline) at 24 months

Analysis used a geometric mean percent change from baseline (back-transformation of a log-transformed fraction from baseline) at Month 24 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP protocol population did not estimate missing data.

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

End point timeframe:

Baseline and 24 months

| End point values                             | Placebo-Ext 1           | Odanacatib 3 mg-Ext 1  | Odanacatib 10 mg-Ext 1   | Odanacatib 25 mg-Ext 1   |
|----------------------------------------------|-------------------------|------------------------|--------------------------|--------------------------|
| Subject group type                           | Reporting group         | Reporting group        | Reporting group          | Reporting group          |
| Number of subjects analysed                  | 56                      | 45                     | 41                       | 51                       |
| Units: Geometric LS Mean percent change      |                         |                        |                          |                          |
| least squares mean (confidence interval 95%) | -4.62 (-18.23 to 11.25) | 12.89 (-4.93 to 34.05) | -40.57 (-50.32 to -28.9) | -38.3 (-47.48 to -27.51) |

|                                              |                           |  |  |  |
|----------------------------------------------|---------------------------|--|--|--|
| <b>End point values</b>                      | Odanacatib 50 mg-Ext 1    |  |  |  |
| Subject group type                           | Reporting group           |  |  |  |
| Number of subjects analysed                  | 38                        |  |  |  |
| Units: Geometric LS Mean percent change      |                           |  |  |  |
| least squares mean (confidence interval 95%) | -51.83 (-60.05 to -41.91) |  |  |  |

## Statistical analyses

|                                                                                                                                                                                                                                                                                                                                             |                                        |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                           | Difference in Least Squares Means      |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                           |                                        |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-NTx) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-NTx) over 24 months. |                                        |
| Comparison groups                                                                                                                                                                                                                                                                                                                           | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                     | 94                                     |
| Analysis specification                                                                                                                                                                                                                                                                                                                      | Pre-specified                          |
| Analysis type                                                                                                                                                                                                                                                                                                                               | other                                  |
| P-value                                                                                                                                                                                                                                                                                                                                     | $\leq 0.001$ <sup>[59]</sup>           |
| Method                                                                                                                                                                                                                                                                                                                                      | ANCOVA                                 |
| Parameter estimate                                                                                                                                                                                                                                                                                                                          | Difference in Least Squares Means      |
| Point estimate                                                                                                                                                                                                                                                                                                                              | -47.21                                 |
| Confidence interval                                                                                                                                                                                                                                                                                                                         |                                        |
| level                                                                                                                                                                                                                                                                                                                                       | 95 %                                   |
| sides                                                                                                                                                                                                                                                                                                                                       | 2-sided                                |
| lower limit                                                                                                                                                                                                                                                                                                                                 | -64.51                                 |
| upper limit                                                                                                                                                                                                                                                                                                                                 | -29.9                                  |

Notes:

[59] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                                                                                                                                                                                                                                                                                                                             |                                        |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                           | Difference in Least Squares Means      |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                           |                                        |
| The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-NTx) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-NTx) over 24 months. |                                        |
| Comparison groups                                                                                                                                                                                                                                                                                                                           | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                     | 107                                    |
| Analysis specification                                                                                                                                                                                                                                                                                                                      | Pre-specified                          |
| Analysis type                                                                                                                                                                                                                                                                                                                               | other                                  |
| P-value                                                                                                                                                                                                                                                                                                                                     | $\leq 0.001$ <sup>[60]</sup>           |
| Method                                                                                                                                                                                                                                                                                                                                      | ANCOVA                                 |
| Parameter estimate                                                                                                                                                                                                                                                                                                                          | Difference in Least Squares Means      |
| Point estimate                                                                                                                                                                                                                                                                                                                              | -33.67                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -51.44  |
| upper limit         | -15.91  |

Notes:

[60] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-NTx) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-NTx) over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 97                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[61]</sup>           |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | -35.94                                 |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -54.15                                 |
| upper limit                             | -17.74                                 |

Notes:

[61] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-NTx) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-NTx) over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 101                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | $= 0.101$ <sup>[62]</sup>             |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | 17.51                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -6.78                                 |
| upper limit                             | 41.8                                  |

Notes:

[62] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

## Secondary: Percentage Change in Biochemical Marker of Bone Turnover (Serum C-telopeptides of Type 1 Collagen [s-CTx]) at 24 Months

|                 |                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change in Biochemical Marker of Bone Turnover (Serum C-telopeptides of Type 1 Collagen [s-CTx]) at 24 Months |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares mean of the log-values percentage change from baseline, in biochemical marker of bone turnover (s-CTx) (relative to baseline) at 24 months.

Analysis used a geometric mean percent change from baseline (back-transformation of a log-transformed fraction from baseline) at Month 24 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP protocol population did not estimate missing data.

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

End point timeframe:

Baseline and 24 months

| End point values                             | Placebo-Ext 1          | Odanacatib 3 mg-Ext 1  | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|------------------------|------------------------|------------------------|------------------------|
| Subject group type                           | Reporting group        | Reporting group        | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 56                     | 45                     | 42                     | 52                     |
| Units: Geometric LS Mean percent change      |                        |                        |                        |                        |
| least squares mean (confidence interval 95%) | 32.77 (13.28 to 55.61) | 54.94 (29.83 to 84.92) | 8.79 (-9.35 to 30.57)  | -6.52 (-20.7 to 10.19) |

| End point values                             | Odanacatib 50 mg-Ext 1  |  |  |  |
|----------------------------------------------|-------------------------|--|--|--|
| Subject group type                           | Reporting group         |  |  |  |
| Number of subjects analysed                  | 39                      |  |  |  |
| Units: Geometric LS Mean percent change      |                         |  |  |  |
| least squares mean (confidence interval 95%) | -30.57 (-42.6 to -16.2) |  |  |  |

## Statistical analyses

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (s-CTx) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (s-CTx) over 24 months.

|                   |                                        |
|-------------------|----------------------------------------|
| Comparison groups | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
|-------------------|----------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 95                                |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | $\leq 0.001$ <sup>[63]</sup>      |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | -63.34                            |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -88.32                            |
| upper limit                             | -38.36                            |

Notes:

[63] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (s-CTx) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (s-CTx) over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
| Number of subjects included in analysis | 108                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $\leq 0.001$ <sup>[64]</sup>           |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | -39.29                                 |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -65.4                                  |
| upper limit                             | -13.18                                 |

Notes:

[64] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (s-CTx) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (s-CTx) over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 98                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | $= 0.124$ <sup>[65]</sup>              |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | -23.98                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -53.04  |
| upper limit         | 5.09    |

Notes:

[65] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (s-CTX) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (s-CTX) over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 101                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | 22.18                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -12.38                                |
| upper limit                             | 56.73                                 |

## Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary Total Deoxypyridinolines [u-DPyr]) at 24 Months

|                 |                                                                                                                                 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary Total Deoxypyridinolines [u-DPyr]) at 24 Months |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares mean of the log-values percentage change from baseline, in biochemical marker of bone turnover (u-DPyr) (relative to baseline) at 24 months.

Analysis used geometric mean percent change from baseline (back-transformation of a log-transformed fraction from baseline) at Month 24 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP protocol population did not estimate missing data.

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

End point timeframe:

Baseline and 24 months

| End point values                             | Placebo-Ext 1          | Odanacatib 3 mg-Ext 1  | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|------------------------|------------------------|------------------------|------------------------|
| Subject group type                           | Reporting group        | Reporting group        | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 56                     | 45                     | 40                     | 51                     |
| Units: Geometric LS Mean percent change      |                        |                        |                        |                        |
| least squares mean (confidence interval 95%) | -5.78 (-18.44 to 8.84) | 15.96 (-1.29 to 36.23) | -7.57 (-22.03 to 9.57) | -14.3 (-26.3 to -0.33) |

| End point values                             | Odanacatib 50 mg-Ext 1   |  |  |  |
|----------------------------------------------|--------------------------|--|--|--|
| Subject group type                           | Reporting group          |  |  |  |
| Number of subjects analysed                  | 38                       |  |  |  |
| Units: Geometric LS Mean percent change      |                          |  |  |  |
| least squares mean (confidence interval 95%) | -22.49 (-34.96 to -7.64) |  |  |  |

## Statistical analyses

| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-DPyr) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-DPyr) over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
| Number of subjects included in analysis | 94                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.015 <sup>[66]</sup>                |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | -16.71                                 |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -36.03                                 |
| upper limit                             | 2.61                                   |

Notes:

[66] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-DPyr) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-DPyr) over 24 months.

|                   |                                        |
|-------------------|----------------------------------------|
| Comparison groups | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
|-------------------|----------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 107                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | = 0.246 <sup>[67]</sup>           |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | -8.51                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -27.31                            |
| upper limit                             | 10.29                             |

Notes:

[67] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-DPyr) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-DPyr) over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 96                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | -1.79                                  |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -22.66                                 |
| upper limit                             | 19.08                                  |

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone resorption (u-DPyr) compared to placebo over 24 months. The secondary hypothesis states that odanacatib will decrease biochemical indices of bone resorption (u-DPyr) over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 101                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | 21.74                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.32   |
| upper limit         | 44.81   |

## Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum Bone-specific Alkaline Phosphatase [s-BSAP]) at 24 Months

|                 |                                                                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum Bone-specific Alkaline Phosphatase [s-BSAP]) at 24 Months |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares mean of the log-values percentage change from baseline, in biochemical marker of bone turnover (s-BSAP) (relative to baseline) at 24 months.

Analysis used a geometric mean percent change from baseline (back-transformation of a log-transformed fraction from baseline) at Month 24 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP protocol population did not estimate missing data.

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

End point timeframe:

Baseline and 24 months

| End point values                             | Placebo-Ext 1         | Odanacatib 3 mg-Ext 1 | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|-----------------------|-----------------------|------------------------|------------------------|
| Subject group type                           | Reporting group       | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 57                    | 47                    | 42                     | 53                     |
| Units: Geometric LS Mean percent change      |                       |                       |                        |                        |
| least squares mean (confidence interval 95%) | 3.38 (-4.94 to 12.44) | 40.17 (27.8 to 53.73) | 2.99 (-6.57 to 13.54)  | 10.62 (1.4 to 20.69)   |

| End point values                             | Odanacatib 50 mg-Ext 1   |  |  |  |
|----------------------------------------------|--------------------------|--|--|--|
| Subject group type                           | Reporting group          |  |  |  |
| Number of subjects analysed                  | 42                       |  |  |  |
| Units: Geometric LS Mean percent change      |                          |  |  |  |
| least squares mean (confidence interval 95%) | -13.62 (-21.36 to -4.32) |  |  |  |

## Statistical analyses

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg

weekly, and 50 mg weekly on biochemical indices of bone formation (s-BSAP) compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
| Number of subjects included in analysis | 99                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.002 <sup>[68]</sup>                |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | -16.64                                 |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -28.84                                 |
| upper limit                             | -4.44                                  |

Notes:

[68] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-BSAP) compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
| Number of subjects included in analysis | 110                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.852 <sup>[69]</sup>                |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 7.24                                   |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -5.73                                  |
| upper limit                             | 20.21                                  |

Notes:

[69] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-BSAP) compared to placebo over 24 months.

|                   |                                        |
|-------------------|----------------------------------------|
| Comparison groups | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
|-------------------|----------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 99                                |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | -0.39                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -13.69                            |
| upper limit                             | 12.92                             |

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-BSAP) compared to placebo over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 104                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | 36.79                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 21.19                                 |
| upper limit                             | 52.38                                 |

### **Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum N-terminal Propeptide of Type 1 Collagen [s-P1NP]) at 24 Months**

|                 |                                                                                                                                               |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum N-terminal Propeptide of Type 1 Collagen [s-P1NP]) at 24 Months |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Back-transformation (geometric mean) of the least squares mean of the log-values percentage change from baseline, in biochemical marker of bone turnover (s-P1NP) (relative to baseline) at 24 months.

Analysis used a geometric mean percent change from baseline (back-transformation of a log-transformed fraction from baseline) at Month 24 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP protocol population did not estimate missing data.

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

End point timeframe:

Baseline and 24 months

| End point values                             | Placebo-Ext 1          | Odanacatib 3 mg-Ext 1  | Odanacatib 10 mg-Ext 1 | Odanacatib 25 mg-Ext 1 |
|----------------------------------------------|------------------------|------------------------|------------------------|------------------------|
| Subject group type                           | Reporting group        | Reporting group        | Reporting group        | Reporting group        |
| Number of subjects analysed                  | 57                     | 47                     | 42                     | 53                     |
| Units: Geometric LS Mean percent change      |                        |                        |                        |                        |
| least squares mean (confidence interval 95%) | 1.29 (-11.11 to 15.43) | 50.52 (30.37 to 73.79) | 9.07 (-6.28 to 26.93)  | 14.6 (0.08 to 31.23)   |

| End point values                             | Odanacatib 50 mg-Ext 1  |  |  |  |
|----------------------------------------------|-------------------------|--|--|--|
| Subject group type                           | Reporting group         |  |  |  |
| Number of subjects analysed                  | 42                      |  |  |  |
| Units: Geometric LS Mean percent change      |                         |  |  |  |
| least squares mean (confidence interval 95%) | -20.2 (-31.49 to -7.05) |  |  |  |

## Statistical analyses

| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-P1NP) compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 50 mg-Ext 1 |
| Number of subjects included in analysis | 99                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.011 <sup>[70]</sup>                |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | -21.49                                 |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -39.55                                 |
| upper limit                             | -3.43                                  |

Notes:

[70] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

| Statistical analysis title | Difference in Least Squares Means |
|----------------------------|-----------------------------------|
|----------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-P1NP) compared to placebo over 24 months.

|                   |                                        |
|-------------------|----------------------------------------|
| Comparison groups | Placebo-Ext 1 v Odanacatib 25 mg-Ext 1 |
|-------------------|----------------------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 110                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | = 0.618 <sup>[71]</sup>           |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | 13.31                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -7.1                              |
| upper limit                             | 33.71                             |

Notes:

[71] - Significance for secondary endpoints was only declared if there was also significance for the primary endpoint. Multiplicity was addressed through stepdown trend-test approach. Multiplicity for multiple endpoints was handled by Hochberg procedure.

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-P1NP) compared to placebo over 24 months.

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 10 mg-Ext 1 |
| Number of subjects included in analysis | 99                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| Method                                  | ANCOVA                                 |
| Parameter estimate                      | Difference in Least Squares Means      |
| Point estimate                          | 7.77                                   |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -13.46                                 |
| upper limit                             | 29.01                                  |

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Difference in Least Squares Means |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The secondary objective was to assess the effect of odanacatib 3 mg weekly, 10 mg weekly, 25 mg weekly, and 50 mg weekly on biochemical indices of bone formation (s-P1NP) compared to placebo over 24 months.

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| Comparison groups                       | Placebo-Ext 1 v Odanacatib 3 mg-Ext 1 |
| Number of subjects included in analysis | 104                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Method                                  | ANCOVA                                |
| Parameter estimate                      | Difference in Least Squares Means     |
| Point estimate                          | 49.23                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 23.86   |
| upper limit         | 74.59   |

### Secondary: Percentage Change From Baseline in Total Hip BMD at 36 Months

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Total Hip BMD at 36 Months |
|-----------------|---------------------------------------------------------------|

End point description:

Percentage change in Total Hip BMD (relative to baseline) at 36 Months.

This analysis was performed at Month 36 using the PP population, which included participants who took at least one dose of extension study medication and had the necessary follow-up information. Missing values were not imputed. No data were carried forward from Month 30 to 36.

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

End point timeframe:

Baseline and 36 months

| End point values                             | Placebo/Placebo-Ext 2 | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|-----------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group       | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                    | 16                             | 17                            | 12                                     |
| Units: Percent Change                        |                       |                                |                               |                                        |
| least squares mean (confidence interval 95%) | -0.77 (-2.92 to 1.38) | 1.16 (-0.86 to 3.17)           | -0.63 (-2.59 to 1.33)         | 2.75 (0.42 to 5.07)                    |

| End point values                             | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 11                             | 9                                       | 12                             | 19                                      |
| Units: Percent Change                        |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | 0.96 (-1.48 to 3.39)           | 4.61 (1.93 to 7.3)                      | 1.64 (-0.69 to 3.97)           | 5.7 (3.85 to 7.54)                      |

| End point values                             | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 15                             | 17                                      |  |  |
| Units: Percent Change                        |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | -0.48 (-2.56 to                | 5.83 (3.87 to                           |  |  |

|      |      |       |
|------|------|-------|
| 95%) | 1.6) | 7.79) |
|------|------|-------|

## Statistical analyses

|                                         |                                                                          |
|-----------------------------------------|--------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Difference in Least Squares Means                                        |
| Comparison groups                       | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis | 32                                                                       |
| Analysis specification                  | Pre-specified                                                            |
| Analysis type                           | other                                                                    |
| Parameter estimate                      | Difference in Least Squares Means                                        |
| Point estimate                          | 6.31                                                                     |
| Confidence interval                     |                                                                          |
| level                                   | 95 %                                                                     |
| sides                                   | 2-sided                                                                  |
| lower limit                             | 3.44                                                                     |
| upper limit                             | 9.17                                                                     |

## Secondary: Percentage Change From Baseline in Femoral Neck BMD at 36 Months

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Femoral Neck BMD at 36 Months |
|-----------------|------------------------------------------------------------------|

End point description:

Percentage change in femoral neck BMD (relative to baseline) at 36 months.

This analysis was performed at Month 36 using the PP population, which included participants who took at least one dose of extension study medication and had the necessary follow-up information. Missing values were not imputed. No data were carried forward from Month 30 to 36.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 36 months |           |

| End point values                             | Placebo/Placebo-Ext 2 | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|-----------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group       | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                    | 16                             | 17                            | 12                                     |
| Units: Percent Change                        |                       |                                |                               |                                        |
| least squares mean (confidence interval 95%) | -0.52 (-2.67 to 1.63) | 1.03 (-0.98 to 3.04)           | -1.04 (-2.99 to 0.92)         | 2.26 (-0.06 to 4.59)                   |

| End point values | Odanacatib 10 | Odanacatib 10 | Odanacatib 25 | Odanacatib 25 |
|------------------|---------------|---------------|---------------|---------------|
|------------------|---------------|---------------|---------------|---------------|

|                                              | mg/Placebo-<br>Ext 2 | mg/Odanacatib<br>50 mg-Ext 2 | mg/Placebo-<br>Ext 2 | mg/Odanacatib<br>50 mg-Ext 2 |
|----------------------------------------------|----------------------|------------------------------|----------------------|------------------------------|
| Subject group type                           | Reporting group      | Reporting group              | Reporting group      | Reporting group              |
| Number of subjects analysed                  | 11                   | 9                            | 12                   | 19                           |
| Units: Percent Change                        |                      |                              |                      |                              |
| least squares mean (confidence interval 95%) | -0.14 (-2.57 to 2.3) | 5.06 (2.38 to 7.74)          | 0.8 (-1.52 to 3.13)  | 7.23 (5.38 to 9.07)          |

|                                              |                                |                                         |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| <b>End point values</b>                      | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 15                             | 17                                      |  |  |
| Units: Percent Change                        |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | 2.26 (0.19 to 4.34)            | 4.97 (3.01 to 6.93)                     |  |  |

### Statistical analyses

|                                         |                                                                          |
|-----------------------------------------|--------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Difference in Least Squares Means                                        |
| Comparison groups                       | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis | 32                                                                       |
| Analysis specification                  | Pre-specified                                                            |
| Analysis type                           | other                                                                    |
| Parameter estimate                      | Difference in Least Squares Means                                        |
| Point estimate                          | 2.71                                                                     |
| Confidence interval                     |                                                                          |
| level                                   | 95 %                                                                     |
| sides                                   | 2-sided                                                                  |
| lower limit                             | -0.16                                                                    |
| upper limit                             | 5.57                                                                     |

### Secondary: Percentage Change From Baseline in Trochanter BMD at 36 Months

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Trochanter BMD at 36 Months |
|-----------------|----------------------------------------------------------------|

End point description:

Percentage change in trochanter BMD (relative to baseline) at 36 months.

This analysis was performed at Month 36 using the PP population, which included participants who took at least one dose of extension study medication and had the necessary follow-up information. Missing values were not imputed. No data were carried forward from Month 30 to 36.

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

End point timeframe:

Baseline and 36 months

| <b>End point values</b>                      | Placebo/Placebo-Ext 2 | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|-----------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group       | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                    | 16                             | 17                            | 12                                     |
| Units: Percent Change                        |                       |                                |                               |                                        |
| least squares mean (confidence interval 95%) | -0.46 (-3.71 to 2.79) | 2.32 (-0.72 to 5.36)           | -1.04 (-4 to 1.92)            | 4.53 (1.01 to 8.04)                    |

| <b>End point values</b>                      | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 11                             | 9                                       | 12                             | 19                                      |
| Units: Percent Change                        |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | 0.66 (-3.02 to 4.34)           | 8.21 (4.16 to 12.27)                    | 1.14 (-2.38 to 4.65)           | 7.97 (5.18 to 10.76)                    |

| <b>End point values</b>                      | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 15                             | 17                                      |  |  |
| Units: Percent Change                        |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | -0.69 (-3.83 to 2.46)          | 7.44 (4.48 to 10.41)                    |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>       | Difference in Least Squares Means                                        |
|-----------------------------------------|--------------------------------------------------------------------------|
| Comparison groups                       | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis | 32                                                                       |
| Analysis specification                  | Pre-specified                                                            |
| Analysis type                           | other                                                                    |
| Parameter estimate                      | Difference in Least Squares Means                                        |
| Point estimate                          | 8.13                                                                     |
| Confidence interval                     |                                                                          |
| level                                   | 95 %                                                                     |
| sides                                   | 2-sided                                                                  |
| lower limit                             | 3.8                                                                      |
| upper limit                             | 12.46                                                                    |

---

**Secondary: Percentage Change From Baseline in Total Body BMD at 36 Months**

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|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Total Body BMD at 36 Months |
|-----------------|----------------------------------------------------------------|

End point description:

Percentage change in total body BMD (relative to baseline) at 36 months.

This analysis was performed at Month 36 using the PP population, which included participants who took at least one dose of extension study medication and had the necessary follow-up information. Missing values were not imputed. No data were carried forward from Month 30 to 36.

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

End point timeframe:

Baseline and 36 months

---

| End point values                                | Placebo/Placebo-<br>o-Ext 2 | Placebo/Odana-<br>catib 50 mg-<br>Ext 2 | Odanacatib 3<br>mg/Placebo-<br>Ext 2 | Odanacatib 3<br>mg/Odanacatib<br>50 mg-Ext 2 |
|-------------------------------------------------|-----------------------------|-----------------------------------------|--------------------------------------|----------------------------------------------|
| Subject group type                              | Reporting group             | Reporting group                         | Reporting group                      | Reporting group                              |
| Number of subjects analysed                     | 14                          | 14                                      | 16                                   | 13                                           |
| Units: Percent Change                           |                             |                                         |                                      |                                              |
| least squares mean (confidence interval<br>95%) | 0.13 (-2.12 to<br>2.38)     | -2.2 (-4.45 to<br>0.05)                 | -3.63 (-5.74 to<br>-1.52)            | 0.28 (-2.07 to<br>2.62)                      |

| End point values                                | Odanacatib 10<br>mg/Placebo-<br>Ext 2 | Odanacatib 10<br>mg/Odanacatib<br>50 mg-Ext 2 | Odanacatib 25<br>mg/Placebo-<br>Ext 2 | Odanacatib 25<br>mg/Odanacatib<br>50 mg-Ext 2 |
|-------------------------------------------------|---------------------------------------|-----------------------------------------------|---------------------------------------|-----------------------------------------------|
| Subject group type                              | Reporting group                       | Reporting group                               | Reporting group                       | Reporting group                               |
| Number of subjects analysed                     | 12                                    | 9                                             | 12                                    | 18                                            |
| Units: Percent Change                           |                                       |                                               |                                       |                                               |
| least squares mean (confidence interval<br>95%) | -2.28 (-4.71 to<br>0.15)              | -1.22 (-4.03 to<br>1.58)                      | -0.85 (-3.29 to<br>1.58)              | 0.56 (-1.43 to<br>2.54)                       |

| End point values                                | Odanacatib 50<br>mg/Placebo-<br>Ext 2 | Odanacatib 50<br>mg/Odanacatib<br>50 mg-Ext 2 |  |  |
|-------------------------------------------------|---------------------------------------|-----------------------------------------------|--|--|
| Subject group type                              | Reporting group                       | Reporting group                               |  |  |
| Number of subjects analysed                     | 15                                    | 17                                            |  |  |
| Units: Percent Change                           |                                       |                                               |  |  |
| least squares mean (confidence interval<br>95%) | -1.84 (-4.02 to<br>0.34)              | -0.38 (-2.43 to<br>1.67)                      |  |  |

## Statistical analyses

|                                         |                                                                          |
|-----------------------------------------|--------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Difference in Least Squares Means                                        |
| Comparison groups                       | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis | 32                                                                       |
| Analysis specification                  | Pre-specified                                                            |
| Analysis type                           | other                                                                    |
| Parameter estimate                      | Difference in Least Squares Means                                        |
| Point estimate                          | 1.46                                                                     |
| Confidence interval                     |                                                                          |
| level                                   | 95 %                                                                     |
| sides                                   | 2-sided                                                                  |
| lower limit                             | -1.54                                                                    |
| upper limit                             | 4.46                                                                     |

## Secondary: Percentage Change From Baseline in Distal Forearm BMD at 36 Months

|                 |                                                                    |
|-----------------|--------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Distal Forearm BMD at 36 Months |
|-----------------|--------------------------------------------------------------------|

End point description:

Percentage change in distal forearm BMD (relative to baseline) at 36 months.

This analysis was performed at Month 36 using the PP population, which included participants who took at least one dose of extension study medication and had the necessary follow-up information. Missing values were not imputed. No data were carried forward from Month 30 to 36.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 36 months |           |

|                                              |                       |                                |                               |                                        |
|----------------------------------------------|-----------------------|--------------------------------|-------------------------------|----------------------------------------|
| <b>End point values</b>                      | Placebo/Placebo-Ext 2 | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
| Subject group type                           | Reporting group       | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                    | 15                             | 16                            | 13                                     |
| Units: Percent Change                        |                       |                                |                               |                                        |
| least squares mean (confidence interval 95%) | -2.08 (-4.6 to 0.43)  | -4.04 (-6.47 to -1.61)         | -6.59 (-8.95 to -4.23)        | -6.34 (-8.96 to -3.73)                 |

|                                              |                                |                                         |                                |                                         |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| <b>End point values</b>                      | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 12                             | 10                                      | 12                             | 18                                      |
| Units: Percent Change                        |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | -1.74 (-4.46 to 0.97)          | -3.74 (-6.71 to -0.76)                  | -2.39 (-5.11 to 0.32)          | 0.53 (-1.69 to 2.74)                    |

|                                              |                                |                                         |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| <b>End point values</b>                      | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 14                             | 17                                      |  |  |
| Units: Percent Change                        |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | -2.73 (-5.25 to -0.22)         | -0.26 (-2.55 to 2.03)                   |  |  |

## Statistical analyses

|                                           |                                                                          |
|-------------------------------------------|--------------------------------------------------------------------------|
| <b>Statistical analysis title</b>         | Difference in Least Squares Means                                        |
| Statistical analysis description:<br>test |                                                                          |
| Comparison groups                         | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis   | 31                                                                       |
| Analysis specification                    | Pre-specified                                                            |
| Analysis type                             | other                                                                    |
| Parameter estimate                        | Difference in Least Squares Means                                        |
| Point estimate                            | 2.47                                                                     |
| Confidence interval                       |                                                                          |
| level                                     | 95 %                                                                     |
| sides                                     | 2-sided                                                                  |
| lower limit                               | -0.93                                                                    |
| upper limit                               | 5.88                                                                     |

## Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary N-telopeptides of Type I Collagen [u-NTx]) at 36 Months

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary N-telopeptides of Type I Collagen [u-NTx]) at 36 Months |
| End point description:<br>Geometric mean percentage change from baseline in biochemical marker of bone turnover (urinary N-telopeptides of Type I collagen [u-NTx]) at 36 months.<br><br>This analysis was geometric mean percent change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 36, using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP approach did not estimate missing data. |                                                                                                                                         |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Secondary                                                                                                                               |
| End point timeframe:<br>Baseline and 36 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                         |

| End point values                             | Placebo/Placebo-Ext 2    | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group          | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                       | 15                             | 13                            | 16                                     |
| Units: Geometric Mean Percent Change         |                          |                                |                               |                                        |
| least squares mean (confidence interval 95%) | -17.43 (-39.06 to 11.86) | -55.12 (-66.51 to 39.85)       | -11.9 (-35.76 to 20.83)       | -57.17 (-67.75 to -43.12)              |

| End point values                             | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 13                             | 11                                      | 10                             | 18                                      |
| Units: Geometric Mean Percent Change         |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | -12.15 (-35.91 to 20.43)       | -49.1 (-63.88 to -28.27)                | 14.26 (-20.17 to 63.53)        | -52.11 (-63.33 to -37.45)               |

| End point values                             | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 14                             | 17                                      |  |  |
| Units: Geometric Mean Percent Change         |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | 27.55 (-5.86 to 72.8)          | -50.51 (-62.44 to -34.81)               |  |  |

## Statistical analyses

| Statistical analysis title              | Difference in Least Squares Means                                        |
|-----------------------------------------|--------------------------------------------------------------------------|
| Comparison groups                       | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis | 31                                                                       |
| Analysis specification                  | Pre-specified                                                            |
| Analysis type                           | other                                                                    |
| Parameter estimate                      | Difference in Least Squares Means                                        |
| Point estimate                          | -78.06                                                                   |
| Confidence interval                     |                                                                          |
| level                                   | 95 %                                                                     |
| sides                                   | 2-sided                                                                  |
| lower limit                             | -119.2                                                                   |
| upper limit                             | -36.92                                                                   |

## Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum C-telopeptides of Type 1 Collagen [s-CTx]) at 36 Months

|                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                       | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum C-telopeptides of Type 1 Collagen [s-CTx]) at 36 Months |
| End point description:                                                                                                                                                                                                                                                                                                                |                                                                                                                                       |
| Geometric mean percentage change from baseline in biochemical marker of bone turnover (serum C-telopeptides of Type 1 collagen [s-CTx]) at 36 Months.                                                                                                                                                                                 |                                                                                                                                       |
| This analysis was geometric mean percent change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 36 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP approach did not estimate missing data. |                                                                                                                                       |
| End point type                                                                                                                                                                                                                                                                                                                        | Secondary                                                                                                                             |
| End point timeframe:                                                                                                                                                                                                                                                                                                                  |                                                                                                                                       |
| Baseline and 36 months                                                                                                                                                                                                                                                                                                                |                                                                                                                                       |

| End point values                             | Placebo/Placebo-Ext 2   | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|-------------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group         | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                      | 15                             | 13                            | 16                                     |
| Units: Geometric Mean Percent Change         |                         |                                |                               |                                        |
| least squares mean (confidence interval 95%) | -0.09 (-28.93 to 40.46) | -41.3 (-57.74 to -18.47)       | -4.69 (-33.13 to 35.85)       | -44.62 (-59.72 to -23.88)              |

| End point values                             | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 13                             | 11                                      | 9                              | 18                                      |
| Units: Geometric Mean Percent Change         |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | 18.24 (-16.98 to 68.41)        | -26.26 (-49.81 to 8.33)                 | 61.14 (5.5 to 146.12)          | -36.71 (-53.09 to -14.6)                |

| End point values                             | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 14                             | 17                                      |  |  |
| Units: Geometric Mean Percent Change         |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | 10.32 (-21.52 to 55.1)         | -23.93 (-44.15 to 3.63)                 |  |  |

## Statistical analyses

|                            |                                                                          |
|----------------------------|--------------------------------------------------------------------------|
| Statistical analysis title | Difference in Least Squares Means                                        |
| Comparison groups          | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 31                                |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | -34.25                            |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -78.7                             |
| upper limit                             | 10.2                              |

### Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary Total Deoxypyridinolines [u-DPyr]) at 36 Months

|                 |                                                                                                                                 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Urinary Total Deoxypyridinolines [u-DPyr]) at 36 Months |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

Geometric mean percentage change from baseline in Biochemical marker of bone turnover (urinary total deoxypyridinolines [u-DPyr]) at 36 months.

This analysis was geometric mean percent change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 36 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP approach did not estimate missing data.

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

End point timeframe:

Baseline and 36 months

| End point values                             | Placebo/Placebo-Ext 2    | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group          | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                       | 15                             | 13                            | 14                                     |
| Units: Geometric Mean Percent Change         |                          |                                |                               |                                        |
| least squares mean (confidence interval 95%) | -18.69 (-41.68 to 13.36) | -14.95 (-38.27 to 17.18)       | -7.82 (-34.76 to 30.26)       | -26.27 (-47.1 to 2.76)                 |

| End point values                             | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 13                             | 11                                      | 10                             | 18                                      |
| Units: Geometric Mean Percent Change         |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | -4.69 (-32.51 to 34.6)         | 0.43 (-31 to 46.19)                     | -9.16 (-38.64 to 34.48)        | -16.41 (-37.59 to 11.97)                |

|                                              |                                |                                         |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| <b>End point values</b>                      | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 14                             | 17                                      |  |  |
| Units: Geometric Mean Percent Change         |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | 22.41 (-12.2 to 70.66)         | -16.84 (-38.49 to 12.45)                |  |  |

## Statistical analyses

|                                         |                                                                          |
|-----------------------------------------|--------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Difference in Least Squares Means                                        |
| Comparison groups                       | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis | 31                                                                       |
| Analysis specification                  | Pre-specified                                                            |
| Analysis type                           | superiority                                                              |
| Parameter estimate                      | Difference in Least Squares Means                                        |
| Point estimate                          | -39.25                                                                   |
| Confidence interval                     |                                                                          |
| level                                   | 95 %                                                                     |
| sides                                   | 2-sided                                                                  |
| lower limit                             | -87.17                                                                   |
| upper limit                             | 8.68                                                                     |

## Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum Bone-specific Alkaline Phosphatase [s-BSAP]) at 36 Months

|                 |                                                                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum Bone-specific Alkaline Phosphatase [s-BSAP]) at 36 Months |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Geometric mean percentage change from baseline, in biochemical marker of bone turnover (serum bone-specific alkaline phosphatase [s-BSAP]) at 36 months.

This analysis was geometric mean percentage change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 36 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP approach did not estimate missing data.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 36 months |           |

| End point values                             | Placebo/Placebo-Ext 2 | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|-----------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group       | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                    | 16                             | 14                            | 16                                     |
| Units: Geometric Mean Percent Change         |                       |                                |                               |                                        |
| least squares mean (confidence interval 95%) | 7.73 (-7.32 to 25.24) | 10.86 (-3.69 to 27.62)         | 14.26 (-1.77 to 32.91)        | 9.13 (-5.2 to 25.62)                   |

| End point values                             | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 13                             | 11                                      | 12                             | 18                                      |
| Units: Geometric Mean Percent Change         |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | 12.95 (-3.41 to 32.08)         | 8.49 (-8.48 to 28.62)                   | 33.74 (13.71 to 57.31)         | 11.12 (-2.67 to 26.86)                  |

| End point values                             | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 14                             | 17                                      |  |  |
| Units: Geometric Mean Percent Change         |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | 1.3 (-12.85 to 17.76)          | 17.9 (2.83 to 35.17)                    |  |  |

## Statistical analyses

| Statistical analysis title              | Difference in Least Squares Means                                        |
|-----------------------------------------|--------------------------------------------------------------------------|
| Comparison groups                       | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis | 31                                                                       |
| Analysis specification                  | Pre-specified                                                            |
| Analysis type                           | other                                                                    |
| Parameter estimate                      | Difference in Least Squares Means                                        |
| Point estimate                          | 16.59                                                                    |
| Confidence interval                     |                                                                          |
| level                                   | 95 %                                                                     |
| sides                                   | 2-sided                                                                  |
| lower limit                             | -5.67                                                                    |
| upper limit                             | 38.85                                                                    |

## Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum N-terminal Propeptide of Type 1 Collagen [s-P1NP]) at 36 Months

|                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                        | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum N-terminal Propeptide of Type 1 Collagen [s-P1NP]) at 36 Months |
| End point description:                                                                                                                                                                                                                                                                                                                 |                                                                                                                                               |
| Geometric mean percentage change from baseline in biochemical marker of bone turnover (serum N-terminal propeptide of Type 1 collagen [s-P1NP]) at 36 months.                                                                                                                                                                          |                                                                                                                                               |
| This analysis was geometric mean percentage change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 36 using a PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP approach did not estimate missing data. |                                                                                                                                               |
| End point type                                                                                                                                                                                                                                                                                                                         | Secondary                                                                                                                                     |
| End point timeframe:                                                                                                                                                                                                                                                                                                                   |                                                                                                                                               |
| Baseline and 36 months                                                                                                                                                                                                                                                                                                                 |                                                                                                                                               |

| End point values                             | Placebo/Placebo-Ext 2   | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|-------------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group         | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                      | 16                             | 14                            | 15                                     |
| Units: Geometric Mean Percent Change         |                         |                                |                               |                                        |
| least squares mean (confidence interval 95%) | -20.79 (-40.08 to 4.72) | -18.79 (-37.44 to 5.42)        | -13.11 (-34.35 to 15)         | -21.08 (-39.75 to 3.37)                |

| End point values                             | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 13                             | 11                                      | 12                             | 18                                      |
| Units: Geometric Mean Percent Change         |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | 8.58 (-18.75 to 45.11)         | 12.44 (-17.98 to 54.13)                 | 22.57 (-9.27 to 65.59)         | -8.14 (-28.14 to 17.42)                 |

| End point values                             | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 14                             | 17                                      |  |  |
| Units: Geometric Mean Percent Change         |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | -0.77 (-24.94 to 31.18)        | -6.2 (-27.2 to 20.86)                   |  |  |

## Statistical analyses

|                            |                                                                          |
|----------------------------|--------------------------------------------------------------------------|
| Statistical analysis title | Difference in Least Squares Means                                        |
| Comparison groups          | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 31                                |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| Parameter estimate                      | Difference in Least Squares Means |
| Point estimate                          | -5.43                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -42.04                            |
| upper limit                             | 31.18                             |

### Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum Bone Tartrate-resistant Acid Phosphatase Isoform 5b [TRAP 5b]) at 36 Months

|                 |                                                                                                                                                           |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum Bone Tartrate-resistant Acid Phosphatase Isoform 5b [TRAP 5b]) at 36 Months |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Geometric mean percentage change from baseline in biochemical marker of bone turnover (serum bone tartrate-resistant acid phosphatase isoform 5b [TRAP 5b]) at 36 months.

This analysis was geometric mean percent change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 36 using the PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP approach did not estimate missing data.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 36 months |           |

| End point values                             | Placebo/Placebo-Ext 2  | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|------------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group        | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 10                     | 11                             | 10                            | 12                                     |
| Units: Geometric Mean Percent Change         |                        |                                |                               |                                        |
| least squares mean (confidence interval 95%) | 52.98 (29.87 to 80.21) | 52.37 (30.34 to 78.12)         | 33.25 (13.12 to 56.97)        | 59.37 (37.24 to 85.08)                 |

| End point values                             | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 10                             | 9                                       | 10                             | 15                                      |
| Units: Geometric Mean Percent Change         |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | 56.71 (33.04 to 84.6)          | 82.94 (53.93 to 117.42)                 | 56.42 (32.79 to 84.26)         | 77.9 (55.63 to 103.36)                  |

|                                              |                                |                                         |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| <b>End point values</b>                      | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 10                             | 15                                      |  |  |
| Units: Geometric Mean Percent Change         |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | 47.61 (25.3 to 73.88)          | 96.7 (72.08 to 124.85)                  |  |  |

## Statistical analyses

|                                         |                                                                          |
|-----------------------------------------|--------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Difference in Least Squares Means                                        |
| Comparison groups                       | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis | 25                                                                       |
| Analysis specification                  | Pre-specified                                                            |
| Analysis type                           | other                                                                    |
| Parameter estimate                      | Difference in Least Squares Means                                        |
| Point estimate                          | 49.1                                                                     |
| Confidence interval                     |                                                                          |
| level                                   | 95 %                                                                     |
| sides                                   | 2-sided                                                                  |
| lower limit                             | 13.37                                                                    |
| upper limit                             | 84.83                                                                    |

## Secondary: Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum Cross-linked Carboxyterminal Telopeptides of Type I Collagen [1-CTP]) at 36 Months

|                 |                                                                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change From Baseline in Biochemical Marker of Bone Turnover (Serum Cross-linked Carboxyterminal Telopeptides of Type I Collagen [1-CTP]) at 36 Months |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Geometric mean percentage change from baseline in biochemical marker of bone turnover (serum cross-linked carboxyterminal telopeptides of Type I collagen [1-CTP]) at 36 Months.

This analysis was geometric mean percentage change from baseline (which is a back-transformation of a log-transformed fraction from baseline) at Month 36 using a PP population, from which participants with important protocol deviations and major protocol violators were excluded. The PP approach did not estimate missing data.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline and 36 months |           |

| End point values                             | Placebo/Placebo-Ext 2 | Placebo/Odanacatib 50 mg-Ext 2 | Odanacatib 3 mg/Placebo-Ext 2 | Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|-----------------------|--------------------------------|-------------------------------|----------------------------------------|
| Subject group type                           | Reporting group       | Reporting group                | Reporting group               | Reporting group                        |
| Number of subjects analysed                  | 14                    | 13                             | 14                            | 16                                     |
| Units: Geometric Mean Percent Change         |                       |                                |                               |                                        |
| least squares mean (confidence interval 95%) | 7.4 (-16.78 to 38.6)  | 193.91 (125.61 to 282.89)      | 1.67 (-21.41 to 31.53)        | 187.37 (126.25 to 264.99)              |

| End point values                             | Odanacatib 10 mg/Placebo-Ext 2 | Odanacatib 10 mg/Odanacatib 50 mg-Ext 2 | Odanacatib 25 mg/Placebo-Ext 2 | Odanacatib 25 mg/Odanacatib 50 mg-Ext 2 |
|----------------------------------------------|--------------------------------|-----------------------------------------|--------------------------------|-----------------------------------------|
| Subject group type                           | Reporting group                | Reporting group                         | Reporting group                | Reporting group                         |
| Number of subjects analysed                  | 12                             | 11                                      | 11                             | 19                                      |
| Units: Geometric Mean Percent Change         |                                |                                         |                                |                                         |
| least squares mean (confidence interval 95%) | 58.76 (20.27 to 109.56)        | 188.5 (116.34 to 284.74)                | 77.94 (33.46 to 137.24)        | 231.93 (166.74 to 313.05)               |

| End point values                             | Odanacatib 50 mg/Placebo-Ext 2 | Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |  |  |
|----------------------------------------------|--------------------------------|-----------------------------------------|--|--|
| Subject group type                           | Reporting group                | Reporting group                         |  |  |
| Number of subjects analysed                  | 15                             | 18                                      |  |  |
| Units: Geometric Mean Percent Change         |                                |                                         |  |  |
| least squares mean (confidence interval 95%) | 27.2 (-0.61 to 62.79)          | 236.64 (168.69 to 321.76)               |  |  |

## Statistical analyses

| Statistical analysis title              | Difference in Least Squares Means                                        |
|-----------------------------------------|--------------------------------------------------------------------------|
| Comparison groups                       | Odanacatib 50 mg/Placebo-Ext 2 v Odanacatib 50 mg/Odanacatib 50 mg-Ext 2 |
| Number of subjects included in analysis | 33                                                                       |
| Analysis specification                  | Pre-specified                                                            |
| Analysis type                           | other                                                                    |
| Parameter estimate                      | Difference in Least Squares Means                                        |
| Point estimate                          | 209.44                                                                   |
| Confidence interval                     |                                                                          |
| level                                   | 95 %                                                                     |
| sides                                   | 2-sided                                                                  |
| lower limit                             | 127.14                                                                   |
| upper limit                             | 291.73                                                                   |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events data were collected up to 120 months (from start of study medication, up to 14 days after the last dose).

Adverse event reporting additional description:

The Safety Analysis was based on the All Participants as Treated (APaT) population, which included all participants who took at least one dose of study medication.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 10.1 |
|--------------------|------|

### Reporting groups

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Years 1-2 Placebo/Placebo-Ext 1 |
|-----------------------|---------------------------------|

Reporting group description:

One placebo tablet once a week

|                       |                                                 |
|-----------------------|-------------------------------------------------|
| Reporting group title | Years 1-2 Odanacatib 3 mg/Odanacatib 3 mg-Ext 1 |
|-----------------------|-------------------------------------------------|

Reporting group description:

One odanacatib 3 mg tablet once a week

|                       |                                                   |
|-----------------------|---------------------------------------------------|
| Reporting group title | Years 1-2 Odanacatib 10 mg/Odanacatib 10 mg-Ext 1 |
|-----------------------|---------------------------------------------------|

Reporting group description:

One odanacatib 10 mg tablet once a week

|                       |                                                   |
|-----------------------|---------------------------------------------------|
| Reporting group title | Years 1-2 Odanacatib 25 mg/Odanacatib 25 mg-Ext 1 |
|-----------------------|---------------------------------------------------|

Reporting group description:

One odanacatib 25 mg tablet once a week

|                       |                                                   |
|-----------------------|---------------------------------------------------|
| Reporting group title | Years 1-2 Odanacatib 50 mg/Odanacatib 50 mg-Ext 1 |
|-----------------------|---------------------------------------------------|

Reporting group description:

One odanacatib 50 mg tablet once a week

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Year 3 Placebo/Placebo-Ext 2 |
|-----------------------|------------------------------|

Reporting group description:

During this 12-month extension (Year 3), participants in this treatment group took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one placebo tablet once a week for 2 years.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Year 3 Placebo/Odanacatib 50 mg-Ext 2 |
|-----------------------|---------------------------------------|

Reporting group description:

During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one placebo tablet once a week for 2 years.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Year 3 Odanacatib 3 mg/Placebo-Ext 2 |
|-----------------------|--------------------------------------|

Reporting group description:

During this 12-month extension (Year 3), participants took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one 3 mg tablet of odanacatib once a week for 2 years.

|                       |                                               |
|-----------------------|-----------------------------------------------|
| Reporting group title | Year 3 Odanacatib 3 mg/Odanacatib 50 mg-Ext 2 |
|-----------------------|-----------------------------------------------|

Reporting group description:

During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one 3 mg tablet of odanacatib once a week for 2 years.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Year 3 Odanacatib 10 mg/Placebo-Ext 2 |
|-----------------------|---------------------------------------|

Reporting group description:

During this 12-month extension (Year 3), participants took one placebo tablet once a week. Before entering this extension, participants had taken one 10 mg tablet of odanacatib once a week for 2 years.

|                                                                                                                                                                                                                                                                                                                                         |                                                  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Year 3 Odanacatib 10 mg/Odanacatib 50 mg-Ext 2   |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group took one 10 mg tablet of odanacatib once a week for 2 years.                                                                                                |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Year 3 Odanacatib 25 mg/Placebo-Ext 2            |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| During this 12-month extension (Year 3), participants in this treatment group took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one 25 mg tablet of odanacatib once a week for 2 years.                                                                               |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Year 3 Odanacatib 25 mg/Odanacatib 50 mg-Ext 2   |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one 25 mg tablet of odanacatib once a week for 2 years.                                                                                           |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Year 3 Odanacatib 50 mg/Placebo-Ext 2            |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| During this 12-month extension (Year 3), participants in this treatment group took one placebo tablet once a week. Before entering this extension, participants in this treatment group had taken one 50 mg tablet of odanacatib once a week for 2 years.                                                                               |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Year 3 Odanacatib 50 mg/Odanacatib 50 mg-Ext 2   |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| During this 12-month extension (Year 3), participants took one 50 mg tablet of odanacatib once a week. Before entering this extension, participants in this treatment group had taken one 50 mg tablet of odanacatib once a week for 2 years.                                                                                           |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Years 4-5 Combined Group A.1: Odanacatib 50 mg   |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| Combined Group A.1 consists of participants who received odanacatib 50 mg once a week during Year 3. During this 24-month extension (Years 4-5), these participants continued to receive odanacatib 50 mg once a week.                                                                                                                  |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Years 4-5 Combined Group A.2: Odanacatib 50 mg   |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| Combined Group A.2 consists of participants who received placebo or odanacatib 3 mg in Years 1, 2 and 3. During this 24-month extension (Years 4-5), these participants received odanacatib 50 mg once a week.                                                                                                                          |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Years 4-5 Combined Group A.3: Placebo            |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| Combined Group A.3 consists of participants who, during this 24-month extension (Years 4-5), received placebo once a week.                                                                                                                                                                                                              |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Years 6-10 Group A: Odanacatib 50 mg once weekly |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| Group A consists of a combination of participants who were treated with odanacatib 25 mg for 2 years, then odanacatib 50 mg for 8 years; and participants who were treated with odanacatib 50 mg for 10 years.                                                                                                                          |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Years 6-10 Group B: Odanacatib 50 mg once weekly |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| Group B consists of a combination participants who were treated with placebo for 2 years, then odanacatib 50 mg for 8 years; participants who were treated with odanacatib 3 mg for 2 years, then odanacatib 50 mg for 8 years; and participants who were treated with odanacatib 10 mg for 2 years, then odanacatib 50 mg for 8 years. |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Years 6-10 Group C: Odanacatib 50 mg once weekly |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| Group C consists of a combination of participants who were treated with placebo for 3 years, then odanacatib 50 mg for 7 years; and participants who were treated with odanacatib 3 mg for 2 years, then placebo for 1 year, then odanacatib 50 mg for 7 years.                                                                         |                                                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                   | Years 6-10 Group D: Odanacatib 50 mg once weekly |
| Reporting group description:                                                                                                                                                                                                                                                                                                            |                                                  |
| Group D consists of a combination of participants who were treated with odanacatib 10 mg for 2 years, then placebo for 3 years, then odanacatib 50 mg for 5 years; participants who were treated with                                                                                                                                   |                                                  |

odanacatib 25 mg for 5 years, then placebo for 3 years, then odanacatib 50 mg for 5 years; and participants who were treated with odanacatib 50 mg for 2 years, then placebo for 3 years, then odanacatib 50 mg for 5 years.

| <b>Serious adverse events</b>                                       | Years 1-2<br>Placebo/Placebo-Ext<br>1 | Years 1-2<br>Odanacatib 3<br>mg/Odanacatib 3<br>mg-Ext 1 | Years 1-2<br>Odanacatib 10<br>mg/Odanacatib 10<br>mg-Ext 1 |
|---------------------------------------------------------------------|---------------------------------------|----------------------------------------------------------|------------------------------------------------------------|
| Total subjects affected by serious adverse events                   |                                       |                                                          |                                                            |
| subjects affected / exposed                                         | 8 / 83 (9.64%)                        | 12 / 82 (14.63%)                                         | 10 / 77 (12.99%)                                           |
| number of deaths (all causes)                                       | 0                                     | 0                                                        | 0                                                          |
| number of deaths resulting from adverse events                      |                                       |                                                          |                                                            |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                       |                                                          |                                                            |
| Anal Cancer                                                         |                                       |                                                          |                                                            |
| subjects affected / exposed                                         | 0 / 83 (0.00%)                        | 0 / 82 (0.00%)                                           | 0 / 77 (0.00%)                                             |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                                    | 0 / 0                                                      |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                                    | 0 / 0                                                      |
| Basal Cell Carcinoma                                                |                                       |                                                          |                                                            |
| subjects affected / exposed                                         | 1 / 83 (1.20%)                        | 1 / 82 (1.22%)                                           | 0 / 77 (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                                                      |
| Breast Cancer                                                       |                                       |                                                          |                                                            |
| subjects affected / exposed                                         | 0 / 83 (0.00%)                        | 0 / 82 (0.00%)                                           | 1 / 77 (1.30%)                                             |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                                    | 0 / 1                                                      |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                                    | 0 / 0                                                      |
| Breast Cancer In Situ                                               |                                       |                                                          |                                                            |
| subjects affected / exposed                                         | 0 / 83 (0.00%)                        | 1 / 82 (1.22%)                                           | 0 / 77 (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                                                      |
| Multiple Myeloma                                                    |                                       |                                                          |                                                            |
| subjects affected / exposed                                         | 0 / 83 (0.00%)                        | 0 / 82 (0.00%)                                           | 1 / 77 (1.30%)                                             |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                                    | 0 / 1                                                      |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                                    | 0 / 0                                                      |
| Non-Hodgkin's Lymphoma                                              |                                       |                                                          |                                                            |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Papillary Thyroid Cancer                        |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sarcoma                                         |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous Cell Carcinoma                         |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Cancer Metastatic                         |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian Neoplasm                                |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Adenoma                                   |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neurilemmoma Benign                             |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bowen's disease                                 |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive breast carcinoma                       |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive ductal breast carcinoma                |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma                              |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma in situ                      |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatic carcinoma metastatic                 |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous cell carcinoma of skin                 |                |                |                |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                                   |                |                |                |
| Hypertension                                         |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 2 / 77 (2.60%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 2          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Orthostatic Hypotension                              |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypotension                                          |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Chest Pain                                           |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders             |                |                |                |
| Genital Prolapse                                     |                |                |                |
| subjects affected / exposed                          | 2 / 83 (2.41%) | 0 / 82 (0.00%) | 0 / 77 (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          |
| Ovarian cyst                                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst torsion                            |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Uterine prolapse                                |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vaginal prolapse                                |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic Obstructive Pulmonary Disease           |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Electrocardiogram ST-T Change                   |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 83 (1.20%) | 0 / 82 (0.00%) | 0 / 77 (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          |
| Weight Decreased                                |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Hip Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Joint Dislocation                               |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Vertebral Fracture                       |                |                |                |
| subjects affected / exposed                     | 1 / 83 (1.20%) | 0 / 82 (0.00%) | 0 / 77 (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          |
| Post Procedural Bile Leak                       |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Head Injury                                     |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ankle Fracture                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fall                                            |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rib Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Femur fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Incarcerated incisional hernia                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Scar                                            |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary retention postoperative                 |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Arteriospasm Coronary                           |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure Congestive                      |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Occlusion                       |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 0 / 77 (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          |
| Myocardial Infarction                           |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atrial Fibrillation                             |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Disease                         |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Palpitations                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Reversible Ischaemic Neurological Deficit       |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 1 / 77 (1.30%) |
| 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                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Facial Palsy                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sciatica                                        |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebral infarction                             |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dementia Alzheimer's type                       |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Headache                                        |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nerve root compression                          |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Paraesthesia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Presyncope                                      |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Immune Thrombocytopenic Purpura                 |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear and labyrinth disorders                     |                |                |                |
| Vertigo                                         |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vertigo Positional                              |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| Cataract                                        |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Macular Hole                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Retinal Detachment                              |                |                |                |
| subjects affected / exposed                     | 1 / 83 (1.20%) | 0 / 82 (0.00%) | 0 / 77 (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          |
| Gastrointestinal disorders                      |                |                |                |
| Anal Fistula                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis                                         |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 0 / 77 (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 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hiatus Hernia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Oesophagitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 0 / 77 (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          |
| Peritonitis                                     |                |                |                |
| subjects affected / exposed                     | 1 / 83 (1.20%) | 0 / 82 (0.00%) | 0 / 77 (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          |
| Stomatitis                                      |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 0 / 77 (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          |
| Abdominal Pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain Lower                            |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reflux Oesophagitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Anal Sphincter Atony                            |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Flatulence                                      |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrooesophageal Reflux Disease                |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal Hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric Ulcer Haemorrhage                       |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nausea                                          |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting                                        |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Cholecystitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 0 / 77 (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          |
| Cholelithiasis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 2 / 77 (2.60%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Erythema Nodosum                                |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Failure Chronic                           |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Endocrine disorders                             |                |                |                |
| Hypoparathyroidism                              |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Foot Deformity                                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 0 / 77 (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 Pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 1 / 83 (1.20%) | 1 / 82 (1.22%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoporotic Fracture                           |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intervertebral Disc Degeneration                |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Chest Pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Trigger Finger                                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Back Pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Spinal Stenosis                          |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bursitis                                        |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rotator cuff syndrome                           |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 1 / 83 (1.20%) | 0 / 82 (0.00%) | 0 / 77 (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          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 1 / 83 (1.20%) | 0 / 82 (0.00%) | 0 / 77 (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          |
| Ear Infection                                   |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 0 / 77 (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          |
| Pneumonia Streptococcal                         |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 0 / 77 (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          |
| Viral Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 1 / 83 (1.20%) | 1 / 82 (1.22%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Tract Infection                     |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Tract Infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wound Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyelonephritis                                  |                |                |                |

|                                                               |                |                |                |
|---------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Sialoadenitis                                                 |                |                |                |
| subjects affected / exposed                                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Arthritis bacterial                                           |                |                |                |
| subjects affected / exposed                                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Bacterial sepsis                                              |                |                |                |
| subjects affected / exposed                                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis intestinal haemorrhagic                        |                |                |                |
| subjects affected / exposed                                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Infective exacerbation of chronic obstructive airways disease |                |                |                |
| subjects affected / exposed                                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders                            |                |                |                |
| Dehydration                                                   |                |                |                |
| subjects affected / exposed                                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                     | Years 1-2<br>Odanacatib 25<br>mg/Odanacatib 25<br>mg-Ext 1 | Years 1-2<br>Odanacatib 50<br>mg/Odanacatib 50<br>mg-Ext 1 | Year 3<br>Placebo/Placebo-Ext<br>2 |
|---------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|------------------------------------|
| Total subjects affected by serious adverse events |                                                            |                                                            |                                    |
| subjects affected / exposed                       | 9 / 79 (11.39%)                                            | 14 / 78 (17.95%)                                           | 2 / 19 (10.53%)                    |
| number of deaths (all causes)                     | 0                                                          | 1                                                          | 0                                  |

|                                                                     |                |                |                |
|---------------------------------------------------------------------|----------------|----------------|----------------|
| number of deaths resulting from adverse events                      |                |                |                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| Anal Cancer                                                         |                |                |                |
| subjects affected / exposed                                         | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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          |
| Basal Cell Carcinoma                                                |                |                |                |
| subjects affected / exposed                                         | 1 / 79 (1.27%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Breast Cancer                                                       |                |                |                |
| subjects affected / exposed                                         | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Breast Cancer In Situ                                               |                |                |                |
| subjects affected / exposed                                         | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Multiple Myeloma                                                    |                |                |                |
| subjects affected / exposed                                         | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-Hodgkin's Lymphoma                                              |                |                |                |
| subjects affected / exposed                                         | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Papillary Thyroid Cancer                                            |                |                |                |
| subjects affected / exposed                                         | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Sarcoma                                                             |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Squamous Cell Carcinoma                         |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Colon Cancer Metastatic                         |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian Neoplasm                                |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Adenoma                                   |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neurilemmoma Benign                             |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bowen's disease                                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive breast carcinoma                       |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive ductal breast carcinoma                |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma                              |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma in situ                      |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatic carcinoma metastatic                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous cell carcinoma of skin                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                              |                |                |                |
| Hypertension                                    |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Orthostatic Hypotension                         |                |                |                |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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          |
| Hypotension                                          |                |                |                |
| subjects affected / exposed                          | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Chest Pain                                           |                |                |                |
| subjects affected / exposed                          | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders             |                |                |                |
| Genital Prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst                                         |                |                |                |
| subjects affected / exposed                          | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst torsion                                 |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Uterine prolapse                                     |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vaginal prolapse                                |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic Obstructive Pulmonary Disease           |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Electrocardiogram ST-T Change                   |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Weight Decreased                                |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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  |                |                |                |
| Hip Fracture                                    |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Joint Dislocation                               |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Post Procedural Bile Leak                       |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Head Injury                                     |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ankle Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fall                                            |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rib Fracture                                    |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Femur fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Incarcerated incisional hernia                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Scar                                            |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary retention postoperative                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Arteriospasm Coronary                           |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Occlusion                       |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Myocardial Infarction                           |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Disease                         |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Palpitations                                    |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Reversible Ischaemic Neurological Deficit       |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Syncope                                         |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Facial Palsy                                    |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sciatica                                        |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebral infarction                             |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dementia Alzheimer's type                       |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Headache                                        |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nerve root compression                          |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Paraesthesia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Presyncope                                      |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Immune Thrombocytopenic Purpura                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear and labyrinth disorders                     |                |                |                |
| Vertigo                                         |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vertigo Positional                              |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| Cataract                                        |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Macular Hole                                    |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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          |
| Retinal Detachment                              |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Anal Fistula                                    |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis                                         |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastritis                                       |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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          |
| Hiatus Hernia                                   |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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          |
| Oesophagitis                                    |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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          |
| Pancreatitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Peritonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Stomatitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain Lower                            |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reflux Oesophagitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Anal Sphincter Atony                            |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Flatulence                                      |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrooesophageal Reflux Disease                |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal Hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric Ulcer Haemorrhage                       |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nausea                                          |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting                                        |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Cholecystitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cholelithiasis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Erythema Nodosum                                |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Failure Chronic                           |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Endocrine disorders                             |                |                |                |
| Hypoparathyroidism                              |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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 |                |                |                |
| Foot Deformity                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Pain                            |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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          |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 2 / 78 (2.56%) | 0 / 19 (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          |
| Osteoporotic Fracture                           |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intervertebral Disc Degeneration                |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Chest Pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Trigger Finger                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Back Pain                                       |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Spinal Stenosis                          |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bursitis                                        |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rotator cuff syndrome                           |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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          |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Ear Infection                                   |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia Streptococcal                         |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral Infection                                 |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (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          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (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          |
| Respiratory Tract Infection                     |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Tract Infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wound Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyelonephritis                                  |                |                |                |

|                                                               |                |                |                |
|---------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Sialoadenitis                                                 |                |                |                |
| subjects affected / exposed                                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Arthritis bacterial                                           |                |                |                |
| subjects affected / exposed                                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Bacterial sepsis                                              |                |                |                |
| subjects affected / exposed                                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis intestinal haemorrhagic                        |                |                |                |
| subjects affected / exposed                                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Infective exacerbation of chronic obstructive airways disease |                |                |                |
| subjects affected / exposed                                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders                            |                |                |                |
| Dehydration                                                   |                |                |                |
| subjects affected / exposed                                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                     | Year 3<br>Placebo/Odanacatib<br>50 mg-Ext 2 | Year 3 Odanacatib 3<br>mg/Placebo-Ext 2 | Year 3 Odanacatib 3<br>mg/Odanacatib 50<br>mg-Ext 2 |
|---------------------------------------------------|---------------------------------------------|-----------------------------------------|-----------------------------------------------------|
| Total subjects affected by serious adverse events |                                             |                                         |                                                     |
| subjects affected / exposed                       | 2 / 22 (9.09%)                              | 3 / 18 (16.67%)                         | 2 / 17 (11.76%)                                     |
| number of deaths (all causes)                     | 0                                           | 0                                       | 0                                                   |
| number of deaths resulting from                   |                                             |                                         |                                                     |

|                                                                     |                |                |                |
|---------------------------------------------------------------------|----------------|----------------|----------------|
| adverse events                                                      |                |                |                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| Anal Cancer                                                         |                |                |                |
| subjects affected / exposed                                         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Basal Cell Carcinoma                                                |                |                |                |
| subjects affected / exposed                                         | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (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          |
| Breast Cancer                                                       |                |                |                |
| subjects affected / exposed                                         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Breast Cancer In Situ                                               |                |                |                |
| subjects affected / exposed                                         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Multiple Myeloma                                                    |                |                |                |
| subjects affected / exposed                                         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-Hodgkin's Lymphoma                                              |                |                |                |
| subjects affected / exposed                                         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Papillary Thyroid Cancer                                            |                |                |                |
| subjects affected / exposed                                         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Sarcoma                                                             |                |                |                |
| subjects affected / exposed                                         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Squamous Cell Carcinoma                         |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Cancer Metastatic                         |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian Neoplasm                                |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (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          |
| Colon Adenoma                                   |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neurilemmoma Benign                             |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bowen's disease                                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive breast carcinoma                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive ductal breast carcinoma                |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma                              |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma in situ                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatic carcinoma metastatic                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous cell carcinoma of skin                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                              |                |                |                |
| Hypertension                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Orthostatic Hypotension                         |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypotension                                     |                |                |                |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Chest Pain                                           |                |                |                |
| subjects affected / exposed                          | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders             |                |                |                |
| Genital Prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst                                         |                |                |                |
| subjects affected / exposed                          | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst torsion                                 |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Uterine prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Vaginal prolapse                                     |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic Obstructive Pulmonary Disease           |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Electrocardiogram ST-T Change                   |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Weight Decreased                                |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Hip Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Joint Dislocation                               |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Vertebral Fracture                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Post Procedural Bile Leak                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Head Injury                                     |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (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          |
| Ankle Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fall                                            |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rib Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Femur fracture                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Incarcerated incisional hernia                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Scar                                            |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary retention postoperative                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Arteriospasm Coronary                           |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure Congestive                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Occlusion                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Myocardial Infarction                           |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atrial Fibrillation                             |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Disease                         |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Palpitations                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Reversible Ischaemic Neurological Deficit       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Syncope                                         |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Facial Palsy                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sciatica                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebral infarction                             |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dementia Alzheimer's type                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Headache                                        |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nerve root compression                          |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Paraesthesia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Presyncope                                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Immune Thrombocytopenic Purpura                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear and labyrinth disorders                     |                |                |                |
| Vertigo                                         |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vertigo Positional                              |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| Cataract                                        |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Macular Hole                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Retinal Detachment                              |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Anal Fistula                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis                                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastritis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hiatus Hernia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Oesophagitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Peritonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Stomatitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain Lower                            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reflux Oesophagitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Anal Sphincter Atony                            |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Flatulence                                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrooesophageal Reflux Disease                |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal Hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric Ulcer Haemorrhage                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nausea                                          |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Cholecystitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cholelithiasis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Erythema Nodosum                                |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Failure Chronic                           |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                |                |                |
| Hypoparathyroidism                              |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Foot Deformity                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoporotic Fracture                           |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intervertebral Disc Degeneration                |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (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          |
| Musculoskeletal Chest Pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Trigger Finger                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Back Pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Spinal Stenosis                          |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bursitis                                        |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rotator cuff syndrome                           |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear Infection                                   |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia Streptococcal                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (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                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Tract Infection                         |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (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          |
| Wound Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (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 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyelonephritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sialoadenitis                                   |                |                |                |

|                                                               |                |                |                |
|---------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Arthritis bacterial                                           |                |                |                |
| subjects affected / exposed                                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Bacterial sepsis                                              |                |                |                |
| subjects affected / exposed                                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis intestinal haemorrhagic                        |                |                |                |
| subjects affected / exposed                                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Infective exacerbation of chronic obstructive airways disease |                |                |                |
| subjects affected / exposed                                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders                            |                |                |                |
| Dehydration                                                   |                |                |                |
| subjects affected / exposed                                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | Year 3 Odanacatib<br>10 mg/Placebo-Ext 2 | Year 3 Odanacatib<br>10 mg/Odanacatib<br>50 mg-Ext 2 | Year 3 Odanacatib<br>25 mg/Placebo-Ext 2 |
|---------------------------------------------------------------------|------------------------------------------|------------------------------------------------------|------------------------------------------|
| Total subjects affected by serious adverse events                   |                                          |                                                      |                                          |
| subjects affected / exposed                                         | 0 / 18 (0.00%)                           | 1 / 17 (5.88%)                                       | 1 / 19 (5.26%)                           |
| number of deaths (all causes)                                       | 0                                        | 0                                                    | 0                                        |
| number of deaths resulting from adverse events                      |                                          |                                                      |                                          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                          |                                                      |                                          |
| Anal Cancer                                                         |                                          |                                                      |                                          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Basal Cell Carcinoma                            |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Breast Cancer                                   |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Breast Cancer In Situ                           |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Multiple Myeloma                                |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-Hodgkin's Lymphoma                          |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Papillary Thyroid Cancer                        |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sarcoma                                         |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous Cell Carcinoma                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Cancer Metastatic                         |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian Neoplasm                                |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Adenoma                                   |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neurilemmoma Benign                             |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bowen's disease                                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive breast carcinoma                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive ductal breast carcinoma                |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma                              |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma in situ                      |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatic carcinoma metastatic                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous cell carcinoma of skin                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                              |                |                |                |
| Hypertension                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Orthostatic Hypotension                         |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypotension                                     |                |                |                |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Chest Pain                                           |                |                |                |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders             |                |                |                |
| Genital Prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst                                         |                |                |                |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst torsion                                 |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Uterine prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Vaginal prolapse                                     |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic Obstructive Pulmonary Disease           |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Electrocardiogram ST-T Change                   |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Weight Decreased                                |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Hip Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Joint Dislocation                               |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Vertebral Fracture                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Post Procedural Bile Leak                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Head Injury                                     |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ankle Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fall                                            |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rib Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Femur fracture                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Incarcerated incisional hernia                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Scar                                            |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary retention postoperative                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Arteriospasm Coronary                           |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure Congestive                      |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Occlusion                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Myocardial Infarction                           |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atrial Fibrillation                             |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Disease                         |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Palpitations                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Reversible Ischaemic Neurological Deficit       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Syncope                                         |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Facial Palsy                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sciatica                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebral infarction                             |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dementia Alzheimer's type                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Headache                                        |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nerve root compression                          |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Paraesthesia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Presyncope                                      |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Immune Thrombocytopenic Purpura                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear and labyrinth disorders                     |                |                |                |
| Vertigo                                         |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vertigo Positional                              |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| Cataract                                        |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (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          |
| Macular Hole                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Retinal Detachment                              |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Anal Fistula                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis                                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastritis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hiatus Hernia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Oesophagitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Peritonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Stomatitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain Lower                            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reflux Oesophagitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Anal Sphincter Atony                            |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Flatulence                                      |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrooesophageal Reflux Disease                |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal Hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric Ulcer Haemorrhage                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nausea                                          |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Cholecystitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cholelithiasis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Erythema Nodosum                                |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Failure Chronic                           |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                |                |                |
| Hypoparathyroidism                              |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Foot Deformity                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoporotic Fracture                           |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intervertebral Disc Degeneration                |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Chest Pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Trigger Finger                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Back Pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Spinal Stenosis                          |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bursitis                                        |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rotator cuff syndrome                           |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear Infection                                   |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia Streptococcal                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Tract Infection                     |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Tract Infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wound Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyelonephritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sialoadenitis                                   |                |                |                |

|                                                               |                |                |                |
|---------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                   | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Arthritis bacterial                                           |                |                |                |
| subjects affected / exposed                                   | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Bacterial sepsis                                              |                |                |                |
| subjects affected / exposed                                   | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis intestinal haemorrhagic                        |                |                |                |
| subjects affected / exposed                                   | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Infective exacerbation of chronic obstructive airways disease |                |                |                |
| subjects affected / exposed                                   | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders                            |                |                |                |
| Dehydration                                                   |                |                |                |
| subjects affected / exposed                                   | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | Year 3 Odanacatib<br>25 mg/Odanacatib<br>50 mg-Ext 2 | Year 3 Odanacatib<br>50 mg/Placebo-Ext 2 | Year 3 Odanacatib<br>50 mg/Odanacatib<br>50 mg-Ext 2 |
|---------------------------------------------------------------------|------------------------------------------------------|------------------------------------------|------------------------------------------------------|
| Total subjects affected by serious adverse events                   |                                                      |                                          |                                                      |
| subjects affected / exposed                                         | 4 / 21 (19.05%)                                      | 2 / 18 (11.11%)                          | 1 / 20 (5.00%)                                       |
| number of deaths (all causes)                                       | 0                                                    | 0                                        | 0                                                    |
| number of deaths resulting from adverse events                      |                                                      |                                          |                                                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                      |                                          |                                                      |
| Anal Cancer                                                         |                                                      |                                          |                                                      |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Basal Cell Carcinoma                            |                |                |                |
| subjects affected / exposed                     | 1 / 21 (4.76%) | 1 / 18 (5.56%) | 0 / 20 (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          |
| Breast Cancer                                   |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Breast Cancer In Situ                           |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Multiple Myeloma                                |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-Hodgkin's Lymphoma                          |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Papillary Thyroid Cancer                        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sarcoma                                         |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous Cell Carcinoma                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Cancer Metastatic                         |                |                |                |
| subjects affected / exposed                     | 1 / 21 (4.76%) | 0 / 18 (0.00%) | 0 / 20 (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          |
| Ovarian Neoplasm                                |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Adenoma                                   |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neurilemmoma Benign                             |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bowen's disease                                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive breast carcinoma                       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive ductal breast carcinoma                |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma                              |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma in situ                      |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatic carcinoma metastatic                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous cell carcinoma of skin                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                              |                |                |                |
| Hypertension                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Orthostatic Hypotension                         |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypotension                                     |                |                |                |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Chest Pain                                           |                |                |                |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders             |                |                |                |
| Genital Prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst                                         |                |                |                |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst torsion                                 |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Uterine prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Vaginal prolapse                                     |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic Obstructive Pulmonary Disease           |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Electrocardiogram ST-T Change                   |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Weight Decreased                                |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Hip Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Joint Dislocation                               |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Vertebral Fracture                       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Post Procedural Bile Leak                       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Head Injury                                     |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist Fracture                                  |                |                |                |
| subjects affected / exposed                     | 1 / 21 (4.76%) | 0 / 18 (0.00%) | 0 / 20 (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          |
| Ankle Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fall                                            |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rib Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Femur fracture                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Incarcerated incisional hernia                  |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Scar                                            |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary retention postoperative                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Arteriospasm Coronary                           |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure Congestive                      |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Occlusion                       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Myocardial Infarction                           |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atrial Fibrillation                             |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Disease                         |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Palpitations                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Reversible Ischaemic Neurological Deficit       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Syncope                                         |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Facial Palsy                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sciatica                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebral infarction                             |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dementia Alzheimer's type                       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Headache                                        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nerve root compression                          |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Paraesthesia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Presyncope                                      |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Immune Thrombocytopenic Purpura                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear and labyrinth disorders                     |                |                |                |
| Vertigo                                         |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (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          |
| Vertigo Positional                              |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| Cataract                                        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Macular Hole                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Retinal Detachment                              |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Anal Fistula                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis                                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastritis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hiatus Hernia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Oesophagitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Peritonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Stomatitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (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          |
| Abdominal Pain Lower                            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reflux Oesophagitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Anal Sphincter Atony                            |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Flatulence                                      |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrooesophageal Reflux Disease                |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal Hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric Ulcer Haemorrhage                       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nausea                                          |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Cholecystitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cholelithiasis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Erythema Nodosum                                |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Failure Chronic                           |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                |                |                |
| Hypoparathyroidism                              |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Foot Deformity                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 1 / 21 (4.76%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoporotic Fracture                           |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intervertebral Disc Degeneration                |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Chest Pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Trigger Finger                                  |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Back Pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Spinal Stenosis                          |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bursitis                                        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rotator cuff syndrome                           |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear Infection                                   |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia Streptococcal                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Tract Infection                     |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Tract Infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wound Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyelonephritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sialoadenitis                                   |                |                |                |

|                                                               |                |                |                |
|---------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Arthritis bacterial                                           |                |                |                |
| subjects affected / exposed                                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Bacterial sepsis                                              |                |                |                |
| subjects affected / exposed                                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis intestinal haemorrhagic                        |                |                |                |
| subjects affected / exposed                                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Infective exacerbation of chronic obstructive airways disease |                |                |                |
| subjects affected / exposed                                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders                            |                |                |                |
| Dehydration                                                   |                |                |                |
| subjects affected / exposed                                   | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (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          |

| <b>Serious adverse events</b>                                       | Years 4-5 Combined<br>Group A.1:<br>Odanacatib 50 mg | Years 4-5 Combined<br>Group A.2:<br>Odanacatib 50 mg | Years 4-5 Combined<br>Group A.3: Placebo |
|---------------------------------------------------------------------|------------------------------------------------------|------------------------------------------------------|------------------------------------------|
| Total subjects affected by serious adverse events                   |                                                      |                                                      |                                          |
| subjects affected / exposed                                         | 16 / 73 (21.92%)                                     | 2 / 27 (7.41%)                                       | 8 / 41 (19.51%)                          |
| number of deaths (all causes)                                       | 0                                                    | 0                                                    | 0                                        |
| number of deaths resulting from adverse events                      |                                                      |                                                      |                                          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                      |                                                      |                                          |
| Anal Cancer                                                         |                                                      |                                                      |                                          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Basal Cell Carcinoma                            |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 3 / 41 (7.32%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 4          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Breast Cancer                                   |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Breast Cancer In Situ                           |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Multiple Myeloma                                |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-Hodgkin's Lymphoma                          |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Papillary Thyroid Cancer                        |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sarcoma                                         |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous Cell Carcinoma                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Colon Cancer Metastatic                         |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian Neoplasm                                |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Adenoma                                   |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Neurilemmoma Benign                             |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 27 (3.70%) | 0 / 41 (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          |
| Bowen's disease                                 |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive breast carcinoma                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive ductal breast carcinoma                |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma                              |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma in situ                      |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatic carcinoma metastatic                 |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous cell carcinoma of skin                 |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                              |                |                |                |
| Hypertension                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Orthostatic Hypotension                         |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypotension                                     |                |                |                |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Chest Pain                                           |                |                |                |
| subjects affected / exposed                          | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders             |                |                |                |
| Genital Prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst                                         |                |                |                |
| subjects affected / exposed                          | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst torsion                                 |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Uterine prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Vaginal prolapse                                     |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic Obstructive Pulmonary Disease           |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Electrocardiogram ST-T Change                   |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Weight Decreased                                |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Hip Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Joint Dislocation                               |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Vertebral Fracture                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Post Procedural Bile Leak                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Head Injury                                     |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ankle Fracture                                  |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Fall                                            |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Rib Fracture                                    |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Incarcerated incisional hernia                  |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Scar                                            |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary retention postoperative                 |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Arteriospasm Coronary                           |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure Congestive                      |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Occlusion                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Myocardial Infarction                           |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atrial Fibrillation                             |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Disease                         |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Palpitations                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Reversible Ischaemic Neurological Deficit       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Syncope                                         |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Facial Palsy                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sciatica                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Cerebral infarction                             |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dementia Alzheimer's type                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Headache                                        |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nerve root compression                          |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Paraesthesia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Presyncope                                      |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Immune Thrombocytopenic Purpura                 |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear and labyrinth disorders                     |                |                |                |
| Vertigo                                         |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vertigo Positional                              |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| Cataract                                        |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Macular Hole                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Retinal Detachment                              |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Anal Fistula                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis                                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastritis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hiatus Hernia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Oesophagitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Peritonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Stomatitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain Lower                            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reflux Oesophagitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Anal Sphincter Atony                            |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Flatulence                                      |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Gastrooesophageal Reflux Disease                |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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 Ulcer Haemorrhage                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nausea                                          |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Cholecystitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cholelithiasis                                  |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Erythema Nodosum                                |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Failure Chronic                           |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                |                |                |
| Hypoparathyroidism                              |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Foot Deformity                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Musculoskeletal Pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 4 / 73 (5.48%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 4          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoporotic Fracture                           |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intervertebral Disc Degeneration                |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Chest Pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Trigger Finger                                  |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Back Pain                                       |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Lumbar Spinal Stenosis                          |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Bursitis                                        |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rotator cuff syndrome                           |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear Infection                                   |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia Streptococcal                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Tract Infection                     |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Tract Infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wound Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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                                  |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (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          |
| Sialoadenitis                                   |                |                |                |

|                                                               |                |                |                |
|---------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                   | 0 / 73 (0.00%) | 1 / 27 (3.70%) | 0 / 41 (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          |
| Arthritis bacterial                                           |                |                |                |
| subjects affected / exposed                                   | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Bacterial sepsis                                              |                |                |                |
| subjects affected / exposed                                   | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis intestinal haemorrhagic                        |                |                |                |
| subjects affected / exposed                                   | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Infective exacerbation of chronic obstructive airways disease |                |                |                |
| subjects affected / exposed                                   | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders                            |                |                |                |
| Dehydration                                                   |                |                |                |
| subjects affected / exposed                                   | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | Years 6-10 Group A:<br>Odanacatib 50 mg<br>once weekly | Years 6-10 Group B:<br>Odanacatib 50 mg<br>once weekly | Years 6-10 Group C:<br>Odanacatib 50 mg<br>once weekly |
|---------------------------------------------------------------------|--------------------------------------------------------|--------------------------------------------------------|--------------------------------------------------------|
| Total subjects affected by serious adverse events                   |                                                        |                                                        |                                                        |
| subjects affected / exposed                                         | 8 / 28 (28.57%)                                        | 14 / 34 (41.18%)                                       | 6 / 23 (26.09%)                                        |
| number of deaths (all causes)                                       | 0                                                      | 1                                                      | 0                                                      |
| number of deaths resulting from adverse events                      | 0                                                      | 0                                                      | 0                                                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                        |                                                        |                                                        |
| Anal Cancer                                                         |                                                        |                                                        |                                                        |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Basal Cell Carcinoma</b>                     |                |                |                |
| subjects affected / exposed                     | 2 / 28 (7.14%) | 1 / 34 (2.94%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 1 / 5          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Breast Cancer</b>                            |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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>Breast Cancer In Situ</b>                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Multiple Myeloma</b>                         |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Non-Hodgkin's Lymphoma</b>                   |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Papillary Thyroid Cancer</b>                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Sarcoma</b>                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Squamous Cell Carcinoma</b>                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Colon Cancer Metastatic                         |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian Neoplasm                                |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Adenoma                                   |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neurilemmoma Benign                             |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bowen's disease                                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Gastric cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive breast carcinoma                       |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Invasive ductal breast carcinoma                |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma                              |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant melanoma in situ                      |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cancer                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Pancreatic carcinoma metastatic                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Squamous cell carcinoma of skin                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                              |                |                |                |
| Hypertension                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Orthostatic Hypotension                         |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypotension                                     |                |                |                |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 1 / 28 (3.57%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| General disorders and administration site conditions |                |                |                |
| Chest Pain                                           |                |                |                |
| subjects affected / exposed                          | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Reproductive system and breast disorders             |                |                |                |
| Genital Prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst                                         |                |                |                |
| subjects affected / exposed                          | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ovarian cyst torsion                                 |                |                |                |
| alternative assessment type: Non-systematic          |                |                |                |
| subjects affected / exposed                          | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Uterine prolapse                                     |                |                |                |
| subjects affected / exposed                          | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Vaginal prolapse                                     |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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, thoracic and mediastinal disorders |                |                |                |
| Chronic Obstructive Pulmonary Disease           |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Electrocardiogram ST-T Change                   |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Weight Decreased                                |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Hip Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Joint Dislocation                               |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lumbar Vertebral Fracture                       |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Post Procedural Bile Leak                       |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Head Injury                                     |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ankle Fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fall                                            |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rib Fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Femur fracture                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 2          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Incarcerated incisional hernia                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Scar                                            |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Urinary retention postoperative                 |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Cardiac disorders                               |                |                |                |
| Arteriospasm Coronary                           |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure Congestive                      |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Occlusion                       |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Myocardial Infarction                           |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Atrial Fibrillation                             |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 2 / 34 (5.88%) | 0 / 23 (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 Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Coronary Artery Disease                         |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Palpitations                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Nervous system disorders                        |                |                |                |
| Reversible Ischaemic Neurological Deficit       |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Syncope                                         |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Facial Palsy                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sciatica                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebral infarction                             |                |                |                |
| alternative assessment type: Non-systematic     |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Dementia Alzheimer's type                       |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Headache                                        |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Nerve root compression                          |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Paraesthesia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Presyncope                                      |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Blood and lymphatic system disorders            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Immune Thrombocytopenic Purpura                 |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Ear and labyrinth disorders                     |                |                |                |
| Vertigo                                         |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vertigo Positional                              |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Eye disorders                                   |                |                |                |
| Cataract                                        |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Macular Hole                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Retinal Detachment                              |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Anal Fistula                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis                                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastritis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hiatus Hernia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Oesophagitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Peritonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Stomatitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Pain Lower                            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reflux Oesophagitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Anal Sphincter Atony                            |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Flatulence                                      |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrooesophageal Reflux Disease                |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal Hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric Ulcer Haemorrhage                       |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nausea                                          |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Hepatobiliary disorders                         |                |                |                |
| Cholecystitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cholelithiasis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Erythema Nodosum                                |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Failure Chronic                           |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                |                |                |
| Hypoparathyroidism                              |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Foot Deformity                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Osteoporotic Fracture                           |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intervertebral Disc Degeneration                |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Chest Pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Trigger Finger                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Back Pain                                       |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Lumbar Spinal Stenosis                          |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bursitis                                        |                |                |                |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Rotator cuff syndrome                           |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Spinal pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear Infection                                   |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia Streptococcal                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Tract Infection                     |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Tract Infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wound Infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyelonephritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sialoadenitis                                   |                |                |                |

|                                                               |                |                |                |
|---------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                   | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Arthritis bacterial                                           |                |                |                |
| subjects affected / exposed                                   | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Bacterial sepsis                                              |                |                |                |
| subjects affected / exposed                                   | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (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          |
| Diverticulitis intestinal haemorrhagic                        |                |                |                |
| subjects affected / exposed                                   | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Infective exacerbation of chronic obstructive airways disease |                |                |                |
| subjects affected / exposed                                   | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (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          |
| Metabolism and nutrition disorders                            |                |                |                |
| Dehydration                                                   |                |                |                |
| subjects affected / exposed                                   | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                                     |                                                        |  |  |
|---------------------------------------------------------------------|--------------------------------------------------------|--|--|
| <b>Serious adverse events</b>                                       | Years 6-10 Group D:<br>Odanacatib 50 mg<br>once weekly |  |  |
| Total subjects affected by serious adverse events                   |                                                        |  |  |
| subjects affected / exposed                                         | 12 / 32 (37.50%)                                       |  |  |
| number of deaths (all causes)                                       | 0                                                      |  |  |
| number of deaths resulting from adverse events                      | 0                                                      |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                        |  |  |
| Anal Cancer                                                         |                                                        |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Basal Cell Carcinoma                            |                |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Breast Cancer                                   |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Breast Cancer In Situ                           |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Multiple Myeloma                                |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Non-Hodgkin's Lymphoma                          |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Papillary Thyroid Cancer                        |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Sarcoma                                         |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Squamous Cell Carcinoma                         |                |  |  |

|                                                 |                |  |  |  |
|-------------------------------------------------|----------------|--|--|--|
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Colon Cancer Metastatic                         |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Ovarian Neoplasm                                |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Colon Adenoma                                   |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Neurilemmoma Benign                             |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Bowen's disease                                 |                |  |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Gastric cancer                                  |                |  |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Invasive breast carcinoma                       |                |  |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Invasive ductal breast carcinoma                |                |  |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Malignant melanoma                              |                |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Malignant melanoma in situ                      |                |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Ovarian cancer                                  |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pancreatic carcinoma metastatic                 |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Squamous cell carcinoma of skin                 |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vascular disorders                              |                |  |  |
| Hypertension                                    |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Orthostatic Hypotension                         |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hypotension                                     |                |  |  |

|                                                      |                |  |  |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Chest Pain                                           |                |  |  |
| subjects affected / exposed                          | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Non-cardiac chest pain                               |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Reproductive system and breast disorders             |                |  |  |
| Genital Prolapse                                     |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Ovarian cyst                                         |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Ovarian cyst torsion                                 |                |  |  |
| alternative assessment type: Non-systematic          |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Uterine prolapse                                     |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Vaginal prolapse                                     |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Chronic Obstructive Pulmonary Disease           |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pneumothorax                                    |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pulmonary embolism                              |                |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Investigations                                  |                |  |  |
| Electrocardiogram ST-T Change                   |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Weight Decreased                                |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Hip Fracture                                    |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Joint Dislocation                               |                |  |  |

|                                                 |                |  |  |  |
|-------------------------------------------------|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Lumbar Vertebral Fracture                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Post Procedural Bile Leak                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Head Injury                                     |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Wrist Fracture                                  |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Ankle Fracture                                  |                |  |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Fall                                            |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Rib Fracture                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Femur fracture                                  |                |  |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Incarcerated incisional hernia                  |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Scar                                            |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urinary retention postoperative                 |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Arteriospasm Coronary                           |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac Failure Congestive                      |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Coronary Artery Occlusion                       |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Myocardial Infarction                           |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Atrial Fibrillation                             |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac Failure                                 |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Coronary Artery Disease                         |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Tachycardia                                     |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Palpitations                                    |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| Reversible Ischaemic Neurological Deficit       |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Syncope                                         |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Facial Palsy                                    |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Sciatica                                        |                |  |  |

|                                                 |                |  |  |  |
|-------------------------------------------------|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cerebral infarction                             |                |  |  |  |
| alternative assessment type: Non-systematic     |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cerebrovascular accident                        |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Dementia Alzheimer's type                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Headache                                        |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Nerve root compression                          |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Paraesthesia                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Presyncope                                      |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Blood and lymphatic system disorders            |                |  |  |  |

|                                                                                                                                                                                  |                                  |  |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|--|--|
| Immune Thrombocytopenic Purpura<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all            | 0 / 32 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Ear and labyrinth disorders<br>Vertigo<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all     | 0 / 32 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Vertigo Positional<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                         | 0 / 32 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Eye disorders<br>Cataract<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                  | 0 / 32 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Macular Hole<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                               | 0 / 32 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Retinal Detachment<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                         | 0 / 32 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Gastrointestinal disorders<br>Anal Fistula<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 32 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Colitis                                                                                                                                                                          |                                  |  |  |

|                                                 |                |  |  |  |
|-------------------------------------------------|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Gastritis                                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Hiatus Hernia                                   |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Oesophagitis                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pancreatitis                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Peritonitis                                     |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Stomatitis                                      |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Abdominal Pain                                  |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Abdominal Pain Lower                            |                |  |  |  |

|                                                 |                |  |  |  |
|-------------------------------------------------|----------------|--|--|--|
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Reflux Oesophagitis                             |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Anal Sphincter Atony                            |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Flatulence                                      |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Gastrooesophageal Reflux Disease                |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Inguinal Hernia                                 |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Gastric Ulcer Haemorrhage                       |                |  |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Nausea                                          |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Vomiting                                        |                |  |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatobiliary disorders                         |                |  |  |
| Cholecystitis                                   |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cholelithiasis                                  |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |
| Erythema Nodosum                                |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| Nephrolithiasis                                 |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal Failure Chronic                           |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Endocrine disorders                             |                |  |  |
| Hypoparathyroidism                              |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Foot Deformity                                  |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal Pain                            |                |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Osteoarthritis                                  |                |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Osteoporotic Fracture                           |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Intervertebral Disc Degeneration                |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal Chest Pain                      |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Trigger Finger                                  |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Back Pain                                       |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Lumbar Spinal Stenosis                          |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Bursitis                                        |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Rotator cuff syndrome                           |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Spinal pain                                     |                |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Bronchitis                                      |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cellulitis                                      |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diverticulitis                                  |                |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Ear Infection                                   |                |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pneumonia Streptococcal                         |                |  |  |

|                                                 |                |  |  |  |
|-------------------------------------------------|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Viral Infection                                 |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumonia                                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Respiratory Tract Infection                     |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Urinary Tract Infection                         |                |  |  |  |
| subjects affected / exposed                     | 1 / 32 (3.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Wound Infection                                 |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Gastroenteritis                                 |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pyelonephritis                                  |                |  |  |  |
| subjects affected / exposed                     | 0 / 32 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Sialoadenitis                                   |                |  |  |  |

|                                                               |                |  |  |
|---------------------------------------------------------------|----------------|--|--|
| subjects affected / exposed                                   | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all               | 0 / 0          |  |  |
| deaths causally related to treatment / all                    | 0 / 0          |  |  |
| Arthritis bacterial                                           |                |  |  |
| subjects affected / exposed                                   | 1 / 32 (3.13%) |  |  |
| occurrences causally related to treatment / all               | 0 / 1          |  |  |
| deaths causally related to treatment / all                    | 0 / 0          |  |  |
| Bacterial sepsis                                              |                |  |  |
| subjects affected / exposed                                   | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all               | 0 / 0          |  |  |
| deaths causally related to treatment / all                    | 0 / 0          |  |  |
| Diverticulitis intestinal haemorrhagic                        |                |  |  |
| subjects affected / exposed                                   | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all               | 0 / 0          |  |  |
| deaths causally related to treatment / all                    | 0 / 0          |  |  |
| Infective exacerbation of chronic obstructive airways disease |                |  |  |
| subjects affected / exposed                                   | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all               | 0 / 0          |  |  |
| deaths causally related to treatment / all                    | 0 / 0          |  |  |
| Metabolism and nutrition disorders                            |                |  |  |
| Dehydration                                                   |                |  |  |
| subjects affected / exposed                                   | 0 / 32 (0.00%) |  |  |
| occurrences causally related to treatment / all               | 0 / 0          |  |  |
| deaths causally related to treatment / all                    | 0 / 0          |  |  |

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

| Non-serious adverse events                                          | Years 1-2<br>Placebo/Placebo-Ext<br>1 | Years 1-2<br>Odanacatib 3<br>mg/Odanacatib 3<br>mg-Ext 1 | Years 1-2<br>Odanacatib 10<br>mg/Odanacatib 10<br>mg-Ext 1 |
|---------------------------------------------------------------------|---------------------------------------|----------------------------------------------------------|------------------------------------------------------------|
| Total subjects affected by non-serious adverse events               |                                       |                                                          |                                                            |
| subjects affected / exposed                                         | 68 / 83 (81.93%)                      | 66 / 82 (80.49%)                                         | 67 / 77 (87.01%)                                           |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                       |                                                          |                                                            |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| Basal Cell Carcinoma                                 |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Fibroma                                              |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Lipoma                                               |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Ovarian Neoplasm                                     |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Thyroid Neoplasm                                     |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Benign neoplasm of thyroid gland                     |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Vascular disorders                                   |                |                |                |
| Flushing                                             |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Haematoma                                            |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Hypertension                                         |                |                |                |
| subjects affected / exposed                          | 4 / 83 (4.82%) | 7 / 82 (8.54%) | 3 / 77 (3.90%) |
| occurrences (all)                                    | 4              | 7              | 3              |
| Phlebitis                                            |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Varicose Vein                                        |                |                |                |
| subjects affected / exposed                          | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| General disorders and administration site conditions |                |                |                |

|                                          |                |                |                |
|------------------------------------------|----------------|----------------|----------------|
| Calcinosis                               |                |                |                |
| subjects affected / exposed              | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Chest Discomfort                         |                |                |                |
| subjects affected / exposed              | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Chest Pain                               |                |                |                |
| subjects affected / exposed              | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Fatigue                                  |                |                |                |
| subjects affected / exposed              | 6 / 83 (7.23%) | 2 / 82 (2.44%) | 2 / 77 (2.60%) |
| occurrences (all)                        | 6              | 2              | 2              |
| Influenza Like Illness                   |                |                |                |
| subjects affected / exposed              | 3 / 83 (3.61%) | 2 / 82 (2.44%) | 3 / 77 (3.90%) |
| occurrences (all)                        | 3              | 2              | 5              |
| Oedema Peripheral                        |                |                |                |
| subjects affected / exposed              | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Wrist Fracture                           |                |                |                |
| subjects affected / exposed              | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Immune system disorders                  |                |                |                |
| Allergy To Arthropod Sting               |                |                |                |
| subjects affected / exposed              | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Drug Hypersensitivity                    |                |                |                |
| subjects affected / exposed              | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Reproductive system and breast disorders |                |                |                |
| Breast Mass                              |                |                |                |
| subjects affected / exposed              | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Fibrocystic Breast Disease               |                |                |                |
| subjects affected / exposed              | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Pelvic Pain                              |                |                |                |

|                                                                             |                     |                     |                     |
|-----------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                            | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Vulvovaginal Discomfort<br>subjects affected / exposed<br>occurrences (all) | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders                             |                     |                     |                     |
| Pharyngolaryngeal Pain<br>subjects affected / exposed<br>occurrences (all)  | 2 / 83 (2.41%)<br>2 | 3 / 82 (3.66%)<br>3 | 3 / 77 (3.90%)<br>3 |
| Allergic Pharyngitis<br>subjects affected / exposed<br>occurrences (all)    | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Asthma<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)               | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Dyspnoea Exertional<br>subjects affected / exposed<br>occurrences (all)     | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Emphysema<br>subjects affected / exposed<br>occurrences (all)               | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Haemoptysis<br>subjects affected / exposed<br>occurrences (all)             | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Cough<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 83 (2.41%)<br>4 | 2 / 82 (2.44%)<br>2 | 2 / 77 (2.60%)<br>5 |
| Psychiatric disorders                                                       |                     |                     |                     |

|                                               |                |                |                |
|-----------------------------------------------|----------------|----------------|----------------|
| Insomnia                                      |                |                |                |
| subjects affected / exposed                   | 7 / 83 (8.43%) | 3 / 82 (3.66%) | 4 / 77 (5.19%) |
| occurrences (all)                             | 7              | 3              | 4              |
| Alcoholism                                    |                |                |                |
| subjects affected / exposed                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Anxiety                                       |                |                |                |
| subjects affected / exposed                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Depression                                    |                |                |                |
| subjects affected / exposed                   | 5 / 83 (6.02%) | 4 / 82 (4.88%) | 5 / 77 (6.49%) |
| occurrences (all)                             | 5              | 4              | 5              |
| Dysthymic Disorder                            |                |                |                |
| subjects affected / exposed                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Stress                                        |                |                |                |
| subjects affected / exposed                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Investigations                                |                |                |                |
| Weight Increased                              |                |                |                |
| subjects affected / exposed                   | 4 / 83 (4.82%) | 2 / 82 (2.44%) | 3 / 77 (3.90%) |
| occurrences (all)                             | 4              | 2              | 3              |
| Alanine Aminotransferase Increased            |                |                |                |
| subjects affected / exposed                   | 1 / 83 (1.20%) | 3 / 82 (3.66%) | 0 / 77 (0.00%) |
| occurrences (all)                             | 1              | 4              | 0              |
| Aspartate Aminotransferase Increased          |                |                |                |
| subjects affected / exposed                   | 1 / 83 (1.20%) | 3 / 82 (3.66%) | 2 / 77 (2.60%) |
| occurrences (all)                             | 1              | 5              | 2              |
| Blood 1,25-Dihydroxycholecalciferol Increased |                |                |                |
| subjects affected / exposed                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Blood Cholesterol Increased                   |                |                |                |
| subjects affected / exposed                   | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Blood Glucose Increased                       |                |                |                |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Blood Parathyroid Hormone Increased |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Blood Pressure Increased            |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Blood Triglycerides Increased       |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Bone Density Decreased              |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Carotid Bruit                       |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Glucose Urine Present               |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| High Density Lipoprotein Decreased  |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Lymphocyte Count Decreased          |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Ultrasound Thyroid Abnormal         |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Weight Decreased                    |                |                |                |
| subjects affected / exposed         | 2 / 83 (2.41%) | 1 / 82 (1.22%) | 2 / 77 (2.60%) |
| occurrences (all)                   | 2              | 1              | 2              |
| White Blood Cells Urine Positive    |                |                |                |
| subjects affected / exposed         | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |

|                                                                                          |                     |                     |                     |
|------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Body height decreased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Injury, poisoning and procedural complications                                           |                     |                     |                     |
| Arthropod Bite<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Arthropod Sting<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                            | 5 / 83 (6.02%)<br>5 | 2 / 82 (2.44%)<br>4 | 5 / 77 (6.49%)<br>8 |
| Device Breakage<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Epicondylitis<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Humerus Fracture<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Joint Sprain<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Limb Injury<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 83 (0.00%)<br>0 | 0 / 82 (0.00%)<br>0 | 0 / 77 (0.00%)<br>0 |
| Muscle Strain                                                                            |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Open Wound                  |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Procedural Pain             |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Radius Fracture             |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rib Fracture                |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Laceration             |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skull Fractured Base        |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Spinal Compression Fracture |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Spinal Fracture             |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Subdural Haematoma          |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Thoracic Vertebral Fracture |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tooth Fracture              |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Vertebral Injury            |                |                |                |

|                                            |                  |                 |                  |
|--------------------------------------------|------------------|-----------------|------------------|
| subjects affected / exposed                | 0 / 83 (0.00%)   | 0 / 82 (0.00%)  | 0 / 77 (0.00%)   |
| occurrences (all)                          | 0                | 0               | 0                |
| Laceration                                 |                  |                 |                  |
| subjects affected / exposed                | 0 / 83 (0.00%)   | 0 / 82 (0.00%)  | 2 / 77 (2.60%)   |
| occurrences (all)                          | 0                | 0               | 2                |
| Ligament sprain                            |                  |                 |                  |
| subjects affected / exposed                | 4 / 83 (4.82%)   | 1 / 82 (1.22%)  | 2 / 77 (2.60%)   |
| occurrences (all)                          | 4                | 1               | 2                |
| Congenital, familial and genetic disorders |                  |                 |                  |
| Congenital Diaphragmatic Hernia            |                  |                 |                  |
| subjects affected / exposed                | 0 / 83 (0.00%)   | 0 / 82 (0.00%)  | 0 / 77 (0.00%)   |
| occurrences (all)                          | 0                | 0               | 0                |
| Cardiac disorders                          |                  |                 |                  |
| Arrhythmia                                 |                  |                 |                  |
| subjects affected / exposed                | 0 / 83 (0.00%)   | 0 / 82 (0.00%)  | 0 / 77 (0.00%)   |
| occurrences (all)                          | 0                | 0               | 0                |
| Atrial Flutter                             |                  |                 |                  |
| subjects affected / exposed                | 0 / 83 (0.00%)   | 0 / 82 (0.00%)  | 0 / 77 (0.00%)   |
| occurrences (all)                          | 0                | 0               | 0                |
| Mitral Valve Prolapse                      |                  |                 |                  |
| subjects affected / exposed                | 0 / 83 (0.00%)   | 0 / 82 (0.00%)  | 0 / 77 (0.00%)   |
| occurrences (all)                          | 0                | 0               | 0                |
| Palpitations                               |                  |                 |                  |
| subjects affected / exposed                | 0 / 83 (0.00%)   | 0 / 82 (0.00%)  | 0 / 77 (0.00%)   |
| occurrences (all)                          | 0                | 0               | 0                |
| Tachycardia                                |                  |                 |                  |
| subjects affected / exposed                | 0 / 83 (0.00%)   | 0 / 82 (0.00%)  | 0 / 77 (0.00%)   |
| occurrences (all)                          | 0                | 0               | 0                |
| Nervous system disorders                   |                  |                 |                  |
| Cervicobrachial Syndrome                   |                  |                 |                  |
| subjects affected / exposed                | 0 / 83 (0.00%)   | 0 / 82 (0.00%)  | 0 / 77 (0.00%)   |
| occurrences (all)                          | 0                | 0               | 0                |
| Headache                                   |                  |                 |                  |
| subjects affected / exposed                | 10 / 83 (12.05%) | 9 / 82 (10.98%) | 10 / 77 (12.99%) |
| occurrences (all)                          | 10               | 9               | 10               |
| Memory Impairment                          |                  |                 |                  |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Migraine                    |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Paraesthesia                |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Sciatica                    |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Somnolence                  |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Tension Headache            |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Tremor                      |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Trigeminal Neuralgia        |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Upper Motor Neuron Lesion   |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Carpal tunnel syndrome      |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Dizziness                   |                |                |                 |
| subjects affected / exposed | 4 / 83 (4.82%) | 7 / 82 (8.54%) | 8 / 77 (10.39%) |
| occurrences (all)           | 5              | 9              | 10              |
| Parkinson's disease         |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Ear and labyrinth disorders |                |                |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Deafness                    |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tinnitus                    |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tympanosclerosis            |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Vertigo                     |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Vertigo Positional          |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Eye disorders               |                |                |                |
| Cataract                    |                |                |                |
| subjects affected / exposed | 2 / 83 (2.41%) | 2 / 82 (2.44%) | 4 / 77 (5.19%) |
| occurrences (all)           | 2              | 2              | 4              |
| Conjunctivitis              |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Conjunctivitis Allergic     |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Eye Pruritus                |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Macular Degeneration        |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Retinal Tear                |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastrointestinal disorders  |                |                |                |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| Abdominal Pain Upper        |                |                |                 |
| subjects affected / exposed | 2 / 83 (2.41%) | 5 / 82 (6.10%) | 5 / 77 (6.49%)  |
| occurrences (all)           | 2              | 5              | 5               |
| Abdominal Pain              |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Anal Fissure                |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Aphthous Stomatitis         |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Colitis                     |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Constipation                |                |                |                 |
| subjects affected / exposed | 3 / 83 (3.61%) | 8 / 82 (9.76%) | 6 / 77 (7.79%)  |
| occurrences (all)           | 3              | 8              | 7               |
| Diarrhoea                   |                |                |                 |
| subjects affected / exposed | 7 / 83 (8.43%) | 4 / 82 (4.88%) | 8 / 77 (10.39%) |
| occurrences (all)           | 7              | 5              | 8               |
| Dry Mouth                   |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Duodenal Ulcer              |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Dyspepsia                   |                |                |                 |
| subjects affected / exposed | 4 / 83 (4.82%) | 2 / 82 (2.44%) | 3 / 77 (3.90%)  |
| occurrences (all)           | 6              | 3              | 4               |
| Faecal Incontinence         |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Flatulence                  |                |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |

|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| Gastric Disorder                 |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastric Polyps                   |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastric Ulcer                    |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastritis                        |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastrointestinal Disorder        |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastrooesophageal Reflux Disease |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 3 / 82 (3.66%) | 4 / 77 (5.19%) |
| occurrences (all)                | 0              | 3              | 4              |
| Gingival Swelling                |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gingivitis                       |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Hiatus Hernia                    |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Inguinal Hernia                  |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Irritable Bowel Syndrome         |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Mouth Ulceration                 |                |                |                |
| subjects affected / exposed      | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| Nausea                                 |                |                |                |
| subjects affected / exposed            | 8 / 83 (9.64%) | 4 / 82 (4.88%) | 6 / 77 (7.79%) |
| occurrences (all)                      | 8              | 6              | 7              |
| Oesophagitis                           |                |                |                |
| subjects affected / exposed            | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Rectal Haemorrhage                     |                |                |                |
| subjects affected / exposed            | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Reflux Oesophagitis                    |                |                |                |
| subjects affected / exposed            | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Toothache                              |                |                |                |
| subjects affected / exposed            | 4 / 83 (4.82%) | 3 / 82 (3.66%) | 4 / 77 (5.19%) |
| occurrences (all)                      | 7              | 4              | 6              |
| Upper Gastrointestinal Haemorrhage     |                |                |                |
| subjects affected / exposed            | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dental caries                          |                |                |                |
| subjects affected / exposed            | 1 / 83 (1.20%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Actinic Keratosis                      |                |                |                |
| subjects affected / exposed            | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dermatitis Atopic                      |                |                |                |
| subjects affected / exposed            | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Ecchymosis                             |                |                |                |
| subjects affected / exposed            | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Granuloma Annulare                     |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Hyperkeratosis              |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Hypertrichosis              |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Lichen Planus               |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Neurodermatitis             |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pruritus                    |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Psoriasis                   |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash                        |                |                |                |
| subjects affected / exposed | 7 / 83 (8.43%) | 4 / 82 (4.88%) | 5 / 77 (6.49%) |
| occurrences (all)           | 10             | 4              | 6              |
| Rash Erythematous           |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash Papular                |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Sebaceous Hyperplasia       |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Irritation             |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Lesion                 |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Urticaria                                       |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Alopecia                                        |                |                |                |
| subjects affected / exposed                     | 2 / 83 (2.41%) | 2 / 82 (2.44%) | 0 / 77 (0.00%) |
| occurrences (all)                               | 2              | 3              | 0              |
| Dermal cyst                                     |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Dermatitis                                      |                |                |                |
| subjects affected / exposed                     | 1 / 83 (1.20%) | 0 / 82 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all)                               | 1              | 0              | 1              |
| Dry skin                                        |                |                |                |
| subjects affected / exposed                     | 3 / 83 (3.61%) | 1 / 82 (1.22%) | 0 / 77 (0.00%) |
| occurrences (all)                               | 3              | 1              | 0              |
| Renal and urinary disorders                     |                |                |                |
| Dysuria                                         |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Micturition Urgency                             |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Endocrine disorders                             |                |                |                |
| Hypothyroidism                                  |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Thyroiditis Chronic                             |                |                |                |
| subjects affected / exposed                     | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Myalgia                                         |                |                |                |
| subjects affected / exposed                     | 3 / 83 (3.61%) | 2 / 82 (2.44%) | 4 / 77 (5.19%) |
| occurrences (all)                               | 3              | 2              | 4              |
| Arthralgia                                      |                |                |                |

|                             |                  |                  |                  |
|-----------------------------|------------------|------------------|------------------|
| subjects affected / exposed | 13 / 83 (15.66%) | 12 / 82 (14.63%) | 12 / 77 (15.58%) |
| occurrences (all)           | 24               | 16               | 13               |
| Back Pain                   |                  |                  |                  |
| subjects affected / exposed | 10 / 83 (12.05%) | 17 / 82 (20.73%) | 9 / 77 (11.69%)  |
| occurrences (all)           | 12               | 19               | 11               |
| Bone Pain                   |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Bursitis                    |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Costochondritis             |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Dupuytren's Contracture     |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Foot Deformity              |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Joint Stiffness             |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Monarthritis                |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Muscle Contracture          |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Muscle Spasms               |                  |                  |                  |
| subjects affected / exposed | 4 / 83 (4.82%)   | 7 / 82 (8.54%)   | 7 / 77 (9.09%)   |
| occurrences (all)           | 4                | 7                | 7                |
| Muscular Weakness           |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Musculoskeletal Chest Pain  |                  |                  |                  |

|                             |                  |                |                 |
|-----------------------------|------------------|----------------|-----------------|
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Musculoskeletal Discomfort  |                  |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Musculoskeletal Pain        |                  |                |                 |
| subjects affected / exposed | 5 / 83 (6.02%)   | 3 / 82 (3.66%) | 5 / 77 (6.49%)  |
| occurrences (all)           | 5                | 3              | 5               |
| Musculoskeletal Stiffness   |                  |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Myalgia Intercostal         |                  |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Neck Pain                   |                  |                |                 |
| subjects affected / exposed | 3 / 83 (3.61%)   | 0 / 82 (0.00%) | 2 / 77 (2.60%)  |
| occurrences (all)           | 3                | 0              | 2               |
| Osteoarthritis              |                  |                |                 |
| subjects affected / exposed | 2 / 83 (2.41%)   | 4 / 82 (4.88%) | 4 / 77 (5.19%)  |
| occurrences (all)           | 2                | 4              | 5               |
| Osteochondrosis             |                  |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Osteosclerosis              |                  |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Pain In Extremity           |                  |                |                 |
| subjects affected / exposed | 10 / 83 (12.05%) | 8 / 82 (9.76%) | 8 / 77 (10.39%) |
| occurrences (all)           | 13               | 10             | 8               |
| Polyarthritis               |                  |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Rotator Cuff Syndrome       |                  |                |                 |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%) | 0 / 77 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Sacroiliitis                |                  |                |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Synovial Cyst               |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tendonitis                  |                |                |                |
| subjects affected / exposed | 1 / 83 (1.20%) | 6 / 82 (7.32%) | 0 / 77 (0.00%) |
| occurrences (all)           | 1              | 6              | 0              |
| Torticollis                 |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Fibromyalgia                |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Joint swelling              |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Spinal osteoarthritis       |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Trigger finger              |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 1 / 82 (1.22%) | 2 / 77 (2.60%) |
| occurrences (all)           | 0              | 1              | 2              |
| Infections and infestations |                |                |                |
| Bacterial Infection         |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Bronchitis                  |                |                |                |
| subjects affected / exposed | 2 / 83 (2.41%) | 4 / 82 (4.88%) | 4 / 77 (5.19%) |
| occurrences (all)           | 5              | 6              | 5              |
| Cellulitis                  |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Chronic Sinusitis           |                |                |                |
| subjects affected / exposed | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

|                             |                  |                  |                  |
|-----------------------------|------------------|------------------|------------------|
| Cystitis                    |                  |                  |                  |
| subjects affected / exposed | 1 / 83 (1.20%)   | 6 / 82 (7.32%)   | 3 / 77 (3.90%)   |
| occurrences (all)           | 3                | 6                | 3                |
| Ear Infection               |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Fungal Infection            |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Furuncle                    |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Gastroenteritis             |                  |                  |                  |
| subjects affected / exposed | 3 / 83 (3.61%)   | 2 / 82 (2.44%)   | 1 / 77 (1.30%)   |
| occurrences (all)           | 4                | 3                | 1                |
| Gastroenteritis Viral       |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Gastrointestinal Infection  |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Herpes Zoster               |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Influenza                   |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Nail Bed Infection Fungal   |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Nasal Abscess               |                  |                  |                  |
| subjects affected / exposed | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%)   |
| occurrences (all)           | 0                | 0                | 0                |
| Nasopharyngitis             |                  |                  |                  |
| subjects affected / exposed | 14 / 83 (16.87%) | 10 / 82 (12.20%) | 16 / 77 (20.78%) |
| occurrences (all)           | 20               | 10               | 20               |

|                                   |                |                |                |
|-----------------------------------|----------------|----------------|----------------|
| Onychomycosis                     |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Oral Candidiasis                  |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Oral Fungal Infection             |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Oral Herpes                       |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Otitis Media Acute                |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Pharyngitis                       |                |                |                |
| subjects affected / exposed       | 4 / 83 (4.82%) | 2 / 82 (2.44%) | 4 / 77 (5.19%) |
| occurrences (all)                 | 4              | 2              | 4              |
| Pharyngitis Streptococcal         |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Pneumonia                         |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Pyoderma                          |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Respiratory Tract Infection       |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Respiratory Tract Infection Viral |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Rhinitis                          |                |                |                |
| subjects affected / exposed       | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |

|                                         |                  |                  |                |
|-----------------------------------------|------------------|------------------|----------------|
| Sinusitis                               |                  |                  |                |
| subjects affected / exposed             | 4 / 83 (4.82%)   | 4 / 82 (4.88%)   | 5 / 77 (6.49%) |
| occurrences (all)                       | 4                | 4                | 6              |
| Tooth Abscess                           |                  |                  |                |
| subjects affected / exposed             | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%) |
| occurrences (all)                       | 0                | 0                | 0              |
| Tooth Infection                         |                  |                  |                |
| subjects affected / exposed             | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%) |
| occurrences (all)                       | 0                | 0                | 0              |
| Upper Respiratory Tract Infection       |                  |                  |                |
| subjects affected / exposed             | 9 / 83 (10.84%)  | 10 / 82 (12.20%) | 7 / 77 (9.09%) |
| occurrences (all)                       | 11               | 12               | 9              |
| Urinary Tract Infection                 |                  |                  |                |
| subjects affected / exposed             | 11 / 83 (13.25%) | 6 / 82 (7.32%)   | 7 / 77 (9.09%) |
| occurrences (all)                       | 11               | 6                | 7              |
| Viral Infection                         |                  |                  |                |
| subjects affected / exposed             | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%) |
| occurrences (all)                       | 0                | 0                | 0              |
| Viral Upper Respiratory Tract Infection |                  |                  |                |
| subjects affected / exposed             | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%) |
| occurrences (all)                       | 0                | 0                | 0              |
| Borrelia infection                      |                  |                  |                |
| subjects affected / exposed             | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%) |
| occurrences (all)                       | 0                | 0                | 0              |
| Eye infection                           |                  |                  |                |
| subjects affected / exposed             | 1 / 83 (1.20%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%) |
| occurrences (all)                       | 1                | 0                | 0              |
| Lower respiratory tract infection       |                  |                  |                |
| subjects affected / exposed             | 2 / 83 (2.41%)   | 1 / 82 (1.22%)   | 0 / 77 (0.00%) |
| occurrences (all)                       | 2                | 2                | 0              |
| Wound infection                         |                  |                  |                |
| subjects affected / exposed             | 0 / 83 (0.00%)   | 0 / 82 (0.00%)   | 0 / 77 (0.00%) |
| occurrences (all)                       | 0                | 0                | 0              |
| Metabolism and nutrition disorders      |                  |                  |                |

|                                             |                |                |                |
|---------------------------------------------|----------------|----------------|----------------|
| Anorexia                                    |                |                |                |
| subjects affected / exposed                 | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Dyslipidaemia                               |                |                |                |
| subjects affected / exposed                 | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Hypercholesterolaemia                       |                |                |                |
| subjects affected / exposed                 | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Hyperlipidaemia                             |                |                |                |
| subjects affected / exposed                 | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Food intolerance                            |                |                |                |
| alternative assessment type: Non-systematic |                |                |                |
| subjects affected / exposed                 | 0 / 83 (0.00%) | 0 / 82 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |

| <b>Non-serious adverse events</b>                                   | Years 1-2<br>Odanacatib 25<br>mg/Odanacatib 25<br>mg-Ext 1 | Years 1-2<br>Odanacatib 50<br>mg/Odanacatib 50<br>mg-Ext 1 | Year 3<br>Placebo/Placebo-Ext<br>2 |
|---------------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|------------------------------------|
| Total subjects affected by non-serious adverse events               |                                                            |                                                            |                                    |
| subjects affected / exposed                                         | 67 / 79 (84.81%)                                           | 66 / 78 (84.62%)                                           | 17 / 19 (89.47%)                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                            |                                                            |                                    |
| Basal Cell Carcinoma                                                |                                                            |                                                            |                                    |
| subjects affected / exposed                                         | 0 / 79 (0.00%)                                             | 0 / 78 (0.00%)                                             | 0 / 19 (0.00%)                     |
| occurrences (all)                                                   | 0                                                          | 0                                                          | 0                                  |
| Fibroma                                                             |                                                            |                                                            |                                    |
| subjects affected / exposed                                         | 0 / 79 (0.00%)                                             | 0 / 78 (0.00%)                                             | 0 / 19 (0.00%)                     |
| occurrences (all)                                                   | 0                                                          | 0                                                          | 0                                  |
| Lipoma                                                              |                                                            |                                                            |                                    |
| subjects affected / exposed                                         | 0 / 79 (0.00%)                                             | 0 / 78 (0.00%)                                             | 0 / 19 (0.00%)                     |
| occurrences (all)                                                   | 0                                                          | 0                                                          | 0                                  |
| Ovarian Neoplasm                                                    |                                                            |                                                            |                                    |
| subjects affected / exposed                                         | 0 / 79 (0.00%)                                             | 0 / 78 (0.00%)                                             | 0 / 19 (0.00%)                     |
| occurrences (all)                                                   | 0                                                          | 0                                                          | 0                                  |
| Thyroid Neoplasm                                                    |                                                            |                                                            |                                    |

|                                                      |                 |                |                 |
|------------------------------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 79 (0.00%)  | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0               |
| Benign neoplasm of thyroid gland                     |                 |                |                 |
| subjects affected / exposed                          | 0 / 79 (0.00%)  | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0               |
| Vascular disorders                                   |                 |                |                 |
| Flushing                                             |                 |                |                 |
| subjects affected / exposed                          | 0 / 79 (0.00%)  | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0               |
| Haematoma                                            |                 |                |                 |
| subjects affected / exposed                          | 0 / 79 (0.00%)  | 0 / 78 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                                    | 0               | 0              | 1               |
| Hypertension                                         |                 |                |                 |
| subjects affected / exposed                          | 8 / 79 (10.13%) | 4 / 78 (5.13%) | 0 / 19 (0.00%)  |
| occurrences (all)                                    | 8               | 4              | 0               |
| Phlebitis                                            |                 |                |                 |
| subjects affected / exposed                          | 0 / 79 (0.00%)  | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0               |
| Varicose Vein                                        |                 |                |                 |
| subjects affected / exposed                          | 0 / 79 (0.00%)  | 0 / 78 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                                    | 0               | 0              | 1               |
| General disorders and administration site conditions |                 |                |                 |
| Calcinosis                                           |                 |                |                 |
| subjects affected / exposed                          | 0 / 79 (0.00%)  | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0               |
| Chest Discomfort                                     |                 |                |                 |
| subjects affected / exposed                          | 0 / 79 (0.00%)  | 0 / 78 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                                    | 0               | 0              | 1               |
| Chest Pain                                           |                 |                |                 |
| subjects affected / exposed                          | 0 / 79 (0.00%)  | 0 / 78 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all)                                    | 0               | 0              | 2               |
| Fatigue                                              |                 |                |                 |
| subjects affected / exposed                          | 1 / 79 (1.27%)  | 3 / 78 (3.85%) | 1 / 19 (5.26%)  |
| occurrences (all)                                    | 1               | 3              | 1               |
| Influenza Like Illness                               |                 |                |                 |

|                                                                                                                               |                     |                     |                     |
|-------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                              | 2 / 79 (2.53%)<br>2 | 7 / 78 (8.97%)<br>7 | 0 / 19 (0.00%)<br>0 |
| Oedema Peripheral<br>subjects affected / exposed<br>occurrences (all)                                                         | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Wrist Fracture<br>subjects affected / exposed<br>occurrences (all)                                                            | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Immune system disorders<br>Allergy To Arthropod Sting<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Drug Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Reproductive system and breast disorders<br>Breast Mass<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Fibrocystic Breast Disease<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Pelvic Pain<br>subjects affected / exposed<br>occurrences (all)                                                               | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1 |
| Vulvovaginal Discomfort<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders<br>Pharyngolaryngeal Pain<br>subjects affected / exposed<br>occurrences (all) | 5 / 79 (6.33%)<br>5 | 1 / 78 (1.28%)<br>1 | 0 / 19 (0.00%)<br>0 |
| Allergic Pharyngitis<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Asthma                                                                                                                        |                     |                     |                     |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Dysphonia                   |                |                |                 |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Dyspnoea                    |                |                |                 |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Dyspnoea Exertional         |                |                |                 |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Emphysema                   |                |                |                 |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Haemoptysis                 |                |                |                 |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Cough                       |                |                |                 |
| subjects affected / exposed | 3 / 79 (3.80%) | 3 / 78 (3.85%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 4              | 3              | 0               |
| Psychiatric disorders       |                |                |                 |
| Insomnia                    |                |                |                 |
| subjects affected / exposed | 3 / 79 (3.80%) | 6 / 78 (7.69%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 3              | 6              | 0               |
| Alcoholism                  |                |                |                 |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Anxiety                     |                |                |                 |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all)           | 0              | 0              | 2               |
| Depression                  |                |                |                 |
| subjects affected / exposed | 3 / 79 (3.80%) | 3 / 78 (3.85%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 3              | 3              | 0               |
| Dysthymic Disorder          |                |                |                 |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |

|                                               |                |                |                |
|-----------------------------------------------|----------------|----------------|----------------|
| Stress                                        |                |                |                |
| subjects affected / exposed                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                             | 0              | 0              | 1              |
| Investigations                                |                |                |                |
| Weight Increased                              |                |                |                |
| subjects affected / exposed                   | 5 / 79 (6.33%) | 3 / 78 (3.85%) | 0 / 19 (0.00%) |
| occurrences (all)                             | 6              | 3              | 0              |
| Alanine Aminotransferase Increased            |                |                |                |
| subjects affected / exposed                   | 5 / 79 (6.33%) | 2 / 78 (2.56%) | 0 / 19 (0.00%) |
| occurrences (all)                             | 7              | 3              | 0              |
| Aspartate Aminotransferase Increased          |                |                |                |
| subjects affected / exposed                   | 4 / 79 (5.06%) | 1 / 78 (1.28%) | 0 / 19 (0.00%) |
| occurrences (all)                             | 6              | 1              | 0              |
| Blood 1,25-Dihydroxycholecalciferol Increased |                |                |                |
| subjects affected / exposed                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                             | 0              | 0              | 2              |
| Blood Cholesterol Increased                   |                |                |                |
| subjects affected / exposed                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Blood Glucose Increased                       |                |                |                |
| subjects affected / exposed                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Blood Parathyroid Hormone Increased           |                |                |                |
| subjects affected / exposed                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                             | 0              | 0              | 2              |
| Blood Pressure Increased                      |                |                |                |
| subjects affected / exposed                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Blood Triglycerides Increased                 |                |                |                |
| subjects affected / exposed                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Bone Density Decreased                        |                |                |                |
| subjects affected / exposed                   | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Carotid Bruit                                 |                |                |                |

|                                                |                |                |                |
|------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Glucose Urine Present                          |                |                |                |
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| High Density Lipoprotein Decreased             |                |                |                |
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Lymphocyte Count Decreased                     |                |                |                |
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Ultrasound Thyroid Abnormal                    |                |                |                |
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Weight Decreased                               |                |                |                |
| subjects affected / exposed                    | 1 / 79 (1.27%) | 4 / 78 (5.13%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 1              | 4              | 0              |
| White Blood Cells Urine Positive               |                |                |                |
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Blood alkaline phosphatase increased           |                |                |                |
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Body height decreased                          |                |                |                |
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Injury, poisoning and procedural complications |                |                |                |
| Arthropod Bite                                 |                |                |                |
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Arthropod Sting                                |                |                |                |
| subjects affected / exposed                    | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Contusion                                      |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 2 / 79 (2.53%) | 3 / 78 (3.85%) | 1 / 19 (5.26%) |
| occurrences (all)           | 3              | 3              | 1              |
| Device Breakage             |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Epicondylitis               |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Fall                        |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Humerus Fracture            |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Joint Sprain                |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Limb Injury                 |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Muscle Strain               |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Open Wound                  |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Procedural Pain             |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Radius Fracture             |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rib Fracture                |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Laceration             |                |                |                |

|                                            |                |                |                |
|--------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Skull Fractured Base                       |                |                |                |
| subjects affected / exposed                | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                          | 0              | 0              | 1              |
| Spinal Compression Fracture                |                |                |                |
| subjects affected / exposed                | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Spinal Fracture                            |                |                |                |
| subjects affected / exposed                | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Subdural Haematoma                         |                |                |                |
| subjects affected / exposed                | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                          | 0              | 0              | 1              |
| Thoracic Vertebral Fracture                |                |                |                |
| subjects affected / exposed                | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Tooth Fracture                             |                |                |                |
| subjects affected / exposed                | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                          | 0              | 0              | 1              |
| Vertebral Injury                           |                |                |                |
| subjects affected / exposed                | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Laceration                                 |                |                |                |
| subjects affected / exposed                | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (0.00%) |
| occurrences (all)                          | 0              | 1              | 0              |
| Ligament sprain                            |                |                |                |
| subjects affected / exposed                | 3 / 79 (3.80%) | 3 / 78 (3.85%) | 0 / 19 (0.00%) |
| occurrences (all)                          | 3              | 5              | 0              |
| Congenital, familial and genetic disorders |                |                |                |
| Congenital Diaphragmatic Hernia            |                |                |                |
| subjects affected / exposed                | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Cardiac disorders                          |                |                |                |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| Arrhythmia                  |                 |                 |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)           | 0               | 0               | 1              |
| Atrial Flutter              |                 |                 |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)           | 0               | 0               | 1              |
| Mitral Valve Prolapse       |                 |                 |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Palpitations                |                 |                 |                |
| subjects affected / exposed | 1 / 79 (1.27%)  | 5 / 78 (6.41%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 2               | 5               | 0              |
| Tachycardia                 |                 |                 |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Nervous system disorders    |                 |                 |                |
| Cervicobrachial Syndrome    |                 |                 |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Headache                    |                 |                 |                |
| subjects affected / exposed | 9 / 79 (11.39%) | 9 / 78 (11.54%) | 0 / 19 (0.00%) |
| occurrences (all)           | 9               | 9               | 0              |
| Memory Impairment           |                 |                 |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Migraine                    |                 |                 |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Paraesthesia                |                 |                 |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Sciatica                    |                 |                 |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Somnolence                  |                 |                 |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tension Headache            |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Tremor                      |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Trigeminal Neuralgia        |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Upper Motor Neuron Lesion   |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Carpal tunnel syndrome      |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dizziness                   |                |                |                |
| subjects affected / exposed | 3 / 79 (3.80%) | 4 / 78 (5.13%) | 0 / 19 (0.00%) |
| occurrences (all)           | 3              | 4              | 0              |
| Parkinson's disease         |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Ear and labyrinth disorders |                |                |                |
| Deafness                    |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tinnitus                    |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tympanosclerosis            |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Vertigo                     |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

|                                                                             |                     |                     |                     |
|-----------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Vertigo Positional<br>subjects affected / exposed<br>occurrences (all)      | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Eye disorders                                                               |                     |                     |                     |
| Cataract<br>subjects affected / exposed<br>occurrences (all)                | 0 / 79 (0.00%)<br>0 | 2 / 78 (2.56%)<br>3 | 0 / 19 (0.00%)<br>0 |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)          | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Conjunctivitis Allergic<br>subjects affected / exposed<br>occurrences (all) | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Eye Pruritus<br>subjects affected / exposed<br>occurrences (all)            | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Macular Degeneration<br>subjects affected / exposed<br>occurrences (all)    | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Retinal Tear<br>subjects affected / exposed<br>occurrences (all)            | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Gastrointestinal disorders                                                  |                     |                     |                     |
| Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all)    | 0 / 79 (0.00%)<br>0 | 5 / 78 (6.41%)<br>5 | 0 / 19 (0.00%)<br>0 |
| Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Anal Fissure<br>subjects affected / exposed<br>occurrences (all)            | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1 |
| Aphthous Stomatitis<br>subjects affected / exposed<br>occurrences (all)     | 0 / 79 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Colitis                                                                     |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Constipation                |                |                |                |
| subjects affected / exposed | 3 / 79 (3.80%) | 1 / 78 (1.28%) | 1 / 19 (5.26%) |
| occurrences (all)           | 3              | 1              | 1              |
| Diarrhoea                   |                |                |                |
| subjects affected / exposed | 3 / 79 (3.80%) | 7 / 78 (8.97%) | 1 / 19 (5.26%) |
| occurrences (all)           | 3              | 10             | 1              |
| Dry Mouth                   |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Duodenal Ulcer              |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dyspepsia                   |                |                |                |
| subjects affected / exposed | 3 / 79 (3.80%) | 6 / 78 (7.69%) | 0 / 19 (0.00%) |
| occurrences (all)           | 3              | 6              | 0              |
| Faecal Incontinence         |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Flatulence                  |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastric Disorder            |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastric Polyps              |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastric Ulcer               |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastritis                   |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Gastrointestinal Disorder   |                |                |                |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Gastrooesophageal Reflux Disease |                |                |                 |
| subjects affected / exposed      | 5 / 79 (6.33%) | 3 / 78 (3.85%) | 2 / 19 (10.53%) |
| occurrences (all)                | 5              | 3              | 2               |
| Gingival Swelling                |                |                |                 |
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Gingivitis                       |                |                |                 |
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Hiatus Hernia                    |                |                |                 |
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Inguinal Hernia                  |                |                |                 |
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Irritable Bowel Syndrome         |                |                |                 |
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Mouth Ulceration                 |                |                |                 |
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Nausea                           |                |                |                 |
| subjects affected / exposed      | 6 / 79 (7.59%) | 5 / 78 (6.41%) | 1 / 19 (5.26%)  |
| occurrences (all)                | 7              | 7              | 1               |
| Oesophagitis                     |                |                |                 |
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Rectal Haemorrhage               |                |                |                 |
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Reflux Oesophagitis              |                |                |                 |
| subjects affected / exposed      | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Toothache                        |                |                |                 |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed            | 2 / 79 (2.53%) | 2 / 78 (2.56%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 2              | 2              | 0              |
| Upper Gastrointestinal Haemorrhage     |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Dental caries                          |                |                |                |
| subjects affected / exposed            | 1 / 79 (1.27%) | 1 / 78 (1.28%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 1              | 1              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Actinic Keratosis                      |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dermatitis Atopic                      |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Ecchymosis                             |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Granuloma Annulare                     |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Hyperkeratosis                         |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Hypertrichosis                         |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Lichen Planus                          |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Neurodermatitis                        |                |                |                |
| subjects affected / exposed            | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                      | 0              | 0              | 1              |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Pruritus                    |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Psoriasis                   |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash                        |                |                |                |
| subjects affected / exposed | 2 / 79 (2.53%) | 3 / 78 (3.85%) | 1 / 19 (5.26%) |
| occurrences (all)           | 2              | 3              | 1              |
| Rash Erythematous           |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash Papular                |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Sebaceous Hyperplasia       |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Irritation             |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Lesion                 |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Urticaria                   |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 3              |
| Alopecia                    |                |                |                |
| subjects affected / exposed | 1 / 79 (1.27%) | 1 / 78 (1.28%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Dermal cyst                 |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dermatitis                  |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 1 / 78 (1.28%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |

|                                                                                                                |                        |                        |                      |
|----------------------------------------------------------------------------------------------------------------|------------------------|------------------------|----------------------|
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 79 (0.00%)<br>0    | 3 / 78 (3.85%)<br>3    | 0 / 19 (0.00%)<br>0  |
| Renal and urinary disorders<br>Dysuria<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 79 (0.00%)<br>0    | 0 / 78 (0.00%)<br>0    | 0 / 19 (0.00%)<br>0  |
| Micturition Urgency<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 79 (0.00%)<br>0    | 0 / 78 (0.00%)<br>0    | 0 / 19 (0.00%)<br>0  |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 79 (0.00%)<br>0    | 0 / 78 (0.00%)<br>0    | 0 / 19 (0.00%)<br>0  |
| Thyroiditis Chronic<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 79 (0.00%)<br>0    | 0 / 78 (0.00%)<br>0    | 0 / 19 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders<br>Myalgia<br>subjects affected / exposed<br>occurrences (all) | 3 / 79 (3.80%)<br>3    | 2 / 78 (2.56%)<br>2    | 0 / 19 (0.00%)<br>0  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                                                 | 14 / 79 (17.72%)<br>17 | 12 / 78 (15.38%)<br>14 | 3 / 19 (15.79%)<br>4 |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)                                                  | 14 / 79 (17.72%)<br>19 | 11 / 78 (14.10%)<br>13 | 2 / 19 (10.53%)<br>2 |
| Bone Pain<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 79 (0.00%)<br>0    | 0 / 78 (0.00%)<br>0    | 1 / 19 (5.26%)<br>1  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 79 (0.00%)<br>0    | 0 / 78 (0.00%)<br>0    | 0 / 19 (0.00%)<br>0  |
| Costochondritis<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 79 (0.00%)<br>0    | 0 / 78 (0.00%)<br>0    | 1 / 19 (5.26%)<br>1  |

|                             |                  |                  |                |
|-----------------------------|------------------|------------------|----------------|
| Dupuytren's Contracture     |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0                | 0              |
| Foot Deformity              |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0                | 0              |
| Joint Stiffness             |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0                | 0              |
| Monarthrititis              |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0                | 0              |
| Muscle Contracture          |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0                | 0              |
| Muscle Spasms               |                  |                  |                |
| subjects affected / exposed | 3 / 79 (3.80%)   | 12 / 78 (15.38%) | 1 / 19 (5.26%) |
| occurrences (all)           | 3                | 12               | 1              |
| Muscular Weakness           |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)           | 0                | 0                | 1              |
| Musculoskeletal Chest Pain  |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0                | 0              |
| Musculoskeletal Discomfort  |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0                | 0              |
| Musculoskeletal Pain        |                  |                  |                |
| subjects affected / exposed | 10 / 79 (12.66%) | 4 / 78 (5.13%)   | 1 / 19 (5.26%) |
| occurrences (all)           | 10               | 4                | 1              |
| Musculoskeletal Stiffness   |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)           | 0                | 0                | 1              |
| Myalgia Intercostal         |                  |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)           | 0                | 0                | 1              |

|                             |                  |                |                |
|-----------------------------|------------------|----------------|----------------|
| Neck Pain                   |                  |                |                |
| subjects affected / exposed | 5 / 79 (6.33%)   | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 5                | 0              | 0              |
| Osteoarthritis              |                  |                |                |
| subjects affected / exposed | 4 / 79 (5.06%)   | 5 / 78 (6.41%) | 0 / 19 (0.00%) |
| occurrences (all)           | 4                | 5              | 0              |
| Osteochondrosis             |                  |                |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0                | 0              | 1              |
| Osteosclerosis              |                  |                |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0              | 0              |
| Pain In Extremity           |                  |                |                |
| subjects affected / exposed | 12 / 79 (15.19%) | 3 / 78 (3.85%) | 1 / 19 (5.26%) |
| occurrences (all)           | 12               | 5              | 1              |
| Polyarthritits              |                  |                |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0                | 0              | 1              |
| Rotator Cuff Syndrome       |                  |                |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0              | 0              |
| Sacroiliitis                |                  |                |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0                | 0              | 1              |
| Synovial Cyst               |                  |                |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0              | 0              |
| Tendonitis                  |                  |                |                |
| subjects affected / exposed | 1 / 79 (1.27%)   | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1                | 0              | 0              |
| Torticollis                 |                  |                |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0              | 0              |
| Fibromyalgia                |                  |                |                |
| subjects affected / exposed | 0 / 79 (0.00%)   | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0                | 0              | 0              |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Joint swelling              |                |                |                |
| subjects affected / exposed | 1 / 79 (1.27%) | 1 / 78 (1.28%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Spinal osteoarthritis       |                |                |                |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Trigger finger              |                |                |                |
| subjects affected / exposed | 2 / 79 (2.53%) | 2 / 78 (2.56%) | 0 / 19 (0.00%) |
| occurrences (all)           | 2              | 3              | 0              |
| Infections and infestations |                |                |                |
| Bacterial Infection         |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Bronchitis                  |                |                |                |
| subjects affected / exposed | 2 / 79 (2.53%) | 1 / 78 (1.28%) | 1 / 19 (5.26%) |
| occurrences (all)           | 2              | 2              | 1              |
| Cellulitis                  |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Chronic Sinusitis           |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Cystitis                    |                |                |                |
| subjects affected / exposed | 1 / 79 (1.27%) | 2 / 78 (2.56%) | 0 / 19 (0.00%) |
| occurrences (all)           | 2              | 2              | 0              |
| Ear Infection               |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Fungal Infection            |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Furuncle                    |                |                |                |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastroenteritis             |                |                |                |

|                             |                 |                  |                |
|-----------------------------|-----------------|------------------|----------------|
| subjects affected / exposed | 4 / 79 (5.06%)  | 1 / 78 (1.28%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 4               | 1                | 0              |
| Gastroenteritis Viral       |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0                | 0              |
| Gastrointestinal Infection  |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0                | 0              |
| Herpes Zoster               |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0                | 0              |
| Influenza                   |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0                | 0              |
| Nail Bed Infection Fungal   |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)           | 0               | 0                | 1              |
| Nasal Abscess               |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)           | 0               | 0                | 2              |
| Nasopharyngitis             |                 |                  |                |
| subjects affected / exposed | 8 / 79 (10.13%) | 14 / 78 (17.95%) | 1 / 19 (5.26%) |
| occurrences (all)           | 10              | 20               | 1              |
| Onychomycosis               |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0                | 0              |
| Oral Candidiasis            |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0                | 0              |
| Oral Fungal Infection       |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0                | 0              |
| Oral Herpes                 |                 |                  |                |
| subjects affected / exposed | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)           | 0               | 0                | 0              |
| Otitis Media Acute          |                 |                  |                |

|                                   |                |                  |                |
|-----------------------------------|----------------|------------------|----------------|
| subjects affected / exposed       | 0 / 79 (0.00%) | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Pharyngitis                       |                |                  |                |
| subjects affected / exposed       | 2 / 79 (2.53%) | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 2              | 0                | 0              |
| Pharyngitis Streptococcal         |                |                  |                |
| subjects affected / exposed       | 0 / 79 (0.00%) | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Pneumonia                         |                |                  |                |
| subjects affected / exposed       | 0 / 79 (0.00%) | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Pyoderma                          |                |                  |                |
| subjects affected / exposed       | 0 / 79 (0.00%) | 0 / 78 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)                 | 0              | 0                | 1              |
| Respiratory Tract Infection       |                |                  |                |
| subjects affected / exposed       | 0 / 79 (0.00%) | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Respiratory Tract Infection Viral |                |                  |                |
| subjects affected / exposed       | 0 / 79 (0.00%) | 0 / 78 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)                 | 0              | 0                | 1              |
| Rhinitis                          |                |                  |                |
| subjects affected / exposed       | 0 / 79 (0.00%) | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Sinusitis                         |                |                  |                |
| subjects affected / exposed       | 4 / 79 (5.06%) | 5 / 78 (6.41%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 5              | 6                | 0              |
| Tooth Abscess                     |                |                  |                |
| subjects affected / exposed       | 0 / 79 (0.00%) | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Tooth Infection                   |                |                  |                |
| subjects affected / exposed       | 0 / 79 (0.00%) | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Upper Respiratory Tract Infection |                |                  |                |
| subjects affected / exposed       | 7 / 79 (8.86%) | 10 / 78 (12.82%) | 1 / 19 (5.26%) |
| occurrences (all)                 | 11             | 14               | 1              |
| Urinary Tract Infection           |                |                  |                |

|                                             |                 |                  |                |
|---------------------------------------------|-----------------|------------------|----------------|
| subjects affected / exposed                 | 8 / 79 (10.13%) | 12 / 78 (15.38%) | 1 / 19 (5.26%) |
| occurrences (all)                           | 8               | 12               | 1              |
| Viral Infection                             |                 |                  |                |
| subjects affected / exposed                 | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                           | 0               | 0                | 0              |
| Viral Upper Respiratory Tract Infection     |                 |                  |                |
| subjects affected / exposed                 | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)                           | 0               | 0                | 1              |
| Borrelia infection                          |                 |                  |                |
| subjects affected / exposed                 | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                           | 0               | 0                | 0              |
| Eye infection                               |                 |                  |                |
| subjects affected / exposed                 | 2 / 79 (2.53%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                           | 2               | 0                | 0              |
| Lower respiratory tract infection           |                 |                  |                |
| subjects affected / exposed                 | 2 / 79 (2.53%)  | 2 / 78 (2.56%)   | 0 / 19 (0.00%) |
| occurrences (all)                           | 5               | 2                | 0              |
| Wound infection                             |                 |                  |                |
| subjects affected / exposed                 | 1 / 79 (1.27%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                           | 1               | 0                | 0              |
| Metabolism and nutrition disorders          |                 |                  |                |
| Anorexia                                    |                 |                  |                |
| subjects affected / exposed                 | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                           | 0               | 0                | 0              |
| Dyslipidaemia                               |                 |                  |                |
| subjects affected / exposed                 | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                           | 0               | 0                | 0              |
| Hypercholesterolaemia                       |                 |                  |                |
| subjects affected / exposed                 | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                           | 0               | 0                | 0              |
| Hyperlipidaemia                             |                 |                  |                |
| subjects affected / exposed                 | 0 / 79 (0.00%)  | 0 / 78 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                           | 0               | 0                | 0              |
| Food intolerance                            |                 |                  |                |
| alternative assessment type: Non-systematic |                 |                  |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 78 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

| <b>Non-serious adverse events</b>                                   | Year 3<br>Placebo/Odanacatib<br>50 mg-Ext 2 | Year 3 Odanacatib 3<br>mg/Placebo-Ext 2 | Year 3 Odanacatib 3<br>mg/Odanacatib 50<br>mg-Ext 2 |
|---------------------------------------------------------------------|---------------------------------------------|-----------------------------------------|-----------------------------------------------------|
| Total subjects affected by non-serious adverse events               |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 13 / 22 (59.09%)                            | 16 / 18 (88.89%)                        | 14 / 17 (82.35%)                                    |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                             |                                         |                                                     |
| Basal Cell Carcinoma                                                |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 0 / 22 (0.00%)                              | 0 / 18 (0.00%)                          | 0 / 17 (0.00%)                                      |
| occurrences (all)                                                   | 0                                           | 0                                       | 0                                                   |
| Fibroma                                                             |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 0 / 22 (0.00%)                              | 0 / 18 (0.00%)                          | 0 / 17 (0.00%)                                      |
| occurrences (all)                                                   | 0                                           | 0                                       | 0                                                   |
| Lipoma                                                              |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 0 / 22 (0.00%)                              | 0 / 18 (0.00%)                          | 0 / 17 (0.00%)                                      |
| occurrences (all)                                                   | 0                                           | 0                                       | 0                                                   |
| Ovarian Neoplasm                                                    |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 0 / 22 (0.00%)                              | 1 / 18 (5.56%)                          | 0 / 17 (0.00%)                                      |
| occurrences (all)                                                   | 0                                           | 1                                       | 0                                                   |
| Thyroid Neoplasm                                                    |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 0 / 22 (0.00%)                              | 0 / 18 (0.00%)                          | 0 / 17 (0.00%)                                      |
| occurrences (all)                                                   | 0                                           | 0                                       | 0                                                   |
| Benign neoplasm of thyroid gland                                    |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 0 / 22 (0.00%)                              | 0 / 18 (0.00%)                          | 0 / 17 (0.00%)                                      |
| occurrences (all)                                                   | 0                                           | 0                                       | 0                                                   |
| Vascular disorders                                                  |                                             |                                         |                                                     |
| Flushing                                                            |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 0 / 22 (0.00%)                              | 0 / 18 (0.00%)                          | 0 / 17 (0.00%)                                      |
| occurrences (all)                                                   | 0                                           | 0                                       | 0                                                   |
| Haematoma                                                           |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 0 / 22 (0.00%)                              | 0 / 18 (0.00%)                          | 1 / 17 (5.88%)                                      |
| occurrences (all)                                                   | 0                                           | 0                                       | 2                                                   |
| Hypertension                                                        |                                             |                                         |                                                     |
| subjects affected / exposed                                         | 1 / 22 (4.55%)                              | 0 / 18 (0.00%)                          | 0 / 17 (0.00%)                                      |
| occurrences (all)                                                   | 1                                           | 0                                       | 0                                                   |
| Phlebitis                                                           |                                             |                                         |                                                     |

|                                                                                |                     |                     |                     |
|--------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                               | 0 / 22 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 17 (0.00%)<br>0 |
| Varicose Vein<br>subjects affected / exposed<br>occurrences (all)              | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| General disorders and administration<br>site conditions                        |                     |                     |                     |
| Calcinosis<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Chest Discomfort<br>subjects affected / exposed<br>occurrences (all)           | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Chest Pain<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 22 (4.55%)<br>2 | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 |
| Influenza Like Illness<br>subjects affected / exposed<br>occurrences (all)     | 0 / 22 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 17 (0.00%)<br>0 |
| Oedema Peripheral<br>subjects affected / exposed<br>occurrences (all)          | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Wrist Fracture<br>subjects affected / exposed<br>occurrences (all)             | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Immune system disorders                                                        |                     |                     |                     |
| Allergy To Arthropod Sting<br>subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Drug Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)      | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Reproductive system and breast<br>disorders                                    |                     |                     |                     |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Breast Mass                                     |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Fibrocystic Breast Disease                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Pelvic Pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Vulvovaginal Discomfort                         |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Pharyngolaryngeal Pain                          |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Allergic Pharyngitis                            |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Asthma                                          |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Dysphonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Dyspnoea                                        |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Dyspnoea Exertional                             |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Emphysema                                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Haemoptysis                                     |                |                |                |

|                                               |                |                |                |
|-----------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                   | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 0              | 1              | 0              |
| Cough                                         |                |                |                |
| subjects affected / exposed                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Psychiatric disorders                         |                |                |                |
| Insomnia                                      |                |                |                |
| subjects affected / exposed                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Alcoholism                                    |                |                |                |
| subjects affected / exposed                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Anxiety                                       |                |                |                |
| subjects affected / exposed                   | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 1              | 0              | 0              |
| Depression                                    |                |                |                |
| subjects affected / exposed                   | 2 / 22 (9.09%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 2              | 0              | 0              |
| Dysthymic Disorder                            |                |                |                |
| subjects affected / exposed                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all)                             | 0              | 0              | 1              |
| Stress                                        |                |                |                |
| subjects affected / exposed                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Investigations                                |                |                |                |
| Weight Increased                              |                |                |                |
| subjects affected / exposed                   | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Alanine Aminotransferase Increased            |                |                |                |
| subjects affected / exposed                   | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 0              | 1              | 0              |
| Aspartate Aminotransferase Increased          |                |                |                |
| subjects affected / exposed                   | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                             | 0              | 1              | 0              |
| Blood 1,25-Dihydroxycholecalciferol Increased |                |                |                |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed         | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 1 / 17 (5.88%) |
| occurrences (all)                   | 0              | 1              | 1              |
| Blood Cholesterol Increased         |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Blood Glucose Increased             |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Blood Parathyroid Hormone Increased |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Blood Pressure Increased            |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Blood Triglycerides Increased       |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                   | 0              | 1              | 0              |
| Bone Density Decreased              |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Carotid Bruit                       |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Glucose Urine Present               |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| High Density Lipoprotein Decreased  |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                   | 0              | 1              | 0              |
| Lymphocyte Count Decreased          |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Ultrasound Thyroid Abnormal         |                |                |                |
| subjects affected / exposed         | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |

|                                                                                          |                     |                     |                     |
|------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Weight Decreased<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 |
| White Blood Cells Urine Positive<br>subjects affected / exposed<br>occurrences (all)     | 1 / 22 (4.55%)<br>1 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Body height decreased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Injury, poisoning and procedural complications                                           |                     |                     |                     |
| Arthropod Bite<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 |
| Arthropod Sting<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 22 (4.55%)<br>1 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>2 |
| Device Breakage<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Epicondylitis<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 22 (4.55%)<br>1 | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 |
| Humerus Fracture<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Joint Sprain                                                                             |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 2              | 0              | 0              |
| Limb Injury                 |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Muscle Strain               |                |                |                |
| subjects affected / exposed | 2 / 22 (9.09%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 2              | 1              | 0              |
| Open Wound                  |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Procedural Pain             |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Radius Fracture             |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rib Fracture                |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Laceration             |                |                |                |
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 2              | 0              | 0              |
| Skull Fractured Base        |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Spinal Compression Fracture |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Spinal Fracture             |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all)           | 0              | 0              | 1              |
| Subdural Haematoma          |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Thoracic Vertebral Fracture |                |                |                |

|                                            |                |                |                |
|--------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Tooth Fracture                             |                |                |                |
| subjects affected / exposed                | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Vertebral Injury                           |                |                |                |
| subjects affected / exposed                | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Laceration                                 |                |                |                |
| subjects affected / exposed                | 2 / 22 (9.09%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 2              | 0              | 0              |
| Ligament sprain                            |                |                |                |
| subjects affected / exposed                | 2 / 22 (9.09%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 2              | 0              | 0              |
| Congenital, familial and genetic disorders |                |                |                |
| Congenital Diaphragmatic Hernia            |                |                |                |
| subjects affected / exposed                | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Cardiac disorders                          |                |                |                |
| Arrhythmia                                 |                |                |                |
| subjects affected / exposed                | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Atrial Flutter                             |                |                |                |
| subjects affected / exposed                | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Mitral Valve Prolapse                      |                |                |                |
| subjects affected / exposed                | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Palpitations                               |                |                |                |
| subjects affected / exposed                | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Tachycardia                                |                |                |                |
| subjects affected / exposed                | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                          | 0              | 1              | 0              |
| Nervous system disorders                   |                |                |                |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| Cervicobrachial Syndrome    |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Headache                    |                |                |                 |
| subjects affected / exposed | 2 / 22 (9.09%) | 1 / 18 (5.56%) | 3 / 17 (17.65%) |
| occurrences (all)           | 2              | 1              | 3               |
| Memory Impairment           |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Migraine                    |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Paraesthesia                |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Sciatica                    |                |                |                 |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 1 / 17 (5.88%)  |
| occurrences (all)           | 1              | 0              | 2               |
| Somnolence                  |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Tension Headache            |                |                |                 |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Tremor                      |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Trigeminal Neuralgia        |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Upper Motor Neuron Lesion   |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Carpal tunnel syndrome      |                |                |                 |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |

|                                                                             |                     |                     |                     |
|-----------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Dizziness<br>subjects affected / exposed<br>occurrences (all)               | 0 / 22 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 1 / 17 (5.88%)<br>1 |
| Parkinson's disease<br>subjects affected / exposed<br>occurrences (all)     | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Ear and labyrinth disorders                                                 |                     |                     |                     |
| Deafness<br>subjects affected / exposed<br>occurrences (all)                | 0 / 22 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 17 (0.00%)<br>0 |
| Tinnitus<br>subjects affected / exposed<br>occurrences (all)                | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Tympanosclerosis<br>subjects affected / exposed<br>occurrences (all)        | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 22 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 17 (0.00%)<br>0 |
| Vertigo Positional<br>subjects affected / exposed<br>occurrences (all)      | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 |
| Eye disorders                                                               |                     |                     |                     |
| Cataract<br>subjects affected / exposed<br>occurrences (all)                | 1 / 22 (4.55%)<br>1 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)          | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Conjunctivitis Allergic<br>subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 |
| Eye Pruritus<br>subjects affected / exposed<br>occurrences (all)            | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Macular Degeneration                                                        |                     |                     |                     |

|                                                                          |                     |                     |                     |
|--------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                         | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Retinal Tear<br>subjects affected / exposed<br>occurrences (all)         | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Gastrointestinal disorders                                               |                     |                     |                     |
| Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)       | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Anal Fissure<br>subjects affected / exposed<br>occurrences (all)         | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Aphthous Stomatitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Colitis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)         | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)            | 2 / 22 (9.09%)<br>2 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Dry Mouth<br>subjects affected / exposed<br>occurrences (all)            | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Duodenal Ulcer<br>subjects affected / exposed<br>occurrences (all)       | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 |

|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| Faecal Incontinence              |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Flatulence                       |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all)                | 0              | 0              | 1              |
| Gastric Disorder                 |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastric Polyps                   |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastric Ulcer                    |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastritis                        |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastrointestinal Disorder        |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastrooesophageal Reflux Disease |                |                |                |
| subjects affected / exposed      | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| Gingival Swelling                |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Gingivitis                       |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Hiatus Hernia                    |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Inguinal Hernia                  |                |                |                |
| subjects affected / exposed      | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| Irritable Bowel Syndrome               |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 1 / 17 (5.88%) |
| occurrences (all)                      | 0              | 1              | 3              |
| Mouth Ulceration                       |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Nausea                                 |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Oesophagitis                           |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Rectal Haemorrhage                     |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Reflux Oesophagitis                    |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Toothache                              |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Upper Gastrointestinal Haemorrhage     |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Dental caries                          |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Actinic Keratosis                      |                |                |                |
| subjects affected / exposed            | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dermatitis Atopic                      |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Ecchymosis                  |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Granuloma Annulare          |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Hyperkeratosis              |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Hypertrichosis              |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Lichen Planus               |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all)           | 0              | 0              | 1              |
| Neurodermatitis             |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pruritus                    |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Psoriasis                   |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash                        |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 2              | 0              |
| Rash Erythematous           |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash Papular                |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Sebaceous Hyperplasia       |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Irritation             |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Skin Lesion                 |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Urticaria                   |                |                |                |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Alopecia                    |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dermal cyst                 |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dermatitis                  |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dry skin                    |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Renal and urinary disorders |                |                |                |
| Dysuria                     |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Micturition Urgency         |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Endocrine disorders         |                |                |                |
| Hypothyroidism              |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Thyroiditis Chronic         |                |                |                |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Myalgia                                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Arthralgia                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 22 (4.55%)  | 1 / 18 (5.56%)  | 1 / 17 (5.88%)  |
| occurrences (all)                               | 1               | 1               | 1               |
| Back Pain                                       |                 |                 |                 |
| subjects affected / exposed                     | 5 / 22 (22.73%) | 1 / 18 (5.56%)  | 2 / 17 (11.76%) |
| occurrences (all)                               | 5               | 1               | 2               |
| Bone Pain                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Bursitis                                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 2 / 17 (11.76%) |
| occurrences (all)                               | 0               | 0               | 3               |
| Costochondritis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Dupuytren's Contracture                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 1 / 17 (5.88%)  |
| occurrences (all)                               | 0               | 0               | 1               |
| Foot Deformity                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 2 / 18 (11.11%) | 0 / 17 (0.00%)  |
| occurrences (all)                               | 0               | 2               | 0               |
| Joint Stiffness                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 1 / 17 (5.88%)  |
| occurrences (all)                               | 0               | 0               | 1               |
| Monarthritis                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Muscle Contracture                              |                 |                 |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Muscle Spasms               |                |                |                |
| subjects affected / exposed | 2 / 22 (9.09%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 3              | 1              | 0              |
| Muscular Weakness           |                |                |                |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Musculoskeletal Chest Pain  |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Musculoskeletal Discomfort  |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Musculoskeletal Pain        |                |                |                |
| subjects affected / exposed | 1 / 22 (4.55%) | 1 / 18 (5.56%) | 1 / 17 (5.88%) |
| occurrences (all)           | 1              | 1              | 1              |
| Musculoskeletal Stiffness   |                |                |                |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Myalgia Intercostal         |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Neck Pain                   |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Osteoarthritis              |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Osteochondrosis             |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Osteosclerosis              |                |                |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pain In Extremity           |                |                |                |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 2 / 22 (9.09%) | 1 / 18 (5.56%) | 2 / 17 (11.76%) |
| occurrences (all)           | 2              | 1              | 2               |
| Polyarthritis               |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Rotator Cuff Syndrome       |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Sacroiliitis                |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Synovial Cyst               |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Tendonitis                  |                |                |                 |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Torticollis                 |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Fibromyalgia                |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Joint swelling              |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Spinal osteoarthritis       |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Trigger finger              |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Infections and infestations |                |                |                 |
| Bacterial Infection         |                |                |                 |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Bronchitis                  |                |                 |                |
| subjects affected / exposed | 2 / 22 (9.09%) | 1 / 18 (5.56%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 3              | 1               | 0              |
| Cellulitis                  |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Chronic Sinusitis           |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Cystitis                    |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Ear Infection               |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Fungal Infection            |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Furuncle                    |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Gastroenteritis             |                |                 |                |
| subjects affected / exposed | 1 / 22 (4.55%) | 2 / 18 (11.11%) | 0 / 17 (0.00%) |
| occurrences (all)           | 1              | 2               | 0              |
| Gastroenteritis Viral       |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Gastrointestinal Infection  |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Herpes Zoster               |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Influenza                   |                |                 |                |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 18 (5.56%)  | 0 / 17 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Nail Bed Infection Fungal   |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Nasal Abscess               |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Nasopharyngitis             |                 |                 |                 |
| subjects affected / exposed | 4 / 22 (18.18%) | 2 / 18 (11.11%) | 2 / 17 (11.76%) |
| occurrences (all)           | 5               | 3               | 2               |
| Onychomycosis               |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Oral Candidiasis            |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Oral Fungal Infection       |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Oral Herpes                 |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Otitis Media Acute          |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Pharyngitis                 |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Pharyngitis Streptococcal   |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Pneumonia                   |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 1 / 17 (5.88%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Pyoderma                    |                 |                 |                 |
| subjects affected / exposed | 0 / 22 (0.00%)  | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |

|                                         |                |                 |                 |
|-----------------------------------------|----------------|-----------------|-----------------|
| Respiratory Tract Infection             |                |                 |                 |
| subjects affected / exposed             | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 1 / 17 (5.88%)  |
| occurrences (all)                       | 0              | 0               | 2               |
| Respiratory Tract Infection Viral       |                |                 |                 |
| subjects affected / exposed             | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Rhinitis                                |                |                 |                 |
| subjects affected / exposed             | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Sinusitis                               |                |                 |                 |
| subjects affected / exposed             | 0 / 22 (0.00%) | 1 / 18 (5.56%)  | 1 / 17 (5.88%)  |
| occurrences (all)                       | 0              | 2               | 1               |
| Tooth Abscess                           |                |                 |                 |
| subjects affected / exposed             | 1 / 22 (4.55%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                       | 1              | 0               | 0               |
| Tooth Infection                         |                |                 |                 |
| subjects affected / exposed             | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 1 / 17 (5.88%)  |
| occurrences (all)                       | 0              | 0               | 1               |
| Upper Respiratory Tract Infection       |                |                 |                 |
| subjects affected / exposed             | 0 / 22 (0.00%) | 3 / 18 (16.67%) | 2 / 17 (11.76%) |
| occurrences (all)                       | 0              | 4               | 2               |
| Urinary Tract Infection                 |                |                 |                 |
| subjects affected / exposed             | 2 / 22 (9.09%) | 1 / 18 (5.56%)  | 2 / 17 (11.76%) |
| occurrences (all)                       | 3              | 1               | 2               |
| Viral Infection                         |                |                 |                 |
| subjects affected / exposed             | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Viral Upper Respiratory Tract Infection |                |                 |                 |
| subjects affected / exposed             | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Borrelia infection                      |                |                 |                 |
| subjects affected / exposed             | 0 / 22 (0.00%) | 0 / 18 (0.00%)  | 0 / 17 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Eye infection                           |                |                 |                 |

|                                                                                                                     |                     |                      |                     |
|---------------------------------------------------------------------------------------------------------------------|---------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                    | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 0 / 17 (0.00%)<br>0 |
| Lower respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 22 (4.55%)<br>1 | 0 / 18 (0.00%)<br>0  | 0 / 17 (0.00%)<br>0 |
| Wound infection<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 0 / 17 (0.00%)<br>0 |
| Metabolism and nutrition disorders                                                                                  |                     |                      |                     |
| Anorexia<br>subjects affected / exposed<br>occurrences (all)                                                        | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 0 / 17 (0.00%)<br>0 |
| Dyslipidaemia<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 0 / 17 (0.00%)<br>0 |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 22 (0.00%)<br>0 | 2 / 18 (11.11%)<br>2 | 0 / 17 (0.00%)<br>0 |
| Hyperlipidaemia<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 0 / 17 (0.00%)<br>0 |
| Food intolerance<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 0 / 17 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>                                                       | Year 3 Odanacatib<br>10 mg/Placebo-Ext 2 | Year 3 Odanacatib<br>10 mg/Odanacatib<br>50 mg-Ext 2 | Year 3 Odanacatib<br>25 mg/Placebo-Ext 2 |
|-----------------------------------------------------------------------------------------|------------------------------------------|------------------------------------------------------|------------------------------------------|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed | 13 / 18 (72.22%)                         | 15 / 17 (88.24%)                                     | 15 / 19 (78.95%)                         |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)                  |                                          |                                                      |                                          |
| Basal Cell Carcinoma<br>subjects affected / exposed<br>occurrences (all)                | 1 / 18 (5.56%)<br>1                      | 0 / 17 (0.00%)<br>0                                  | 0 / 19 (0.00%)<br>0                      |
| Fibroma                                                                                 |                                          |                                                      |                                          |

|                                                                                                                           |                     |                     |                      |
|---------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                                                          | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Lipoma<br>subjects affected / exposed<br>occurrences (all)                                                                | 1 / 18 (5.56%)<br>1 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Ovarian Neoplasm<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Thyroid Neoplasm<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Benign neoplasm of thyroid gland<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Vascular disorders<br>Flushing<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 | 0 / 19 (0.00%)<br>0  |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)                                                             | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)                                                          | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 2 / 19 (10.53%)<br>0 |
| Phlebitis<br>subjects affected / exposed<br>occurrences (all)                                                             | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Varicose Vein<br>subjects affected / exposed<br>occurrences (all)                                                         | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| General disorders and administration<br>site conditions<br>Calcinosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Chest Discomfort                                                                                                          |                     |                     |                      |

|                                                                                                             |                     |                     |                     |
|-------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                            | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Chest Pain<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 | 0 / 19 (0.00%)<br>0 |
| Influenza Like Illness<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 | 0 / 19 (0.00%)<br>0 |
| Oedema Peripheral<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 18 (5.56%)<br>1 | 1 / 17 (5.88%)<br>1 | 1 / 19 (5.26%)<br>1 |
| Wrist Fracture<br>subjects affected / exposed<br>occurrences (all)                                          | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1 |
| Immune system disorders<br>Allergy To Arthropod Sting<br>subjects affected / exposed<br>occurrences (all)   | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Drug Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Reproductive system and breast disorders<br>Breast Mass<br>subjects affected / exposed<br>occurrences (all) | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1 |
| Fibrocystic Breast Disease<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Pelvic Pain<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Vulvovaginal Discomfort                                                                                     |                     |                     |                     |

|                                                  |                     |                     |                     |
|--------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders  |                     |                     |                     |
| Pharyngolaryngeal Pain                           |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 17 (0.00%)      | 0 / 19 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Allergic Pharyngitis                             |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 17 (0.00%)      | 0 / 19 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Asthma                                           |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 17 (0.00%)      | 1 / 19 (5.26%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Dysphonia                                        |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 17 (0.00%)      | 0 / 19 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Dyspnoea                                         |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 17 (0.00%)      | 0 / 19 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Dyspnoea Exertional                              |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 17 (0.00%)      | 1 / 19 (5.26%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Emphysema                                        |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 17 (0.00%)      | 0 / 19 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Haemoptysis                                      |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 17 (0.00%)      | 0 / 19 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Cough                                            |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 2 / 17 (11.76%)     | 0 / 19 (0.00%)      |
| occurrences (all)                                | 0                   | 2                   | 0                   |
| Psychiatric disorders                            |                     |                     |                     |
| Insomnia                                         |                     |                     |                     |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 17 (0.00%)      | 0 / 19 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Alcoholism                                       |                     |                     |                     |

|                                               |                |                 |                |
|-----------------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed                   | 0 / 18 (0.00%) | 1 / 17 (5.88%)  | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 1               | 0              |
| Anxiety                                       |                |                 |                |
| subjects affected / exposed                   | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0               | 0              |
| Depression                                    |                |                 |                |
| subjects affected / exposed                   | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0               | 0              |
| Dysthymic Disorder                            |                |                 |                |
| subjects affected / exposed                   | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0               | 0              |
| Stress                                        |                |                 |                |
| subjects affected / exposed                   | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0               | 0              |
| Investigations                                |                |                 |                |
| Weight Increased                              |                |                 |                |
| subjects affected / exposed                   | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0               | 0              |
| Alanine Aminotransferase Increased            |                |                 |                |
| subjects affected / exposed                   | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)                             | 0              | 0               | 1              |
| Aspartate Aminotransferase Increased          |                |                 |                |
| subjects affected / exposed                   | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0               | 0              |
| Blood 1,25-Dihydroxycholecalciferol Increased |                |                 |                |
| subjects affected / exposed                   | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 0               | 0              |
| Blood Cholesterol Increased                   |                |                 |                |
| subjects affected / exposed                   | 0 / 18 (0.00%) | 2 / 17 (11.76%) | 0 / 19 (0.00%) |
| occurrences (all)                             | 0              | 2               | 0              |
| Blood Glucose Increased                       |                |                 |                |
| subjects affected / exposed                   | 1 / 18 (5.56%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                             | 1              | 0               | 0              |
| Blood Parathyroid Hormone Increased           |                |                 |                |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed          | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 5              | 0              |
| Blood Pressure Increased             |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood Triglycerides Increased        |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Bone Density Decreased               |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Carotid Bruit                        |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Glucose Urine Present                |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| High Density Lipoprotein Decreased   |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Lymphocyte Count Decreased           |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Ultrasound Thyroid Abnormal          |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0              |
| Weight Decreased                     |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0              |
| White Blood Cells Urine Positive     |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood alkaline phosphatase increased |                |                |                |
| subjects affected / exposed          | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Body height decreased                |                |                |                |

|                                                |                |                |                |
|------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Arthropod Bite                                 |                |                |                |
| subjects affected / exposed                    | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Arthropod Sting                                |                |                |                |
| subjects affected / exposed                    | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Contusion                                      |                |                |                |
| subjects affected / exposed                    | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Device Breakage                                |                |                |                |
| subjects affected / exposed                    | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Epicondylitis                                  |                |                |                |
| subjects affected / exposed                    | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Fall                                           |                |                |                |
| subjects affected / exposed                    | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Humerus Fracture                               |                |                |                |
| subjects affected / exposed                    | 1 / 18 (5.56%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 2              | 1              | 0              |
| Joint Sprain                                   |                |                |                |
| subjects affected / exposed                    | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                              | 1              | 0              | 1              |
| Limb Injury                                    |                |                |                |
| subjects affected / exposed                    | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Muscle Strain                                  |                |                |                |
| subjects affected / exposed                    | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Open Wound                                     |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Procedural Pain             |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Radius Fracture             |                |                |                |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Rib Fracture                |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Laceration             |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skull Fractured Base        |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Spinal Compression Fracture |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Spinal Fracture             |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Subdural Haematoma          |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Thoracic Vertebral Fracture |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Tooth Fracture              |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Vertebral Injury            |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Laceration                  |                |                |                |

|                                                                                                                                   |                     |                     |                     |
|-----------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                                  | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Ligament sprain<br>subjects affected / exposed<br>occurrences (all)                                                               | 1 / 18 (5.56%)<br>1 | 0 / 17 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1 |
| Congenital, familial and genetic disorders<br>Congenital Diaphragmatic Hernia<br>subjects affected / exposed<br>occurrences (all) | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Cardiac disorders<br>Arrhythmia<br>subjects affected / exposed<br>occurrences (all)                                               | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Atrial Flutter<br>subjects affected / exposed<br>occurrences (all)                                                                | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Mitral Valve Prolapse<br>subjects affected / exposed<br>occurrences (all)                                                         | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 | 0 / 19 (0.00%)<br>0 |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                                                   | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Nervous system disorders<br>Cervicobrachial Syndrome<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 |
| Headache<br>subjects affected / exposed<br>occurrences (all)                                                                      | 1 / 18 (5.56%)<br>1 | 1 / 17 (5.88%)<br>1 | 1 / 19 (5.26%)<br>1 |
| Memory Impairment<br>subjects affected / exposed<br>occurrences (all)                                                             | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 | 0 / 19 (0.00%)<br>0 |
| Migraine                                                                                                                          |                     |                     |                     |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0               | 1              |
| Paraesthesia                |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 17 (5.88%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Sciatica                    |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Somnolence                  |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 17 (5.88%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Tension Headache            |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Tremor                      |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 17 (11.76%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 2               | 0              |
| Trigeminal Neuralgia        |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Upper Motor Neuron Lesion   |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0               | 1              |
| Carpal tunnel syndrome      |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Dizziness                   |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 17 (5.88%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Parkinson's disease         |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Ear and labyrinth disorders |                |                 |                |
| Deafness                    |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| Tinnitus                    |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Tympanosclerosis            |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Vertigo                     |                 |                |                 |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0               |
| Vertigo Positional          |                 |                |                 |
| subjects affected / exposed | 1 / 18 (5.56%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Eye disorders               |                 |                |                 |
| Cataract                    |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all)           | 0               | 0              | 3               |
| Conjunctivitis              |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Conjunctivitis Allergic     |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Eye Pruritus                |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Macular Degeneration        |                 |                |                 |
| subjects affected / exposed | 1 / 18 (5.56%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Retinal Tear                |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Gastrointestinal disorders  |                 |                |                 |
| Abdominal Pain Upper        |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Abdominal Pain              |                 |                |                 |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 17 (11.76%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 2               | 0              |
| Anal Fissure                |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Aphthous Stomatitis         |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0               | 1              |
| Colitis                     |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Constipation                |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Diarrhoea                   |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Dry Mouth                   |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 17 (5.88%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Duodenal Ulcer              |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Dyspepsia                   |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0               | 1              |
| Faecal Incontinence         |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Flatulence                  |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Gastric Disorder            |                |                 |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0               | 1              |
| Gastric Polyps              |                |                 |                |

|                                 |                |                |                |
|---------------------------------|----------------|----------------|----------------|
| subjects affected / exposed     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)               | 0              | 0              | 1              |
| Gastric Ulcer                   |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)               | 0              | 0              | 1              |
| Gastritis                       |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 1 / 19 (5.26%) |
| occurrences (all)               | 0              | 1              | 1              |
| Gastrointestinal Disorder       |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Gastroesophageal Reflux Disease |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Gingival Swelling               |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Gingivitis                      |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Hiatus Hernia                   |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Inguinal Hernia                 |                |                |                |
| subjects affected / exposed     | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)               | 2              | 0              | 0              |
| Irritable Bowel Syndrome        |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)               | 0              | 1              | 0              |
| Mouth Ulceration                |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Nausea                          |                |                |                |
| subjects affected / exposed     | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)               | 0              | 1              | 0              |
| Oesophagitis                    |                |                |                |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed            | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 1 / 19 (5.26%) |
| occurrences (all)                      | 0              | 2              | 1              |
| Rectal Haemorrhage                     |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Reflux Oesophagitis                    |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Toothache                              |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Upper Gastrointestinal Haemorrhage     |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dental caries                          |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Actinic Keratosis                      |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dermatitis Atopic                      |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Ecchymosis                             |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Granuloma Annulare                     |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Hyperkeratosis                         |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Hypertrichosis              |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Lichen Planus               |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Neurodermatitis             |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pruritus                    |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Psoriasis                   |                |                |                |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Rash                        |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash Erythematous           |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash Papular                |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Sebaceous Hyperplasia       |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Skin Irritation             |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Lesion                 |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Urticaria                   |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

|                                                                                                                |                     |                     |                      |
|----------------------------------------------------------------------------------------------------------------|---------------------|---------------------|----------------------|
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Dermal cyst<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Dermatitis<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Renal and urinary disorders<br>Dysuria<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Micturition Urgency<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |
| Thyroiditis Chronic<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 18 (0.00%)<br>0 | 1 / 17 (5.88%)<br>1 | 0 / 19 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders<br>Myalgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 18 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                                                 | 1 / 18 (5.56%)<br>1 | 0 / 17 (0.00%)<br>0 | 2 / 19 (10.53%)<br>2 |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)                                                  | 1 / 18 (5.56%)<br>1 | 1 / 17 (5.88%)<br>1 | 4 / 19 (21.05%)<br>5 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Bone Pain                   |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Bursitis                    |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Costochondritis             |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dupuytren's Contracture     |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Foot Deformity              |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Joint Stiffness             |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Monarthrits                 |                |                |                |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Muscle Contracture          |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Muscle Spasms               |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Muscular Weakness           |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Musculoskeletal Chest Pain  |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Musculoskeletal Discomfort  |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| Musculoskeletal Pain        |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Musculoskeletal Stiffness   |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Myalgia Intercostal         |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Neck Pain                   |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)           | 0               | 0              | 2               |
| Osteoarthritis              |                 |                |                 |
| subjects affected / exposed | 2 / 18 (11.11%) | 1 / 17 (5.88%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 2               | 1              | 0               |
| Osteochondrosis             |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Osteosclerosis              |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)           | 0               | 0              | 2               |
| Pain In Extremity           |                 |                |                 |
| subjects affected / exposed | 3 / 18 (16.67%) | 1 / 17 (5.88%) | 3 / 19 (15.79%) |
| occurrences (all)           | 3               | 1              | 4               |
| Polyarthritis               |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Rotator Cuff Syndrome       |                 |                |                 |
| subjects affected / exposed | 1 / 18 (5.56%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Sacroiliitis                |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Synovial Cyst               |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Tendonitis                  |                |                |                |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Torticollis                 |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Fibromyalgia                |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Joint swelling              |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Spinal osteoarthritis       |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Trigger finger              |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Infections and infestations |                |                |                |
| Bacterial Infection         |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Bronchitis                  |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 3              | 1              |
| Cellulitis                  |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Chronic Sinusitis           |                |                |                |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Cystitis                    |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0              | 1              |
| Ear Infection               |                |                |                |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Fungal Infection            |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Furuncle                    |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 1 / 17 (5.88%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |
| Gastroenteritis             |                 |                |                 |
| subjects affected / exposed | 1 / 18 (5.56%)  | 1 / 17 (5.88%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 1               | 1              | 0               |
| Gastroenteritis Viral       |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Gastrointestinal Infection  |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Herpes Zoster               |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 1 / 17 (5.88%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |
| Influenza                   |                 |                |                 |
| subjects affected / exposed | 1 / 18 (5.56%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Nail Bed Infection Fungal   |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Nasal Abscess               |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Nasopharyngitis             |                 |                |                 |
| subjects affected / exposed | 3 / 18 (16.67%) | 0 / 17 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all)           | 3               | 0              | 2               |
| Onychomycosis               |                 |                |                 |
| subjects affected / exposed | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Oral Candidiasis            |                 |                |                 |

|                                   |                 |                |                 |
|-----------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                 | 0               | 0              | 1               |
| Oral Fungal Infection             |                 |                |                 |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Oral Herpes                       |                 |                |                 |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Otitis Media Acute                |                 |                |                 |
| subjects affected / exposed       | 1 / 18 (5.56%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                 | 1               | 0              | 0               |
| Pharyngitis                       |                 |                |                 |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all)                 | 0               | 0              | 2               |
| Pharyngitis Streptococcal         |                 |                |                 |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                 | 0               | 0              | 1               |
| Pneumonia                         |                 |                |                 |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                 | 0               | 0              | 1               |
| Pyoderma                          |                 |                |                 |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Respiratory Tract Infection       |                 |                |                 |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Respiratory Tract Infection Viral |                 |                |                 |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Rhinitis                          |                 |                |                 |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 17 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Sinusitis                         |                 |                |                 |
| subjects affected / exposed       | 2 / 18 (11.11%) | 0 / 17 (0.00%) | 1 / 19 (5.26%)  |
| occurrences (all)                 | 2               | 0              | 1               |
| Tooth Abscess                     |                 |                |                 |

|                                         |                |                |                |
|-----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed             | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Tooth Infection                         |                |                |                |
| subjects affected / exposed             | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Upper Respiratory Tract Infection       |                |                |                |
| subjects affected / exposed             | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Urinary Tract Infection                 |                |                |                |
| subjects affected / exposed             | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Viral Infection                         |                |                |                |
| subjects affected / exposed             | 0 / 18 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 0              | 1              | 0              |
| Viral Upper Respiratory Tract Infection |                |                |                |
| subjects affected / exposed             | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Borrelia infection                      |                |                |                |
| subjects affected / exposed             | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Eye infection                           |                |                |                |
| subjects affected / exposed             | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Lower respiratory tract infection       |                |                |                |
| subjects affected / exposed             | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Wound infection                         |                |                |                |
| subjects affected / exposed             | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Metabolism and nutrition disorders      |                |                |                |
| Anorexia                                |                |                |                |
| subjects affected / exposed             | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Dyslipidaemia                           |                |                |                |

|                                             |                |                |                |
|---------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                 | 1 / 18 (5.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                           | 1              | 0              | 0              |
| Hypercholesterolaemia                       |                |                |                |
| subjects affected / exposed                 | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Hyperlipidaemia                             |                |                |                |
| subjects affected / exposed                 | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all)                           | 0              | 0              | 1              |
| Food intolerance                            |                |                |                |
| alternative assessment type: Non-systematic |                |                |                |
| subjects affected / exposed                 | 0 / 18 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |

| <b>Non-serious adverse events</b>                                   | Year 3 Odanacatib<br>25 mg/Odanacatib<br>50 mg-Ext 2 | Year 3 Odanacatib<br>50 mg/Placebo-Ext 2 | Year 3 Odanacatib<br>50 mg/Odanacatib<br>50 mg-Ext 2 |
|---------------------------------------------------------------------|------------------------------------------------------|------------------------------------------|------------------------------------------------------|
| Total subjects affected by non-serious adverse events               |                                                      |                                          |                                                      |
| subjects affected / exposed                                         | 17 / 21 (80.95%)                                     | 14 / 18 (77.78%)                         | 15 / 20 (75.00%)                                     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                      |                                          |                                                      |
| Basal Cell Carcinoma                                                |                                                      |                                          |                                                      |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                       | 0 / 18 (0.00%)                           | 0 / 20 (0.00%)                                       |
| occurrences (all)                                                   | 0                                                    | 0                                        | 0                                                    |
| Fibroma                                                             |                                                      |                                          |                                                      |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                       | 0 / 18 (0.00%)                           | 1 / 20 (5.00%)                                       |
| occurrences (all)                                                   | 0                                                    | 0                                        | 1                                                    |
| Lipoma                                                              |                                                      |                                          |                                                      |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                       | 0 / 18 (0.00%)                           | 0 / 20 (0.00%)                                       |
| occurrences (all)                                                   | 0                                                    | 0                                        | 0                                                    |
| Ovarian Neoplasm                                                    |                                                      |                                          |                                                      |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                       | 0 / 18 (0.00%)                           | 0 / 20 (0.00%)                                       |
| occurrences (all)                                                   | 0                                                    | 0                                        | 0                                                    |
| Thyroid Neoplasm                                                    |                                                      |                                          |                                                      |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                       | 0 / 18 (0.00%)                           | 1 / 20 (5.00%)                                       |
| occurrences (all)                                                   | 0                                                    | 0                                        | 1                                                    |
| Benign neoplasm of thyroid gland                                    |                                                      |                                          |                                                      |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                       | 0 / 18 (0.00%)                           | 0 / 20 (0.00%)                                       |
| occurrences (all)                                                   | 0                                                    | 0                                        | 0                                                    |

|                                                      |                |                 |                 |
|------------------------------------------------------|----------------|-----------------|-----------------|
| Vascular disorders                                   |                |                 |                 |
| Flushing                                             |                |                 |                 |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                    | 0              | 0               | 0               |
| Haematoma                                            |                |                 |                 |
| subjects affected / exposed                          | 1 / 21 (4.76%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                    | 1              | 0               | 0               |
| Hypertension                                         |                |                 |                 |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 2 / 18 (11.11%) | 0 / 20 (0.00%)  |
| occurrences (all)                                    | 0              | 2               | 0               |
| Phlebitis                                            |                |                 |                 |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                    | 0              | 0               | 0               |
| Varicose Vein                                        |                |                 |                 |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                    | 0              | 0               | 0               |
| General disorders and administration site conditions |                |                 |                 |
| Calcinosis                                           |                |                 |                 |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                                    | 0              | 0               | 1               |
| Chest Discomfort                                     |                |                 |                 |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                    | 0              | 0               | 0               |
| Chest Pain                                           |                |                 |                 |
| subjects affected / exposed                          | 1 / 21 (4.76%) | 0 / 18 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                                    | 1              | 0               | 1               |
| Fatigue                                              |                |                 |                 |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                    | 0              | 1               | 0               |
| Influenza Like Illness                               |                |                 |                 |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                    | 0              | 1               | 0               |
| Oedema Peripheral                                    |                |                 |                 |
| subjects affected / exposed                          | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 3 / 20 (15.00%) |
| occurrences (all)                                    | 0              | 0               | 3               |
| Wrist Fracture                                       |                |                 |                 |

|                                                                                |                     |                     |                     |
|--------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                               | 1 / 21 (4.76%)<br>1 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 |
| Immune system disorders                                                        |                     |                     |                     |
| Allergy To Arthropod Sting<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 20 (0.00%)<br>0 |
| Drug Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)      | 1 / 21 (4.76%)<br>1 | 0 / 18 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1 |
| Reproductive system and breast disorders                                       |                     |                     |                     |
| Breast Mass<br>subjects affected / exposed<br>occurrences (all)                | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 |
| Fibrocystic Breast Disease<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 20 (0.00%)<br>0 |
| Pelvic Pain<br>subjects affected / exposed<br>occurrences (all)                | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 |
| Vulvovaginal Discomfort<br>subjects affected / exposed<br>occurrences (all)    | 0 / 21 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 20 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders                                |                     |                     |                     |
| Pharyngolaryngeal Pain<br>subjects affected / exposed<br>occurrences (all)     | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 |
| Allergic Pharyngitis<br>subjects affected / exposed<br>occurrences (all)       | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1 |
| Asthma<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1 |
| Dyspnoea                                                                       |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Dyspnoea Exertional         |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Emphysema                   |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Haemoptysis                 |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Cough                       |                |                |                |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all)           | 1              | 1              | 1              |
| Psychiatric disorders       |                |                |                |
| Insomnia                    |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Alcoholism                  |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Anxiety                     |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Depression                  |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dysthymic Disorder          |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Stress                      |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Investigations              |                |                |                |
| Weight Increased            |                |                |                |

|                                               |                |                |                |
|-----------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Alanine Aminotransferase Increased            |                |                |                |
| subjects affected / exposed                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Aspartate Aminotransferase Increased          |                |                |                |
| subjects affected / exposed                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Blood 1,25-Dihydroxycholecalciferol Increased |                |                |                |
| subjects affected / exposed                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Blood Cholesterol Increased                   |                |                |                |
| subjects affected / exposed                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Blood Glucose Increased                       |                |                |                |
| subjects affected / exposed                   | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 1              | 0              |
| Blood Parathyroid Hormone Increased           |                |                |                |
| subjects affected / exposed                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)                             | 0              | 0              | 1              |
| Blood Pressure Increased                      |                |                |                |
| subjects affected / exposed                   | 2 / 21 (9.52%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 2              | 1              | 0              |
| Blood Triglycerides Increased                 |                |                |                |
| subjects affected / exposed                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Bone Density Decreased                        |                |                |                |
| subjects affected / exposed                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Carotid Bruit                                 |                |                |                |
| subjects affected / exposed                   | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 0              | 0              |
| Glucose Urine Present                         |                |                |                |

|                                                |                |                 |                |
|------------------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed                    | 0 / 21 (0.00%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 1               | 0              |
| High Density Lipoprotein Decreased             |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Lymphocyte Count Decreased                     |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 3 / 18 (16.67%) | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 3               | 0              |
| Ultrasound Thyroid Abnormal                    |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Weight Decreased                               |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 1               | 0              |
| White Blood Cells Urine Positive               |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Blood alkaline phosphatase increased           |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Body height decreased                          |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Injury, poisoning and procedural complications |                |                 |                |
| Arthropod Bite                                 |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Arthropod Sting                                |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 1               | 0              |
| Contusion                                      |                |                 |                |
| subjects affected / exposed                    | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Device Breakage                                |                |                 |                |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Epicondylitis               |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Fall                        |                |                 |                |
| subjects affected / exposed | 1 / 21 (4.76%) | 2 / 18 (11.11%) | 0 / 20 (0.00%) |
| occurrences (all)           | 1              | 2               | 0              |
| Humerus Fracture            |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Joint Sprain                |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Limb Injury                 |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Muscle Strain               |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Open Wound                  |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Procedural Pain             |                |                 |                |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 2              | 1               | 0              |
| Radius Fracture             |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Rib Fracture                |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 0               | 1              |
| Skin Laceration             |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Skull Fractured Base        |                |                 |                |

|                                            |                |                |                |
|--------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Spinal Compression Fracture                |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Spinal Fracture                            |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Subdural Haematoma                         |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Thoracic Vertebral Fracture                |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Tooth Fracture                             |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Vertebral Injury                           |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Laceration                                 |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 1              | 0              |
| Ligament sprain                            |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Congenital, familial and genetic disorders |                |                |                |
| Congenital Diaphragmatic Hernia            |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)                          | 0              | 0              | 1              |
| Cardiac disorders                          |                |                |                |
| Arrhythmia                                 |                |                |                |
| subjects affected / exposed                | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Atrial Flutter                             |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Mitral Valve Prolapse       |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Palpitations                |                |                |                |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Tachycardia                 |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Nervous system disorders    |                |                |                |
| Cervicobrachial Syndrome    |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Headache                    |                |                |                |
| subjects affected / exposed | 2 / 21 (9.52%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all)           | 2              | 1              | 1              |
| Memory Impairment           |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Migraine                    |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Paraesthesia                |                |                |                |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)           | 1              | 0              | 1              |
| Sciatica                    |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Somnolence                  |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tension Headache            |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Tremor                      |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Trigeminal Neuralgia        |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Upper Motor Neuron Lesion   |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Carpal tunnel syndrome      |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Dizziness                   |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 2 / 18 (11.11%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 3               | 1              |
| Parkinson's disease         |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Ear and labyrinth disorders |                |                 |                |
| Deafness                    |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Tinnitus                    |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Tympanosclerosis            |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Vertigo                     |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Vertigo Positional          |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Eye disorders               |                |                 |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Cataract                    |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Conjunctivitis              |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Conjunctivitis Allergic     |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Eye Pruritus                |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Macular Degeneration        |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Retinal Tear                |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Gastrointestinal disorders  |                |                |                |
| Abdominal Pain Upper        |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Abdominal Pain              |                |                |                |
| subjects affected / exposed | 2 / 21 (9.52%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)           | 2              | 1              | 0              |
| Anal Fissure                |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Aphthous Stomatitis         |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Colitis                     |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Constipation                |                |                |                |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed      | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Diarrhoea                        |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 3 / 20 (15.00%) |
| occurrences (all)                | 0              | 1              | 0               |
| Dry Mouth                        |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Duodenal Ulcer                   |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0               |
| Dyspepsia                        |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Faecal Incontinence              |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Flatulence                       |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Gastric Disorder                 |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Gastric Polyps                   |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Gastric Ulcer                    |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0               |
| Gastritis                        |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Gastrointestinal Disorder        |                |                |                 |
| subjects affected / exposed      | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Gastrooesophageal Reflux Disease |                |                |                 |

|                                    |                |                |                |
|------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed        | 2 / 21 (9.52%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)                  | 2              | 0              | 0              |
| Gingival Swelling                  |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Gingivitis                         |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Hiatus Hernia                      |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Inguinal Hernia                    |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Irritable Bowel Syndrome           |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Mouth Ulceration                   |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Nausea                             |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Oesophagitis                       |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Rectal Haemorrhage                 |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 1              | 0              |
| Reflux Oesophagitis                |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Toothache                          |                |                |                |
| subjects affected / exposed        | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)                  | 0              | 1              | 0              |
| Upper Gastrointestinal Haemorrhage |                |                |                |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed            | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dental caries                          |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Actinic Keratosis                      |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Dermatitis Atopic                      |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Ecchymosis                             |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Granuloma Annulare                     |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Hyperkeratosis                         |                |                |                |
| subjects affected / exposed            | 1 / 21 (4.76%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Hypertrichosis                         |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Lichen Planus                          |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Neurodermatitis                        |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Pruritus                               |                |                |                |
| subjects affected / exposed            | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Psoriasis                   |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Rash                        |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 2 / 18 (11.11%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 2               | 3              |
| Rash Erythematous           |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Rash Papular                |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Sebaceous Hyperplasia       |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Skin Irritation             |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Skin Lesion                 |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Urticaria                   |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Alopecia                    |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Dermal cyst                 |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Dermatitis                  |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Dry skin                    |                |                 |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |

|                                                 |                 |                |                 |
|-------------------------------------------------|-----------------|----------------|-----------------|
| Renal and urinary disorders                     |                 |                |                 |
| Dysuria                                         |                 |                |                 |
| subjects affected / exposed                     | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                               | 0               | 0              | 1               |
| Micturition Urgency                             |                 |                |                 |
| subjects affected / exposed                     | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                               | 0               | 0              | 1               |
| Endocrine disorders                             |                 |                |                 |
| Hypothyroidism                                  |                 |                |                 |
| subjects affected / exposed                     | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Thyroiditis Chronic                             |                 |                |                 |
| subjects affected / exposed                     | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Musculoskeletal and connective tissue disorders |                 |                |                 |
| Myalgia                                         |                 |                |                 |
| subjects affected / exposed                     | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Arthralgia                                      |                 |                |                 |
| subjects affected / exposed                     | 3 / 21 (14.29%) | 0 / 18 (0.00%) | 3 / 20 (15.00%) |
| occurrences (all)                               | 4               | 0              | 4               |
| Back Pain                                       |                 |                |                 |
| subjects affected / exposed                     | 2 / 21 (9.52%)  | 1 / 18 (5.56%) | 0 / 20 (0.00%)  |
| occurrences (all)                               | 2               | 1              | 0               |
| Bone Pain                                       |                 |                |                 |
| subjects affected / exposed                     | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Bursitis                                        |                 |                |                 |
| subjects affected / exposed                     | 1 / 21 (4.76%)  | 0 / 18 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                               | 1               | 0              | 1               |
| Costochondritis                                 |                 |                |                 |
| subjects affected / exposed                     | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Dupuytren's Contracture                         |                 |                |                 |
| subjects affected / exposed                     | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Foot Deformity              |                 |                 |                 |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Joint Stiffness             |                 |                 |                 |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Monarthrititis              |                 |                 |                 |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Muscle Contracture          |                 |                 |                 |
| subjects affected / exposed | 0 / 21 (0.00%)  | 1 / 18 (5.56%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Muscle Spasms               |                 |                 |                 |
| subjects affected / exposed | 1 / 21 (4.76%)  | 1 / 18 (5.56%)  | 2 / 20 (10.00%) |
| occurrences (all)           | 1               | 1               | 2               |
| Muscular Weakness           |                 |                 |                 |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Musculoskeletal Chest Pain  |                 |                 |                 |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Musculoskeletal Discomfort  |                 |                 |                 |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Musculoskeletal Pain        |                 |                 |                 |
| subjects affected / exposed | 3 / 21 (14.29%) | 2 / 18 (11.11%) | 0 / 20 (0.00%)  |
| occurrences (all)           | 3               | 2               | 0               |
| Musculoskeletal Stiffness   |                 |                 |                 |
| subjects affected / exposed | 1 / 21 (4.76%)  | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 2               | 0               | 0               |
| Myalgia Intercostal         |                 |                 |                 |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Neck Pain                   |                 |                 |                 |
| subjects affected / exposed | 2 / 21 (9.52%)  | 0 / 18 (0.00%)  | 4 / 20 (20.00%) |
| occurrences (all)           | 2               | 0               | 4               |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| Osteoarthritis              |                 |                |                |
| subjects affected / exposed | 3 / 21 (14.29%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all)           | 3               | 2              | 1              |
| Osteochondrosis             |                 |                |                |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Osteosclerosis              |                 |                |                |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Pain In Extremity           |                 |                |                |
| subjects affected / exposed | 2 / 21 (9.52%)  | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)           | 2               | 1              | 0              |
| Polyarthrititis             |                 |                |                |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Rotator Cuff Syndrome       |                 |                |                |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Sacroiliitis                |                 |                |                |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Synovial Cyst               |                 |                |                |
| subjects affected / exposed | 0 / 21 (0.00%)  | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0               | 1              | 0              |
| Tendonitis                  |                 |                |                |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Torticollis                 |                 |                |                |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Fibromyalgia                |                 |                |                |
| subjects affected / exposed | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Joint swelling              |                 |                |                |
| subjects affected / exposed | 1 / 21 (4.76%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 1               | 0              | 0              |

|                                                                           |                     |                     |                      |
|---------------------------------------------------------------------------|---------------------|---------------------|----------------------|
| Spinal osteoarthritis<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  |
| Trigger finger<br>subjects affected / exposed<br>occurrences (all)        | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  |
| Infections and infestations                                               |                     |                     |                      |
| Bacterial Infection<br>subjects affected / exposed<br>occurrences (all)   | 0 / 21 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 20 (0.00%)<br>0  |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)            | 1 / 21 (4.76%)<br>1 | 1 / 18 (5.56%)<br>1 | 0 / 20 (0.00%)<br>0  |
| Cellulitis<br>subjects affected / exposed<br>occurrences (all)            | 0 / 21 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 20 (0.00%)<br>0  |
| Chronic Sinusitis<br>subjects affected / exposed<br>occurrences (all)     | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  |
| Cystitis<br>subjects affected / exposed<br>occurrences (all)              | 1 / 21 (4.76%)<br>1 | 0 / 18 (0.00%)<br>0 | 2 / 20 (10.00%)<br>2 |
| Ear Infection<br>subjects affected / exposed<br>occurrences (all)         | 1 / 21 (4.76%)<br>1 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  |
| Fungal Infection<br>subjects affected / exposed<br>occurrences (all)      | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  |
| Furuncle<br>subjects affected / exposed<br>occurrences (all)              | 0 / 21 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)       | 1 / 21 (4.76%)<br>1 | 1 / 18 (5.56%)<br>1 | 0 / 20 (0.00%)<br>0  |
| Gastroenteritis Viral                                                     |                     |                     |                      |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastrointestinal Infection  |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Herpes Zoster               |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Influenza                   |                |                |                |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 2              | 0              | 0              |
| Nail Bed Infection Fungal   |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Nasal Abscess               |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Nasopharyngitis             |                |                |                |
| subjects affected / exposed | 2 / 21 (9.52%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all)           | 2              | 1              | 2              |
| Onychomycosis               |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Oral Candidiasis            |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Oral Fungal Infection       |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Oral Herpes                 |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Otitis Media Acute          |                |                |                |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pharyngitis                 |                |                |                |

|                                   |                 |                |                 |
|-----------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed       | 1 / 21 (4.76%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 1               | 0              | 0               |
| Pharyngitis Streptococcal         |                 |                |                 |
| subjects affected / exposed       | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Pneumonia                         |                 |                |                 |
| subjects affected / exposed       | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Pyoderma                          |                 |                |                 |
| subjects affected / exposed       | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Respiratory Tract Infection       |                 |                |                 |
| subjects affected / exposed       | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Respiratory Tract Infection Viral |                 |                |                 |
| subjects affected / exposed       | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Rhinitis                          |                 |                |                 |
| subjects affected / exposed       | 0 / 21 (0.00%)  | 1 / 18 (5.56%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 0               | 1              | 0               |
| Sinusitis                         |                 |                |                 |
| subjects affected / exposed       | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0               |
| Tooth Abscess                     |                 |                |                 |
| subjects affected / exposed       | 0 / 21 (0.00%)  | 1 / 18 (5.56%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 0               | 1              | 0               |
| Tooth Infection                   |                 |                |                 |
| subjects affected / exposed       | 0 / 21 (0.00%)  | 0 / 18 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                 | 0               | 0              | 1               |
| Upper Respiratory Tract Infection |                 |                |                 |
| subjects affected / exposed       | 2 / 21 (9.52%)  | 0 / 18 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                 | 3               | 0              | 0               |
| Urinary Tract Infection           |                 |                |                 |
| subjects affected / exposed       | 3 / 21 (14.29%) | 0 / 18 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all)                 | 3               | 0              | 3               |
| Viral Infection                   |                 |                |                 |

|                                             |                |                |                |
|---------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Viral Upper Respiratory Tract Infection     |                |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Borrelia infection                          |                |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Eye infection                               |                |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)                           | 0              | 0              | 1              |
| Lower respiratory tract infection           |                |                |                |
| subjects affected / exposed                 | 1 / 21 (4.76%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                           | 1              | 0              | 0              |
| Wound infection                             |                |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Metabolism and nutrition disorders          |                |                |                |
| Anorexia                                    |                |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 1 / 18 (5.56%) | 0 / 20 (0.00%) |
| occurrences (all)                           | 0              | 1              | 0              |
| Dyslipidaemia                               |                |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)                           | 0              | 0              | 1              |
| Hypercholesterolaemia                       |                |                |                |
| subjects affected / exposed                 | 1 / 21 (4.76%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                           | 1              | 0              | 0              |
| Hyperlipidaemia                             |                |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Food intolerance                            |                |                |                |
| alternative assessment type: Non-systematic |                |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 18 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |

| <b>Non-serious adverse events</b>                                   | <b>Years 4-5 Combined<br/>Group A.1:<br/>Odanacatib 50 mg</b> | <b>Years 4-5 Combined<br/>Group A.2:<br/>Odanacatib 50 mg</b> | <b>Years 4-5 Combined<br/>Group A.3: Placebo</b> |
|---------------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|--------------------------------------------------|
| Total subjects affected by non-serious adverse events               |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 65 / 73 (89.04%)                                              | 23 / 27 (85.19%)                                              | 33 / 41 (80.49%)                                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                               |                                                               |                                                  |
| Basal Cell Carcinoma                                                |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)                                                | 0 / 27 (0.00%)                                                | 0 / 41 (0.00%)                                   |
| occurrences (all)                                                   | 0                                                             | 0                                                             | 0                                                |
| Fibroma                                                             |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)                                                | 0 / 27 (0.00%)                                                | 0 / 41 (0.00%)                                   |
| occurrences (all)                                                   | 0                                                             | 0                                                             | 0                                                |
| Lipoma                                                              |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)                                                | 0 / 27 (0.00%)                                                | 0 / 41 (0.00%)                                   |
| occurrences (all)                                                   | 0                                                             | 0                                                             | 0                                                |
| Ovarian Neoplasm                                                    |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)                                                | 0 / 27 (0.00%)                                                | 0 / 41 (0.00%)                                   |
| occurrences (all)                                                   | 0                                                             | 0                                                             | 0                                                |
| Thyroid Neoplasm                                                    |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)                                                | 0 / 27 (0.00%)                                                | 0 / 41 (0.00%)                                   |
| occurrences (all)                                                   | 0                                                             | 0                                                             | 0                                                |
| Benign neoplasm of thyroid gland                                    |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)                                                | 0 / 27 (0.00%)                                                | 0 / 41 (0.00%)                                   |
| occurrences (all)                                                   | 0                                                             | 0                                                             | 0                                                |
| Vascular disorders                                                  |                                                               |                                                               |                                                  |
| Flushing                                                            |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)                                                | 0 / 27 (0.00%)                                                | 0 / 41 (0.00%)                                   |
| occurrences (all)                                                   | 0                                                             | 0                                                             | 0                                                |
| Haematoma                                                           |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 2 / 73 (2.74%)                                                | 0 / 27 (0.00%)                                                | 0 / 41 (0.00%)                                   |
| occurrences (all)                                                   | 3                                                             | 0                                                             | 0                                                |
| Hypertension                                                        |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 5 / 73 (6.85%)                                                | 2 / 27 (7.41%)                                                | 2 / 41 (4.88%)                                   |
| occurrences (all)                                                   | 6                                                             | 2                                                             | 2                                                |
| Phlebitis                                                           |                                                               |                                                               |                                                  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)                                                | 0 / 27 (0.00%)                                                | 0 / 41 (0.00%)                                   |
| occurrences (all)                                                   | 0                                                             | 0                                                             | 0                                                |
| Varicose Vein                                                       |                                                               |                                                               |                                                  |

|                                                         |                     |                     |                     |
|---------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)        | 1 / 73 (1.37%)<br>1 | 0 / 27 (0.00%)<br>0 | 2 / 41 (4.88%)<br>2 |
| General disorders and administration<br>site conditions |                     |                     |                     |
| Calcinosis                                              |                     |                     |                     |
| subjects affected / exposed                             | 1 / 73 (1.37%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                       | 1                   | 0                   | 0                   |
| Chest Discomfort                                        |                     |                     |                     |
| subjects affected / exposed                             | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |
| Chest Pain                                              |                     |                     |                     |
| subjects affected / exposed                             | 1 / 73 (1.37%)      | 1 / 27 (3.70%)      | 1 / 41 (2.44%)      |
| occurrences (all)                                       | 1                   | 1                   | 1                   |
| Fatigue                                                 |                     |                     |                     |
| subjects affected / exposed                             | 2 / 73 (2.74%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                       | 3                   | 0                   | 0                   |
| Influenza Like Illness                                  |                     |                     |                     |
| subjects affected / exposed                             | 1 / 73 (1.37%)      | 1 / 27 (3.70%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                       | 2                   | 1                   | 0                   |
| Oedema Peripheral                                       |                     |                     |                     |
| subjects affected / exposed                             | 2 / 73 (2.74%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                       | 2                   | 0                   | 0                   |
| Wrist Fracture                                          |                     |                     |                     |
| subjects affected / exposed                             | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |
| Immune system disorders                                 |                     |                     |                     |
| Allergy To Arthropod Sting                              |                     |                     |                     |
| subjects affected / exposed                             | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 1 / 41 (2.44%)      |
| occurrences (all)                                       | 0                   | 0                   | 2                   |
| Drug Hypersensitivity                                   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 73 (0.00%)      | 1 / 27 (3.70%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                       | 0                   | 1                   | 0                   |
| Reproductive system and breast<br>disorders             |                     |                     |                     |
| Breast Mass                                             |                     |                     |                     |
| subjects affected / exposed                             | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |
| Fibrocystic Breast Disease                              |                     |                     |                     |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Pelvic Pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Vulvovaginal Discomfort                         |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Pharyngolaryngeal Pain                          |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Allergic Pharyngitis                            |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 1 / 27 (3.70%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 1              | 1              | 0              |
| Asthma                                          |                |                |                |
| subjects affected / exposed                     | 4 / 73 (5.48%) | 0 / 27 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all)                               | 4              | 0              | 3              |
| Dysphonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Dyspnoea                                        |                |                |                |
| subjects affected / exposed                     | 4 / 73 (5.48%) | 0 / 27 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all)                               | 4              | 0              | 3              |
| Dyspnoea Exertional                             |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                               | 1              | 0              | 1              |
| Emphysema                                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Haemoptysis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Cough                                           |                |                |                |

|                                                  |                     |                     |                     |
|--------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 4 / 73 (5.48%)<br>4 | 0 / 27 (0.00%)<br>0 | 3 / 41 (7.32%)<br>3 |
| Psychiatric disorders                            |                     |                     |                     |
| Insomnia                                         |                     |                     |                     |
| subjects affected / exposed                      | 2 / 73 (2.74%)      | 0 / 27 (0.00%)      | 2 / 41 (4.88%)      |
| occurrences (all)                                | 2                   | 0                   | 2                   |
| Alcoholism                                       |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Anxiety                                          |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Depression                                       |                     |                     |                     |
| subjects affected / exposed                      | 1 / 73 (1.37%)      | 3 / 27 (11.11%)     | 1 / 41 (2.44%)      |
| occurrences (all)                                | 1                   | 3                   | 1                   |
| Dysthymic Disorder                               |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Stress                                           |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 1 / 27 (3.70%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Investigations                                   |                     |                     |                     |
| Weight Increased                                 |                     |                     |                     |
| subjects affected / exposed                      | 1 / 73 (1.37%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Alanine Aminotransferase Increased               |                     |                     |                     |
| subjects affected / exposed                      | 1 / 73 (1.37%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Aspartate Aminotransferase Increased             |                     |                     |                     |
| subjects affected / exposed                      | 1 / 73 (1.37%)      | 1 / 27 (3.70%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 1                   | 1                   | 0                   |
| Blood 1,25-Dihydroxycholecalciferol Increased    |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Blood Cholesterol Increased                      |                     |                     |                     |

|                                     |                |                 |                |
|-------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed         | 2 / 73 (2.74%) | 0 / 27 (0.00%)  | 1 / 41 (2.44%) |
| occurrences (all)                   | 2              | 0               | 1              |
| Blood Glucose Increased             |                |                 |                |
| subjects affected / exposed         | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 1 / 41 (2.44%) |
| occurrences (all)                   | 0              | 0               | 1              |
| Blood Parathyroid Hormone Increased |                |                 |                |
| subjects affected / exposed         | 5 / 73 (6.85%) | 3 / 27 (11.11%) | 2 / 41 (4.88%) |
| occurrences (all)                   | 13             | 5               | 3              |
| Blood Pressure Increased            |                |                 |                |
| subjects affected / exposed         | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                   | 0              | 0               | 0              |
| Blood Triglycerides Increased       |                |                 |                |
| subjects affected / exposed         | 1 / 73 (1.37%) | 0 / 27 (0.00%)  | 2 / 41 (4.88%) |
| occurrences (all)                   | 1              | 0               | 2              |
| Bone Density Decreased              |                |                 |                |
| subjects affected / exposed         | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                   | 0              | 0               | 0              |
| Carotid Bruit                       |                |                 |                |
| subjects affected / exposed         | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 1 / 41 (2.44%) |
| occurrences (all)                   | 0              | 0               | 1              |
| Glucose Urine Present               |                |                 |                |
| subjects affected / exposed         | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                   | 0              | 0               | 0              |
| High Density Lipoprotein Decreased  |                |                 |                |
| subjects affected / exposed         | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                   | 0              | 0               | 0              |
| Lymphocyte Count Decreased          |                |                 |                |
| subjects affected / exposed         | 1 / 73 (1.37%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                   | 1              | 0               | 0              |
| Ultrasound Thyroid Abnormal         |                |                 |                |
| subjects affected / exposed         | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                   | 0              | 0               | 0              |
| Weight Decreased                    |                |                 |                |
| subjects affected / exposed         | 1 / 73 (1.37%) | 1 / 27 (3.70%)  | 1 / 41 (2.44%) |
| occurrences (all)                   | 1              | 1               | 1              |

|                                                                                          |                     |                     |                     |
|------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| White Blood Cells Urine Positive<br>subjects affected / exposed<br>occurrences (all)     | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Body height decreased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Injury, poisoning and procedural complications                                           |                     |                     |                     |
| Arthropod Bite<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 73 (1.37%)<br>2 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Arthropod Sting<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 73 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1 | 1 / 41 (2.44%)<br>2 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                            | 4 / 73 (5.48%)<br>6 | 0 / 27 (0.00%)<br>0 | 2 / 41 (4.88%)<br>2 |
| Device Breakage<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Epicondylitis<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 73 (1.37%)<br>1 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                                 | 3 / 73 (4.11%)<br>4 | 0 / 27 (0.00%)<br>0 | 2 / 41 (4.88%)<br>2 |
| Humerus Fracture<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Joint Sprain<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Limb Injury                                                                              |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Muscle Strain               |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all)           | 0              | 0              | 2              |
| Open Wound                  |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Procedural Pain             |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 27 (3.70%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Radius Fracture             |                |                |                |
| subjects affected / exposed | 1 / 73 (1.37%) | 2 / 27 (7.41%) | 0 / 41 (0.00%) |
| occurrences (all)           | 1              | 2              | 0              |
| Rib Fracture                |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)           | 0              | 0              | 3              |
| Skin Laceration             |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skull Fractured Base        |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Spinal Compression Fracture |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Spinal Fracture             |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Subdural Haematoma          |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Thoracic Vertebral Fracture |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tooth Fracture              |                |                |                |

|                                            |                |                |                |
|--------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                          | 2              | 0              | 0              |
| Vertebral Injury                           |                |                |                |
| subjects affected / exposed                | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Laceration                                 |                |                |                |
| subjects affected / exposed                | 1 / 73 (1.37%) | 1 / 27 (3.70%) | 3 / 41 (7.32%) |
| occurrences (all)                          | 1              | 1              | 3              |
| Ligament sprain                            |                |                |                |
| subjects affected / exposed                | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                          | 1              | 0              | 1              |
| Congenital, familial and genetic disorders |                |                |                |
| Congenital Diaphragmatic Hernia            |                |                |                |
| subjects affected / exposed                | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Cardiac disorders                          |                |                |                |
| Arrhythmia                                 |                |                |                |
| subjects affected / exposed                | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                          | 1              | 0              | 0              |
| Atrial Flutter                             |                |                |                |
| subjects affected / exposed                | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Mitral Valve Prolapse                      |                |                |                |
| subjects affected / exposed                | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Palpitations                               |                |                |                |
| subjects affected / exposed                | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Tachycardia                                |                |                |                |
| subjects affected / exposed                | 0 / 73 (0.00%) | 1 / 27 (3.70%) | 0 / 41 (0.00%) |
| occurrences (all)                          | 0              | 1              | 0              |
| Nervous system disorders                   |                |                |                |
| Cervicobrachial Syndrome                   |                |                |                |
| subjects affected / exposed                | 2 / 73 (2.74%) | 1 / 27 (3.70%) | 0 / 41 (0.00%) |
| occurrences (all)                          | 2              | 1              | 0              |
| Headache                                   |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 2 / 73 (2.74%) | 2 / 27 (7.41%) | 1 / 41 (2.44%) |
| occurrences (all)           | 2              | 2              | 2              |
| Memory Impairment           |                |                |                |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Migraine                    |                |                |                |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 2              | 0              | 0              |
| Paraesthesia                |                |                |                |
| subjects affected / exposed | 3 / 73 (4.11%) | 1 / 27 (3.70%) | 2 / 41 (4.88%) |
| occurrences (all)           | 3              | 1              | 3              |
| Sciatica                    |                |                |                |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)           | 3              | 0              | 1              |
| Somnolence                  |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tension Headache            |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tremor                      |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Trigeminal Neuralgia        |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Upper Motor Neuron Lesion   |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Carpal tunnel syndrome      |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dizziness                   |                |                |                |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 3              | 0              | 0              |
| Parkinson's disease         |                |                |                |

|                                                  |                     |                     |                     |
|--------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Ear and labyrinth disorders                      |                     |                     |                     |
| Deafness                                         |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Tinnitus                                         |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 1 / 27 (3.70%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Tympanosclerosis                                 |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Vertigo                                          |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Vertigo Positional                               |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Eye disorders                                    |                     |                     |                     |
| Cataract                                         |                     |                     |                     |
| subjects affected / exposed                      | 2 / 73 (2.74%)      | 2 / 27 (7.41%)      | 3 / 41 (7.32%)      |
| occurrences (all)                                | 2                   | 4                   | 3                   |
| Conjunctivitis                                   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Conjunctivitis Allergic                          |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 1 / 41 (2.44%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Eye Pruritus                                     |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Macular Degeneration                             |                     |                     |                     |
| subjects affected / exposed                      | 1 / 73 (1.37%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Retinal Tear                                     |                     |                     |                     |

|                                                  |                     |                     |                     |
|--------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Gastrointestinal disorders                       |                     |                     |                     |
| Abdominal Pain Upper                             |                     |                     |                     |
| subjects affected / exposed                      | 1 / 73 (1.37%)      | 2 / 27 (7.41%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 1                   | 2                   | 0                   |
| Abdominal Pain                                   |                     |                     |                     |
| subjects affected / exposed                      | 1 / 73 (1.37%)      | 0 / 27 (0.00%)      | 2 / 41 (4.88%)      |
| occurrences (all)                                | 1                   | 0                   | 3                   |
| Anal Fissure                                     |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Aphthous Stomatitis                              |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Colitis                                          |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Constipation                                     |                     |                     |                     |
| subjects affected / exposed                      | 3 / 73 (4.11%)      | 1 / 27 (3.70%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 4                   | 1                   | 0                   |
| Diarrhoea                                        |                     |                     |                     |
| subjects affected / exposed                      | 2 / 73 (2.74%)      | 3 / 27 (11.11%)     | 0 / 41 (0.00%)      |
| occurrences (all)                                | 3                   | 3                   | 0                   |
| Dry Mouth                                        |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 1 / 27 (3.70%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Duodenal Ulcer                                   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Dyspepsia                                        |                     |                     |                     |
| subjects affected / exposed                      | 3 / 73 (4.11%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 4                   | 0                   | 0                   |
| Faecal Incontinence                              |                     |                     |                     |
| subjects affected / exposed                      | 0 / 73 (0.00%)      | 0 / 27 (0.00%)      | 0 / 41 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |

|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| Flatulence                       |                |                |                |
| subjects affected / exposed      | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                | 0              | 0              | 1              |
| Gastric Disorder                 |                |                |                |
| subjects affected / exposed      | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastric Polyps                   |                |                |                |
| subjects affected / exposed      | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastric Ulcer                    |                |                |                |
| subjects affected / exposed      | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                | 0              | 0              | 1              |
| Gastritis                        |                |                |                |
| subjects affected / exposed      | 0 / 73 (0.00%) | 1 / 27 (3.70%) | 0 / 41 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Gastrointestinal Disorder        |                |                |                |
| subjects affected / exposed      | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastrooesophageal Reflux Disease |                |                |                |
| subjects affected / exposed      | 3 / 73 (4.11%) | 2 / 27 (7.41%) | 0 / 41 (0.00%) |
| occurrences (all)                | 3              | 2              | 0              |
| Gingival Swelling                |                |                |                |
| subjects affected / exposed      | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gingivitis                       |                |                |                |
| subjects affected / exposed      | 1 / 73 (1.37%) | 1 / 27 (3.70%) | 1 / 41 (2.44%) |
| occurrences (all)                | 1              | 1              | 1              |
| Hiatus Hernia                    |                |                |                |
| subjects affected / exposed      | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Inguinal Hernia                  |                |                |                |
| subjects affected / exposed      | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Irritable Bowel Syndrome         |                |                |                |
| subjects affected / exposed      | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| Mouth Ulceration                       |                |                |                |
| subjects affected / exposed            | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Nausea                                 |                |                |                |
| subjects affected / exposed            | 1 / 73 (1.37%) | 2 / 27 (7.41%) | 1 / 41 (2.44%) |
| occurrences (all)                      | 1              | 2              | 1              |
| Oesophagitis                           |                |                |                |
| subjects affected / exposed            | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                      | 2              | 0              | 0              |
| Rectal Haemorrhage                     |                |                |                |
| subjects affected / exposed            | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                      | 2              | 0              | 0              |
| Reflux Oesophagitis                    |                |                |                |
| subjects affected / exposed            | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Toothache                              |                |                |                |
| subjects affected / exposed            | 4 / 73 (5.48%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                      | 4              | 0              | 0              |
| Upper Gastrointestinal Haemorrhage     |                |                |                |
| subjects affected / exposed            | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 2 / 73 (2.74%) | 1 / 27 (3.70%) | 1 / 41 (2.44%) |
| occurrences (all)                      | 2              | 1              | 1              |
| Dental caries                          |                |                |                |
| subjects affected / exposed            | 2 / 73 (2.74%) | 1 / 27 (3.70%) | 1 / 41 (2.44%) |
| occurrences (all)                      | 2              | 1              | 1              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Actinic Keratosis                      |                |                |                |
| subjects affected / exposed            | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Dermatitis Atopic                      |                |                |                |
| subjects affected / exposed            | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Ecchymosis                             |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Granuloma Annulare          |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Hyperkeratosis              |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 27 (3.70%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Hypertrichosis              |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Lichen Planus               |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Neurodermatitis             |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pruritus                    |                |                |                |
| subjects affected / exposed | 1 / 73 (1.37%) | 1 / 27 (3.70%) | 1 / 41 (2.44%) |
| occurrences (all)           | 2              | 1              | 1              |
| Psoriasis                   |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash                        |                |                |                |
| subjects affected / exposed | 1 / 73 (1.37%) | 1 / 27 (3.70%) | 1 / 41 (2.44%) |
| occurrences (all)           | 2              | 1              | 1              |
| Rash Erythematous           |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash Papular                |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Sebaceous Hyperplasia       |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Irritation             |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Skin Lesion                                     |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 27 (3.70%) | 1 / 41 (2.44%) |
| occurrences (all)                               | 0              | 1              | 2              |
| Urticaria                                       |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                               | 0              | 0              | 2              |
| Alopecia                                        |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Dermal cyst                                     |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Dermatitis                                      |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                               | 1              | 0              | 1              |
| Dry skin                                        |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                               | 1              | 0              | 1              |
| Renal and urinary disorders                     |                |                |                |
| Dysuria                                         |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                               | 1              | 0              | 1              |
| Micturition Urgency                             |                |                |                |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Endocrine disorders                             |                |                |                |
| Hypothyroidism                                  |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Thyroiditis Chronic                             |                |                |                |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Myalgia                     |                 |                 |                 |
| subjects affected / exposed | 2 / 73 (2.74%)  | 1 / 27 (3.70%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 2               | 1               | 0               |
| Arthralgia                  |                 |                 |                 |
| subjects affected / exposed | 9 / 73 (12.33%) | 4 / 27 (14.81%) | 6 / 41 (14.63%) |
| occurrences (all)           | 13              | 4               | 8               |
| Back Pain                   |                 |                 |                 |
| subjects affected / exposed | 8 / 73 (10.96%) | 5 / 27 (18.52%) | 1 / 41 (2.44%)  |
| occurrences (all)           | 11              | 7               | 1               |
| Bone Pain                   |                 |                 |                 |
| subjects affected / exposed | 1 / 73 (1.37%)  | 1 / 27 (3.70%)  | 1 / 41 (2.44%)  |
| occurrences (all)           | 1               | 1               | 1               |
| Bursitis                    |                 |                 |                 |
| subjects affected / exposed | 2 / 73 (2.74%)  | 2 / 27 (7.41%)  | 1 / 41 (2.44%)  |
| occurrences (all)           | 2               | 2               | 1               |
| Costochondritis             |                 |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)  | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Dupuytren's Contracture     |                 |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)  | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Foot Deformity              |                 |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)  | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Joint Stiffness             |                 |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)  | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Monarthrititis              |                 |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)  | 0 / 27 (0.00%)  | 1 / 41 (2.44%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Muscle Contracture          |                 |                 |                 |
| subjects affected / exposed | 1 / 73 (1.37%)  | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Muscle Spasms               |                 |                 |                 |
| subjects affected / exposed | 3 / 73 (4.11%)  | 1 / 27 (3.70%)  | 1 / 41 (2.44%)  |
| occurrences (all)           | 3               | 1               | 1               |

|                             |                  |                 |                 |
|-----------------------------|------------------|-----------------|-----------------|
| Muscular Weakness           |                  |                 |                 |
| subjects affected / exposed | 1 / 73 (1.37%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 1                | 0               | 0               |
| Musculoskeletal Chest Pain  |                  |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 1 / 41 (2.44%)  |
| occurrences (all)           | 0                | 0               | 1               |
| Musculoskeletal Discomfort  |                  |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Musculoskeletal Pain        |                  |                 |                 |
| subjects affected / exposed | 4 / 73 (5.48%)   | 1 / 27 (3.70%)  | 6 / 41 (14.63%) |
| occurrences (all)           | 5                | 1               | 6               |
| Musculoskeletal Stiffness   |                  |                 |                 |
| subjects affected / exposed | 1 / 73 (1.37%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 1                | 0               | 0               |
| Myalgia Intercostal         |                  |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Neck Pain                   |                  |                 |                 |
| subjects affected / exposed | 3 / 73 (4.11%)   | 2 / 27 (7.41%)  | 1 / 41 (2.44%)  |
| occurrences (all)           | 3                | 2               | 1               |
| Osteoarthritis              |                  |                 |                 |
| subjects affected / exposed | 6 / 73 (8.22%)   | 2 / 27 (7.41%)  | 1 / 41 (2.44%)  |
| occurrences (all)           | 7                | 3               | 2               |
| Osteochondrosis             |                  |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Osteosclerosis              |                  |                 |                 |
| subjects affected / exposed | 1 / 73 (1.37%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 1                | 0               | 0               |
| Pain In Extremity           |                  |                 |                 |
| subjects affected / exposed | 12 / 73 (16.44%) | 4 / 27 (14.81%) | 2 / 41 (4.88%)  |
| occurrences (all)           | 15               | 5               | 2               |
| Polyarthritis               |                  |                 |                 |
| subjects affected / exposed | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Rotator Cuff Syndrome       |                |                 |                |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 27 (0.00%)  | 1 / 41 (2.44%) |
| occurrences (all)           | 2              | 0               | 1              |
| Sacroiliitis                |                |                 |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Synovial Cyst               |                |                 |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Tendonitis                  |                |                 |                |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)           | 1              | 0               | 0              |
| Torticollis                 |                |                 |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Fibromyalgia                |                |                 |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Joint swelling              |                |                 |                |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)           | 1              | 0               | 0              |
| Spinal osteoarthritis       |                |                 |                |
| subjects affected / exposed | 2 / 73 (2.74%) | 1 / 27 (3.70%)  | 0 / 41 (0.00%) |
| occurrences (all)           | 3              | 1               | 0              |
| Trigger finger              |                |                 |                |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)           | 1              | 0               | 0              |
| Infections and infestations |                |                 |                |
| Bacterial Infection         |                |                 |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Bronchitis                  |                |                 |                |
| subjects affected / exposed | 4 / 73 (5.48%) | 4 / 27 (14.81%) | 4 / 41 (9.76%) |
| occurrences (all)           | 7              | 4               | 4              |
| Cellulitis                  |                |                 |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 27 (3.70%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Chronic Sinusitis           |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Cystitis                    |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)           | 0              | 0              | 1              |
| Ear Infection               |                |                |                |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Fungal Infection            |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 27 (3.70%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Furuncle                    |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastroenteritis             |                |                |                |
| subjects affected / exposed | 2 / 73 (2.74%) | 2 / 27 (7.41%) | 0 / 41 (0.00%) |
| occurrences (all)           | 2              | 2              | 0              |
| Gastroenteritis Viral       |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all)           | 0              | 0              | 1              |
| Gastrointestinal Infection  |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Herpes Zoster               |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Influenza                   |                |                |                |
| subjects affected / exposed | 4 / 73 (5.48%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 4              | 0              | 0              |
| Nail Bed Infection Fungal   |                |                |                |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 27 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Nasal Abscess               |                |                |                |

|                                   |                  |                 |                  |
|-----------------------------------|------------------|-----------------|------------------|
| subjects affected / exposed       | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)   |
| occurrences (all)                 | 0                | 0               | 0                |
| Nasopharyngitis                   |                  |                 |                  |
| subjects affected / exposed       | 13 / 73 (17.81%) | 6 / 27 (22.22%) | 10 / 41 (24.39%) |
| occurrences (all)                 | 16               | 13              | 13               |
| Onychomycosis                     |                  |                 |                  |
| subjects affected / exposed       | 2 / 73 (2.74%)   | 1 / 27 (3.70%)  | 0 / 41 (0.00%)   |
| occurrences (all)                 | 2                | 1               | 0                |
| Oral Candidiasis                  |                  |                 |                  |
| subjects affected / exposed       | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 1 / 41 (2.44%)   |
| occurrences (all)                 | 0                | 0               | 1                |
| Oral Fungal Infection             |                  |                 |                  |
| subjects affected / exposed       | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)   |
| occurrences (all)                 | 0                | 0               | 0                |
| Oral Herpes                       |                  |                 |                  |
| subjects affected / exposed       | 2 / 73 (2.74%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)   |
| occurrences (all)                 | 2                | 0               | 0                |
| Otitis Media Acute                |                  |                 |                  |
| subjects affected / exposed       | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)   |
| occurrences (all)                 | 0                | 0               | 0                |
| Pharyngitis                       |                  |                 |                  |
| subjects affected / exposed       | 1 / 73 (1.37%)   | 0 / 27 (0.00%)  | 1 / 41 (2.44%)   |
| occurrences (all)                 | 1                | 0               | 1                |
| Pharyngitis Streptococcal         |                  |                 |                  |
| subjects affected / exposed       | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 1 / 41 (2.44%)   |
| occurrences (all)                 | 0                | 0               | 1                |
| Pneumonia                         |                  |                 |                  |
| subjects affected / exposed       | 1 / 73 (1.37%)   | 1 / 27 (3.70%)  | 2 / 41 (4.88%)   |
| occurrences (all)                 | 1                | 1               | 3                |
| Pyoderma                          |                  |                 |                  |
| subjects affected / exposed       | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)   |
| occurrences (all)                 | 0                | 0               | 0                |
| Respiratory Tract Infection       |                  |                 |                  |
| subjects affected / exposed       | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%)   |
| occurrences (all)                 | 0                | 0               | 0                |
| Respiratory Tract Infection Viral |                  |                 |                  |

|                                         |                  |                 |                |
|-----------------------------------------|------------------|-----------------|----------------|
| subjects affected / exposed             | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                       | 0                | 0               | 0              |
| Rhinitis                                |                  |                 |                |
| subjects affected / exposed             | 1 / 73 (1.37%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                       | 1                | 0               | 0              |
| Sinusitis                               |                  |                 |                |
| subjects affected / exposed             | 3 / 73 (4.11%)   | 3 / 27 (11.11%) | 2 / 41 (4.88%) |
| occurrences (all)                       | 3                | 5               | 2              |
| Tooth Abscess                           |                  |                 |                |
| subjects affected / exposed             | 1 / 73 (1.37%)   | 0 / 27 (0.00%)  | 1 / 41 (2.44%) |
| occurrences (all)                       | 1                | 0               | 1              |
| Tooth Infection                         |                  |                 |                |
| subjects affected / exposed             | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                       | 0                | 0               | 0              |
| Upper Respiratory Tract Infection       |                  |                 |                |
| subjects affected / exposed             | 3 / 73 (4.11%)   | 0 / 27 (0.00%)  | 1 / 41 (2.44%) |
| occurrences (all)                       | 4                | 0               | 1              |
| Urinary Tract Infection                 |                  |                 |                |
| subjects affected / exposed             | 10 / 73 (13.70%) | 4 / 27 (14.81%) | 2 / 41 (4.88%) |
| occurrences (all)                       | 12               | 4               | 3              |
| Viral Infection                         |                  |                 |                |
| subjects affected / exposed             | 2 / 73 (2.74%)   | 1 / 27 (3.70%)  | 0 / 41 (0.00%) |
| occurrences (all)                       | 2                | 1               | 0              |
| Viral Upper Respiratory Tract Infection |                  |                 |                |
| subjects affected / exposed             | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                       | 0                | 0               | 0              |
| Borrelia infection                      |                  |                 |                |
| subjects affected / exposed             | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                       | 0                | 0               | 0              |
| Eye infection                           |                  |                 |                |
| subjects affected / exposed             | 1 / 73 (1.37%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                       | 1                | 0               | 0              |
| Lower respiratory tract infection       |                  |                 |                |
| subjects affected / exposed             | 0 / 73 (0.00%)   | 0 / 27 (0.00%)  | 0 / 41 (0.00%) |
| occurrences (all)                       | 0                | 0               | 0              |

|                                                                                                                     |                     |                     |                     |
|---------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Wound infection<br>subjects affected / exposed<br>occurrences (all)                                                 | 1 / 73 (1.37%)<br>1 | 0 / 27 (0.00%)<br>0 | 1 / 41 (2.44%)<br>1 |
| Metabolism and nutrition disorders                                                                                  |                     |                     |                     |
| Anorexia<br>subjects affected / exposed<br>occurrences (all)                                                        | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Dyslipidaemia<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 1 / 41 (2.44%)<br>1 |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)                                           | 2 / 73 (2.74%)<br>2 | 2 / 27 (7.41%)<br>2 | 0 / 41 (0.00%)<br>0 |
| Hyperlipidaemia<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |
| Food intolerance<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 0 / 73 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>                                                    | Years 6-10 Group A:<br>Odanacatib 50 mg<br>once weekly | Years 6-10 Group B:<br>Odanacatib 50 mg<br>once weekly | Years 6-10 Group C:<br>Odanacatib 50 mg<br>once weekly |
|--------------------------------------------------------------------------------------|--------------------------------------------------------|--------------------------------------------------------|--------------------------------------------------------|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 27 / 28 (96.43%)                                       | 34 / 34 (100.00%)                                      | 23 / 23 (100.00%)                                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)                  |                                                        |                                                        |                                                        |
| Basal Cell Carcinoma<br>subjects affected / exposed<br>occurrences (all)             | 0 / 28 (0.00%)<br>0                                    | 0 / 34 (0.00%)<br>0                                    | 0 / 23 (0.00%)<br>0                                    |
| Fibroma<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 28 (0.00%)<br>0                                    | 0 / 34 (0.00%)<br>0                                    | 0 / 23 (0.00%)<br>0                                    |
| Lipoma<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 28 (0.00%)<br>0                                    | 0 / 34 (0.00%)<br>0                                    | 0 / 23 (0.00%)<br>0                                    |
| Ovarian Neoplasm                                                                     |                                                        |                                                        |                                                        |

|                                                                                      |                      |                      |                      |
|--------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                     | 0 / 28 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Thyroid Neoplasm<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 28 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Benign neoplasm of thyroid gland<br>subjects affected / exposed<br>occurrences (all) | 2 / 28 (7.14%)<br>2  | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Vascular disorders                                                                   |                      |                      |                      |
| Flushing<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 28 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 28 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 28 (10.71%)<br>3 | 6 / 34 (17.65%)<br>7 | 5 / 23 (21.74%)<br>5 |
| Phlebitis<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 28 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Varicose Vein<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 28 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1  |
| General disorders and administration<br>site conditions                              |                      |                      |                      |
| Calcinosis<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 28 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Chest Discomfort<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 28 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Chest Pain<br>subjects affected / exposed<br>occurrences (all)                       | 2 / 28 (7.14%)<br>3  | 1 / 34 (2.94%)<br>1  | 1 / 23 (4.35%)<br>2  |
| Fatigue                                                                              |                      |                      |                      |

|                                                                                                                               |                     |                     |                     |
|-------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                              | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0 |
| Influenza Like Illness<br>subjects affected / exposed<br>occurrences (all)                                                    | 1 / 28 (3.57%)<br>1 | 1 / 34 (2.94%)<br>1 | 1 / 23 (4.35%)<br>1 |
| Oedema Peripheral<br>subjects affected / exposed<br>occurrences (all)                                                         | 1 / 28 (3.57%)<br>2 | 2 / 34 (5.88%)<br>2 | 2 / 23 (8.70%)<br>3 |
| Wrist Fracture<br>subjects affected / exposed<br>occurrences (all)                                                            | 1 / 28 (3.57%)<br>1 | 1 / 34 (2.94%)<br>1 | 0 / 23 (0.00%)<br>0 |
| Immune system disorders<br>Allergy To Arthropod Sting<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0 |
| Drug Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                                                     | 1 / 28 (3.57%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0 |
| Reproductive system and breast disorders<br>Breast Mass<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 28 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 1 / 23 (4.35%)<br>1 |
| Fibrocystic Breast Disease<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0 |
| Pelvic Pain<br>subjects affected / exposed<br>occurrences (all)                                                               | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0 |
| Vulvovaginal Discomfort<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders<br>Pharyngolaryngeal Pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0 |
| Allergic Pharyngitis                                                                                                          |                     |                     |                     |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Asthma                      |                 |                |                |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0               | 1              | 0              |
| Dysphonia                   |                 |                |                |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0               | 0              | 1              |
| Dyspnoea                    |                 |                |                |
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 34 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all)           | 3               | 0              | 1              |
| Dyspnoea Exertional         |                 |                |                |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0               | 1              | 1              |
| Emphysema                   |                 |                |                |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Haemoptysis                 |                 |                |                |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Cough                       |                 |                |                |
| subjects affected / exposed | 0 / 28 (0.00%)  | 2 / 34 (5.88%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0               | 2              | 0              |
| Psychiatric disorders       |                 |                |                |
| Insomnia                    |                 |                |                |
| subjects affected / exposed | 2 / 28 (7.14%)  | 1 / 34 (2.94%) | 1 / 23 (4.35%) |
| occurrences (all)           | 2               | 1              | 1              |
| Alcoholism                  |                 |                |                |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Anxiety                     |                 |                |                |
| subjects affected / exposed | 1 / 28 (3.57%)  | 1 / 34 (2.94%) | 1 / 23 (4.35%) |
| occurrences (all)           | 1               | 1              | 1              |
| Depression                  |                 |                |                |
| subjects affected / exposed | 4 / 28 (14.29%) | 3 / 34 (8.82%) | 2 / 23 (8.70%) |
| occurrences (all)           | 5               | 3              | 4              |

|                                                                                                   |                     |                     |                      |
|---------------------------------------------------------------------------------------------------|---------------------|---------------------|----------------------|
| Dysthymic Disorder<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Stress<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 28 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 1 / 23 (4.35%)<br>1  |
| Investigations                                                                                    |                     |                     |                      |
| Weight Increased<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Alanine Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 4 / 23 (17.39%)<br>4 |
| Aspartate Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 4 / 23 (17.39%)<br>4 |
| Blood 1,25-Dihydroxycholecalciferol Increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Blood Cholesterol Increased<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Blood Glucose Increased<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Blood Parathyroid Hormone Increased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Blood Pressure Increased<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Blood Triglycerides Increased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Bone Density Decreased                                                                            |                     |                     |                      |

|                                                |                |                |                |
|------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Carotid Bruit                                  |                |                |                |
| subjects affected / exposed                    | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Glucose Urine Present                          |                |                |                |
| subjects affected / exposed                    | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| High Density Lipoprotein Decreased             |                |                |                |
| subjects affected / exposed                    | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Lymphocyte Count Decreased                     |                |                |                |
| subjects affected / exposed                    | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Ultrasound Thyroid Abnormal                    |                |                |                |
| subjects affected / exposed                    | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Weight Decreased                               |                |                |                |
| subjects affected / exposed                    | 0 / 28 (0.00%) | 2 / 34 (5.88%) | 2 / 23 (8.70%) |
| occurrences (all)                              | 0              | 3              | 2              |
| White Blood Cells Urine Positive               |                |                |                |
| subjects affected / exposed                    | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Blood alkaline phosphatase increased           |                |                |                |
| subjects affected / exposed                    | 2 / 28 (7.14%) | 0 / 34 (0.00%) | 2 / 23 (8.70%) |
| occurrences (all)                              | 2              | 0              | 2              |
| Body height decreased                          |                |                |                |
| subjects affected / exposed                    | 1 / 28 (3.57%) | 3 / 34 (8.82%) | 2 / 23 (8.70%) |
| occurrences (all)                              | 1              | 4              | 2              |
| Injury, poisoning and procedural complications |                |                |                |
| Arthropod Bite                                 |                |                |                |
| subjects affected / exposed                    | 1 / 28 (3.57%) | 1 / 34 (2.94%) | 0 / 23 (0.00%) |
| occurrences (all)                              | 1              | 1              | 0              |
| Arthropod Sting                                |                |                |                |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Contusion                   |                 |                 |                 |
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 34 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 3               | 0               | 2               |
| Device Breakage             |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Epicondylitis               |                 |                 |                 |
| subjects affected / exposed | 2 / 28 (7.14%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 2               | 0               | 0               |
| Fall                        |                 |                 |                 |
| subjects affected / exposed | 3 / 28 (10.71%) | 4 / 34 (11.76%) | 5 / 23 (21.74%) |
| occurrences (all)           | 12              | 8               | 6               |
| Humerus Fracture            |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Joint Sprain                |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Limb Injury                 |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Muscle Strain               |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Open Wound                  |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Procedural Pain             |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Radius Fracture             |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Rib Fracture                |                 |                 |                 |

|                                            |                |                |                |
|--------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 1 / 23 (4.35%) |
| occurrences (all)                          | 0              | 1              | 1              |
| Skin Laceration                            |                |                |                |
| subjects affected / exposed                | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Skull Fractured Base                       |                |                |                |
| subjects affected / exposed                | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Spinal Compression Fracture                |                |                |                |
| subjects affected / exposed                | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Spinal Fracture                            |                |                |                |
| subjects affected / exposed                | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Subdural Haematoma                         |                |                |                |
| subjects affected / exposed                | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Thoracic Vertebral Fracture                |                |                |                |
| subjects affected / exposed                | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Tooth Fracture                             |                |                |                |
| subjects affected / exposed                | 1 / 28 (3.57%) | 1 / 34 (2.94%) | 2 / 23 (8.70%) |
| occurrences (all)                          | 1              | 2              | 4              |
| Vertebral Injury                           |                |                |                |
| subjects affected / exposed                | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                          | 0              | 0              | 0              |
| Laceration                                 |                |                |                |
| subjects affected / exposed                | 1 / 28 (3.57%) | 2 / 34 (5.88%) | 1 / 23 (4.35%) |
| occurrences (all)                          | 1              | 3              | 1              |
| Ligament sprain                            |                |                |                |
| subjects affected / exposed                | 1 / 28 (3.57%) | 2 / 34 (5.88%) | 0 / 23 (0.00%) |
| occurrences (all)                          | 1              | 2              | 0              |
| Congenital, familial and genetic disorders |                |                |                |
| Congenital Diaphragmatic Hernia            |                |                |                |

|                                                  |                     |                     |                     |
|--------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 28 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0 |
| Cardiac disorders                                |                     |                     |                     |
| Arrhythmia                                       |                     |                     |                     |
| subjects affected / exposed                      | 0 / 28 (0.00%)      | 0 / 34 (0.00%)      | 0 / 23 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Atrial Flutter                                   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 28 (0.00%)      | 0 / 34 (0.00%)      | 0 / 23 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Mitral Valve Prolapse                            |                     |                     |                     |
| subjects affected / exposed                      | 0 / 28 (0.00%)      | 0 / 34 (0.00%)      | 0 / 23 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Palpitations                                     |                     |                     |                     |
| subjects affected / exposed                      | 0 / 28 (0.00%)      | 1 / 34 (2.94%)      | 0 / 23 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Tachycardia                                      |                     |                     |                     |
| subjects affected / exposed                      | 0 / 28 (0.00%)      | 0 / 34 (0.00%)      | 0 / 23 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Nervous system disorders                         |                     |                     |                     |
| Cervicobrachial Syndrome                         |                     |                     |                     |
| subjects affected / exposed                      | 1 / 28 (3.57%)      | 0 / 34 (0.00%)      | 0 / 23 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Headache                                         |                     |                     |                     |
| subjects affected / exposed                      | 2 / 28 (7.14%)      | 1 / 34 (2.94%)      | 3 / 23 (13.04%)     |
| occurrences (all)                                | 3                   | 1                   | 4                   |
| Memory Impairment                                |                     |                     |                     |
| subjects affected / exposed                      | 0 / 28 (0.00%)      | 0 / 34 (0.00%)      | 0 / 23 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Migraine                                         |                     |                     |                     |
| subjects affected / exposed                      | 0 / 28 (0.00%)      | 0 / 34 (0.00%)      | 1 / 23 (4.35%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Paraesthesia                                     |                     |                     |                     |
| subjects affected / exposed                      | 2 / 28 (7.14%)      | 1 / 34 (2.94%)      | 1 / 23 (4.35%)      |
| occurrences (all)                                | 2                   | 1                   | 1                   |
| Sciatica                                         |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Somnolence                  |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tension Headache            |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tremor                      |                |                |                |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Trigeminal Neuralgia        |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Upper Motor Neuron Lesion   |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Carpal tunnel syndrome      |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 3 / 34 (8.82%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 3              | 0              |
| Dizziness                   |                |                |                |
| subjects affected / exposed | 2 / 28 (7.14%) | 3 / 34 (8.82%) | 2 / 23 (8.70%) |
| occurrences (all)           | 2              | 3              | 2              |
| Parkinson's disease         |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 2 / 34 (5.88%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 2              | 0              |
| Ear and labyrinth disorders |                |                |                |
| Deafness                    |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tinnitus                    |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 2 / 34 (5.88%) | 2 / 23 (8.70%) |
| occurrences (all)           | 0              | 3              | 2              |
| Tympanosclerosis            |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| Vertigo                     |                |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 5 / 34 (14.71%) | 1 / 23 (4.35%)  |
| occurrences (all)           | 0              | 7               | 1               |
| Vertigo Positional          |                |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Eye disorders               |                |                 |                 |
| Cataract                    |                |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 6 / 34 (17.65%) | 6 / 23 (26.09%) |
| occurrences (all)           | 0              | 9               | 10              |
| Conjunctivitis              |                |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 34 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 1              | 0               | 1               |
| Conjunctivitis Allergic     |                |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Eye Pruritus                |                |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Macular Degeneration        |                |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Retinal Tear                |                |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Gastrointestinal disorders  |                |                 |                 |
| Abdominal Pain Upper        |                |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 34 (2.94%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 1              | 1               | 1               |
| Abdominal Pain              |                |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Anal Fissure                |                |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Aphthous Stomatitis         |                |                 |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Colitis                     |                |                |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Constipation                |                |                |                 |
| subjects affected / exposed | 2 / 28 (7.14%) | 2 / 34 (5.88%) | 1 / 23 (4.35%)  |
| occurrences (all)           | 3              | 2              | 2               |
| Diarrhoea                   |                |                |                 |
| subjects affected / exposed | 2 / 28 (7.14%) | 2 / 34 (5.88%) | 4 / 23 (17.39%) |
| occurrences (all)           | 2              | 3              | 5               |
| Dry Mouth                   |                |                |                 |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Duodenal Ulcer              |                |                |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Dyspepsia                   |                |                |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 4 / 23 (17.39%) |
| occurrences (all)           | 0              | 1              | 4               |
| Faecal Incontinence         |                |                |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Flatulence                  |                |                |                 |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Gastric Disorder            |                |                |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Gastric Polyps              |                |                |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Gastric Ulcer               |                |                |                 |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Gastritis                   |                |                |                 |

|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed      | 1 / 28 (3.57%) | 2 / 34 (5.88%) | 1 / 23 (4.35%) |
| occurrences (all)                | 1              | 2              | 1              |
| Gastrointestinal Disorder        |                |                |                |
| subjects affected / exposed      | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastrooesophageal Reflux Disease |                |                |                |
| subjects affected / exposed      | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 2 / 23 (8.70%) |
| occurrences (all)                | 1              | 0              | 2              |
| Gingival Swelling                |                |                |                |
| subjects affected / exposed      | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gingivitis                       |                |                |                |
| subjects affected / exposed      | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Hiatus Hernia                    |                |                |                |
| subjects affected / exposed      | 0 / 28 (0.00%) | 2 / 34 (5.88%) | 0 / 23 (0.00%) |
| occurrences (all)                | 0              | 2              | 0              |
| Inguinal Hernia                  |                |                |                |
| subjects affected / exposed      | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Irritable Bowel Syndrome         |                |                |                |
| subjects affected / exposed      | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| Mouth Ulceration                 |                |                |                |
| subjects affected / exposed      | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| Nausea                           |                |                |                |
| subjects affected / exposed      | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Oesophagitis                     |                |                |                |
| subjects affected / exposed      | 0 / 28 (0.00%) | 3 / 34 (8.82%) | 0 / 23 (0.00%) |
| occurrences (all)                | 0              | 3              | 0              |
| Rectal Haemorrhage               |                |                |                |
| subjects affected / exposed      | 1 / 28 (3.57%) | 1 / 34 (2.94%) | 0 / 23 (0.00%) |
| occurrences (all)                | 1              | 1              | 0              |
| Reflux Oesophagitis              |                |                |                |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed            | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Toothache                              |                |                |                |
| subjects affected / exposed            | 1 / 28 (3.57%) | 1 / 34 (2.94%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 1              | 1              | 0              |
| Upper Gastrointestinal Haemorrhage     |                |                |                |
| subjects affected / exposed            | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 1 / 23 (4.35%) |
| occurrences (all)                      | 0              | 1              | 1              |
| Dental caries                          |                |                |                |
| subjects affected / exposed            | 0 / 28 (0.00%) | 2 / 34 (5.88%) | 2 / 23 (8.70%) |
| occurrences (all)                      | 0              | 2              | 2              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Actinic Keratosis                      |                |                |                |
| subjects affected / exposed            | 2 / 28 (7.14%) | 1 / 34 (2.94%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 2              | 1              | 0              |
| Dermatitis Atopic                      |                |                |                |
| subjects affected / exposed            | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 2 / 23 (8.70%) |
| occurrences (all)                      | 0              | 0              | 3              |
| Ecchymosis                             |                |                |                |
| subjects affected / exposed            | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Granuloma Annulare                     |                |                |                |
| subjects affected / exposed            | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Hyperkeratosis                         |                |                |                |
| subjects affected / exposed            | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Hypertrichosis                         |                |                |                |
| subjects affected / exposed            | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Lichen Planus                          |                |                |                |
| subjects affected / exposed            | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Neurodermatitis             |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pruritus                    |                |                |                |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 2              | 0              | 0              |
| Psoriasis                   |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash                        |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 2 / 34 (5.88%) | 2 / 23 (8.70%) |
| occurrences (all)           | 0              | 2              | 2              |
| Rash Erythematous           |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash Papular                |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0              | 0              | 1              |
| Sebaceous Hyperplasia       |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Irritation             |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Lesion                 |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Urticaria                   |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0              | 1              | 2              |
| Alopecia                    |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 2 / 23 (8.70%) |
| occurrences (all)           | 0              | 0              | 2              |
| Dermal cyst                 |                |                |                |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

|                                                                                                                |                       |                      |                      |
|----------------------------------------------------------------------------------------------------------------|-----------------------|----------------------|----------------------|
| Dermatitis<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 28 (0.00%)<br>0   | 2 / 34 (5.88%)<br>3  | 1 / 23 (4.35%)<br>1  |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 28 (0.00%)<br>0   | 1 / 34 (2.94%)<br>1  | 2 / 23 (8.70%)<br>2  |
| Renal and urinary disorders<br>Dysuria<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 28 (0.00%)<br>0   | 1 / 34 (2.94%)<br>1  | 1 / 23 (4.35%)<br>1  |
| Micturition Urgency<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 28 (0.00%)<br>0   | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 28 (0.00%)<br>0   | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Thyroiditis Chronic<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 28 (0.00%)<br>0   | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders<br>Myalgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 28 (3.57%)<br>1   | 2 / 34 (5.88%)<br>2  | 2 / 23 (8.70%)<br>2  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                                                 | 5 / 28 (17.86%)<br>10 | 4 / 34 (11.76%)<br>4 | 8 / 23 (34.78%)<br>8 |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)                                                  | 6 / 28 (21.43%)<br>6  | 7 / 34 (20.59%)<br>9 | 5 / 23 (21.74%)<br>7 |
| Bone Pain<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 28 (0.00%)<br>0   | 0 / 34 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)                                                   | 1 / 28 (3.57%)<br>1   | 1 / 34 (2.94%)<br>1  | 1 / 23 (4.35%)<br>1  |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Costochondritis             |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Dupuytren's Contracture     |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1               | 1               | 0               |
| Foot Deformity              |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Joint Stiffness             |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Monarthrititis              |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Muscle Contracture          |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Muscle Spasms               |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 1 / 34 (2.94%)  | 2 / 23 (8.70%)  |
| occurrences (all)           | 1               | 1               | 2               |
| Muscular Weakness           |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 2 / 34 (5.88%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0               | 2               | 1               |
| Musculoskeletal Chest Pain  |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Musculoskeletal Discomfort  |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Musculoskeletal Pain        |                 |                 |                 |
| subjects affected / exposed | 3 / 28 (10.71%) | 4 / 34 (11.76%) | 5 / 23 (21.74%) |
| occurrences (all)           | 6               | 4               | 6               |
| Musculoskeletal Stiffness   |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Myalgia Intercostal         |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Neck Pain                   |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 3 / 34 (8.82%)  | 3 / 23 (13.04%) |
| occurrences (all)           | 0               | 4               | 4               |
| Osteoarthritis              |                 |                 |                 |
| subjects affected / exposed | 3 / 28 (10.71%) | 5 / 34 (14.71%) | 2 / 23 (8.70%)  |
| occurrences (all)           | 3               | 6               | 2               |
| Osteochondrosis             |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Osteosclerosis              |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Pain In Extremity           |                 |                 |                 |
| subjects affected / exposed | 6 / 28 (21.43%) | 1 / 34 (2.94%)  | 2 / 23 (8.70%)  |
| occurrences (all)           | 6               | 1               | 3               |
| Polyarthritis               |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Rotator Cuff Syndrome       |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Sacroiliitis                |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Synovial Cyst               |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Tendonitis                  |                 |                 |                 |
| subjects affected / exposed | 2 / 28 (7.14%)  | 3 / 34 (8.82%)  | 2 / 23 (8.70%)  |
| occurrences (all)           | 2               | 3               | 2               |
| Torticollis                 |                 |                 |                 |
| subjects affected / exposed | 2 / 28 (7.14%)  | 3 / 34 (8.82%)  | 2 / 23 (8.70%)  |
| occurrences (all)           | 2               | 3               | 2               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Fibromyalgia                |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 2 / 23 (8.70%)  |
| occurrences (all)           | 0               | 1               | 2               |
| Joint swelling              |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 2 / 34 (5.88%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0               | 3               | 2               |
| Spinal osteoarthritis       |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Trigger finger              |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 2 / 34 (5.88%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0               | 2               | 1               |
| Infections and infestations |                 |                 |                 |
| Bacterial Infection         |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Bronchitis                  |                 |                 |                 |
| subjects affected / exposed | 3 / 28 (10.71%) | 5 / 34 (14.71%) | 5 / 23 (21.74%) |
| occurrences (all)           | 4               | 5               | 9               |
| Cellulitis                  |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Chronic Sinusitis           |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Cystitis                    |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 0 / 34 (0.00%)  | 2 / 23 (8.70%)  |
| occurrences (all)           | 1               | 0               | 2               |
| Ear Infection               |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 2 / 34 (5.88%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1               | 2               | 0               |
| Fungal Infection            |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Furuncle                    |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Gastroenteritis             |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Gastroenteritis Viral       |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Gastrointestinal Infection  |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Herpes Zoster               |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 2 / 34 (5.88%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 1               | 2               | 1               |
| Influenza                   |                 |                 |                 |
| subjects affected / exposed | 1 / 28 (3.57%)  | 4 / 34 (11.76%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 1               | 4               | 0               |
| Nail Bed Infection Fungal   |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Nasal Abscess               |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Nasopharyngitis             |                 |                 |                 |
| subjects affected / exposed | 7 / 28 (25.00%) | 8 / 34 (23.53%) | 5 / 23 (21.74%) |
| occurrences (all)           | 9               | 15              | 9               |
| Onychomycosis               |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 2 / 34 (5.88%)  | 3 / 23 (13.04%) |
| occurrences (all)           | 0               | 3               | 4               |
| Oral Candidiasis            |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Oral Fungal Infection       |                 |                 |                 |
| subjects affected / exposed | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Oral Herpes                 |                 |                 |                 |

|                                   |                |                |                 |
|-----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed       | 2 / 28 (7.14%) | 1 / 34 (2.94%) | 0 / 23 (0.00%)  |
| occurrences (all)                 | 2              | 1              | 0               |
| Otitis Media Acute                |                |                |                 |
| subjects affected / exposed       | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%)  |
| occurrences (all)                 | 0              | 0              | 1               |
| Pharyngitis                       |                |                |                 |
| subjects affected / exposed       | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%)  |
| occurrences (all)                 | 0              | 0              | 2               |
| Pharyngitis Streptococcal         |                |                |                 |
| subjects affected / exposed       | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 1 / 23 (4.35%)  |
| occurrences (all)                 | 0              | 3              | 1               |
| Pneumonia                         |                |                |                 |
| subjects affected / exposed       | 0 / 28 (0.00%) | 1 / 34 (2.94%) | 1 / 23 (4.35%)  |
| occurrences (all)                 | 0              | 3              | 1               |
| Pyoderma                          |                |                |                 |
| subjects affected / exposed       | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Respiratory Tract Infection       |                |                |                 |
| subjects affected / exposed       | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 1 / 23 (4.35%)  |
| occurrences (all)                 | 1              | 0              | 2               |
| Respiratory Tract Infection Viral |                |                |                 |
| subjects affected / exposed       | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Rhinitis                          |                |                |                 |
| subjects affected / exposed       | 1 / 28 (3.57%) | 2 / 34 (5.88%) | 0 / 23 (0.00%)  |
| occurrences (all)                 | 1              | 2              | 0               |
| Sinusitis                         |                |                |                 |
| subjects affected / exposed       | 1 / 28 (3.57%) | 1 / 34 (2.94%) | 4 / 23 (17.39%) |
| occurrences (all)                 | 2              | 1              | 4               |
| Tooth Abscess                     |                |                |                 |
| subjects affected / exposed       | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 1 / 23 (4.35%)  |
| occurrences (all)                 | 0              | 0              | 1               |
| Tooth Infection                   |                |                |                 |
| subjects affected / exposed       | 0 / 28 (0.00%) | 0 / 34 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Upper Respiratory Tract Infection |                |                |                 |

|                                         |                 |                 |                 |
|-----------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed             | 2 / 28 (7.14%)  | 3 / 34 (8.82%)  | 2 / 23 (8.70%)  |
| occurrences (all)                       | 7               | 5               | 2               |
| Urinary Tract Infection                 |                 |                 |                 |
| subjects affected / exposed             | 9 / 28 (32.14%) | 9 / 34 (26.47%) | 6 / 23 (26.09%) |
| occurrences (all)                       | 15              | 19              | 20              |
| Viral Infection                         |                 |                 |                 |
| subjects affected / exposed             | 1 / 28 (3.57%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)                       | 1               | 1               | 0               |
| Viral Upper Respiratory Tract Infection |                 |                 |                 |
| subjects affected / exposed             | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                       | 0               | 0               | 0               |
| Borrelia infection                      |                 |                 |                 |
| subjects affected / exposed             | 2 / 28 (7.14%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)                       | 2               | 1               | 0               |
| Eye infection                           |                 |                 |                 |
| subjects affected / exposed             | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                       | 0               | 0               | 0               |
| Lower respiratory tract infection       |                 |                 |                 |
| subjects affected / exposed             | 0 / 28 (0.00%)  | 1 / 34 (2.94%)  | 2 / 23 (8.70%)  |
| occurrences (all)                       | 0               | 6               | 3               |
| Wound infection                         |                 |                 |                 |
| subjects affected / exposed             | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                       | 0               | 0               | 0               |
| Metabolism and nutrition disorders      |                 |                 |                 |
| Anorexia                                |                 |                 |                 |
| subjects affected / exposed             | 0 / 28 (0.00%)  | 0 / 34 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                       | 0               | 0               | 0               |
| Dyslipidaemia                           |                 |                 |                 |
| subjects affected / exposed             | 1 / 28 (3.57%)  | 1 / 34 (2.94%)  | 0 / 23 (0.00%)  |
| occurrences (all)                       | 1               | 1               | 0               |
| Hypercholesterolaemia                   |                 |                 |                 |
| subjects affected / exposed             | 3 / 28 (10.71%) | 1 / 34 (2.94%)  | 1 / 23 (4.35%)  |
| occurrences (all)                       | 3               | 1               | 1               |
| Hyperlipidaemia                         |                 |                 |                 |

|                                             |                |                |                |
|---------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                 | 1 / 28 (3.57%) | 0 / 34 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)                           | 1              | 0              | 0              |
| Food intolerance                            |                |                |                |
| alternative assessment type: Non-systematic |                |                |                |
| subjects affected / exposed                 | 0 / 28 (0.00%) | 2 / 34 (5.88%) | 0 / 23 (0.00%) |
| occurrences (all)                           | 0              | 2              | 0              |

|                                                                     |                                                        |  |  |
|---------------------------------------------------------------------|--------------------------------------------------------|--|--|
| <b>Non-serious adverse events</b>                                   | Years 6-10 Group D:<br>Odanacatib 50 mg<br>once weekly |  |  |
| Total subjects affected by non-serious adverse events               |                                                        |  |  |
| subjects affected / exposed                                         | 32 / 32 (100.00%)                                      |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                        |  |  |
| Basal Cell Carcinoma                                                |                                                        |  |  |
| subjects affected / exposed                                         | 1 / 32 (3.13%)                                         |  |  |
| occurrences (all)                                                   | 1                                                      |  |  |
| Fibroma                                                             |                                                        |  |  |
| subjects affected / exposed                                         | 0 / 32 (0.00%)                                         |  |  |
| occurrences (all)                                                   | 0                                                      |  |  |
| Lipoma                                                              |                                                        |  |  |
| subjects affected / exposed                                         | 0 / 32 (0.00%)                                         |  |  |
| occurrences (all)                                                   | 0                                                      |  |  |
| Ovarian Neoplasm                                                    |                                                        |  |  |
| subjects affected / exposed                                         | 0 / 32 (0.00%)                                         |  |  |
| occurrences (all)                                                   | 0                                                      |  |  |
| Thyroid Neoplasm                                                    |                                                        |  |  |
| subjects affected / exposed                                         | 1 / 32 (3.13%)                                         |  |  |
| occurrences (all)                                                   | 1                                                      |  |  |
| Benign neoplasm of thyroid gland                                    |                                                        |  |  |
| subjects affected / exposed                                         | 0 / 32 (0.00%)                                         |  |  |
| occurrences (all)                                                   | 0                                                      |  |  |
| Vascular disorders                                                  |                                                        |  |  |
| Flushing                                                            |                                                        |  |  |
| subjects affected / exposed                                         | 0 / 32 (0.00%)                                         |  |  |
| occurrences (all)                                                   | 0                                                      |  |  |
| Haematoma                                                           |                                                        |  |  |

|                                                      |                |  |  |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences (all)                                    | 0              |  |  |
| Hypertension                                         |                |  |  |
| subjects affected / exposed                          | 3 / 32 (9.38%) |  |  |
| occurrences (all)                                    | 3              |  |  |
| Phlebitis                                            |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences (all)                                    | 0              |  |  |
| Varicose Vein                                        |                |  |  |
| subjects affected / exposed                          | 1 / 32 (3.13%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| General disorders and administration site conditions |                |  |  |
| Calcinosis                                           |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences (all)                                    | 0              |  |  |
| Chest Discomfort                                     |                |  |  |
| subjects affected / exposed                          | 1 / 32 (3.13%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Chest Pain                                           |                |  |  |
| subjects affected / exposed                          | 2 / 32 (6.25%) |  |  |
| occurrences (all)                                    | 2              |  |  |
| Fatigue                                              |                |  |  |
| subjects affected / exposed                          | 1 / 32 (3.13%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Influenza Like Illness                               |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences (all)                                    | 0              |  |  |
| Oedema Peripheral                                    |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences (all)                                    | 0              |  |  |
| Wrist Fracture                                       |                |  |  |
| subjects affected / exposed                          | 0 / 32 (0.00%) |  |  |
| occurrences (all)                                    | 0              |  |  |
| Immune system disorders                              |                |  |  |

|                                                                                                                               |                     |  |  |
|-------------------------------------------------------------------------------------------------------------------------------|---------------------|--|--|
| Allergy To Arthropod Sting<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 32 (0.00%)<br>0 |  |  |
| Drug Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 32 (0.00%)<br>0 |  |  |
| Reproductive system and breast disorders<br>Breast Mass<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 32 (3.13%)<br>1 |  |  |
| Fibrocystic Breast Disease<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 32 (0.00%)<br>0 |  |  |
| Pelvic Pain<br>subjects affected / exposed<br>occurrences (all)                                                               | 1 / 32 (3.13%)<br>1 |  |  |
| Vulvovaginal Discomfort<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 32 (0.00%)<br>0 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Pharyngolaryngeal Pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 32 (0.00%)<br>0 |  |  |
| Allergic Pharyngitis<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 32 (0.00%)<br>0 |  |  |
| Asthma<br>subjects affected / exposed<br>occurrences (all)                                                                    | 1 / 32 (3.13%)<br>1 |  |  |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)                                                                 | 0 / 32 (0.00%)<br>0 |  |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 32 (0.00%)<br>0 |  |  |
| Dyspnoea Exertional                                                                                                           |                     |  |  |

|                                    |                |  |  |
|------------------------------------|----------------|--|--|
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Emphysema                          |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Haemoptysis                        |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Cough                              |                |  |  |
| subjects affected / exposed        | 1 / 32 (3.13%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Psychiatric disorders              |                |  |  |
| Insomnia                           |                |  |  |
| subjects affected / exposed        | 1 / 32 (3.13%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Alcoholism                         |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Anxiety                            |                |  |  |
| subjects affected / exposed        | 1 / 32 (3.13%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Depression                         |                |  |  |
| subjects affected / exposed        | 2 / 32 (6.25%) |  |  |
| occurrences (all)                  | 2              |  |  |
| Dysthymic Disorder                 |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Stress                             |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Investigations                     |                |  |  |
| Weight Increased                   |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Alanine Aminotransferase Increased |                |  |  |

|                                               |                |  |  |
|-----------------------------------------------|----------------|--|--|
| subjects affected / exposed                   | 3 / 32 (9.38%) |  |  |
| occurrences (all)                             | 3              |  |  |
| Aspartate Aminotransferase Increased          |                |  |  |
| subjects affected / exposed                   | 2 / 32 (6.25%) |  |  |
| occurrences (all)                             | 2              |  |  |
| Blood 1,25-Dihydroxycholecalciferol Increased |                |  |  |
| subjects affected / exposed                   | 0 / 32 (0.00%) |  |  |
| occurrences (all)                             | 0              |  |  |
| Blood Cholesterol Increased                   |                |  |  |
| subjects affected / exposed                   | 0 / 32 (0.00%) |  |  |
| occurrences (all)                             | 0              |  |  |
| Blood Glucose Increased                       |                |  |  |
| subjects affected / exposed                   | 1 / 32 (3.13%) |  |  |
| occurrences (all)                             | 1              |  |  |
| Blood Parathyroid Hormone Increased           |                |  |  |
| subjects affected / exposed                   | 0 / 32 (0.00%) |  |  |
| occurrences (all)                             | 0              |  |  |
| Blood Pressure Increased                      |                |  |  |
| subjects affected / exposed                   | 0 / 32 (0.00%) |  |  |
| occurrences (all)                             | 0              |  |  |
| Blood Triglycerides Increased                 |                |  |  |
| subjects affected / exposed                   | 0 / 32 (0.00%) |  |  |
| occurrences (all)                             | 0              |  |  |
| Bone Density Decreased                        |                |  |  |
| subjects affected / exposed                   | 0 / 32 (0.00%) |  |  |
| occurrences (all)                             | 0              |  |  |
| Carotid Bruit                                 |                |  |  |
| subjects affected / exposed                   | 0 / 32 (0.00%) |  |  |
| occurrences (all)                             | 0              |  |  |
| Glucose Urine Present                         |                |  |  |
| subjects affected / exposed                   | 0 / 32 (0.00%) |  |  |
| occurrences (all)                             | 0              |  |  |
| High Density Lipoprotein Decreased            |                |  |  |

|                                                |                 |  |  |
|------------------------------------------------|-----------------|--|--|
| subjects affected / exposed                    | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Lymphocyte Count Decreased                     |                 |  |  |
| subjects affected / exposed                    | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Ultrasound Thyroid Abnormal                    |                 |  |  |
| subjects affected / exposed                    | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Weight Decreased                               |                 |  |  |
| subjects affected / exposed                    | 2 / 32 (6.25%)  |  |  |
| occurrences (all)                              | 2               |  |  |
| White Blood Cells Urine Positive               |                 |  |  |
| subjects affected / exposed                    | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Blood alkaline phosphatase increased           |                 |  |  |
| subjects affected / exposed                    | 6 / 32 (18.75%) |  |  |
| occurrences (all)                              | 6               |  |  |
| Body height decreased                          |                 |  |  |
| subjects affected / exposed                    | 2 / 32 (6.25%)  |  |  |
| occurrences (all)                              | 2               |  |  |
| Injury, poisoning and procedural complications |                 |  |  |
| Arthropod Bite                                 |                 |  |  |
| subjects affected / exposed                    | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Arthropod Sting                                |                 |  |  |
| subjects affected / exposed                    | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Contusion                                      |                 |  |  |
| subjects affected / exposed                    | 3 / 32 (9.38%)  |  |  |
| occurrences (all)                              | 7               |  |  |
| Device Breakage                                |                 |  |  |
| subjects affected / exposed                    | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Epicondylitis                                  |                 |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Fall                        |                 |  |  |
| subjects affected / exposed | 4 / 32 (12.50%) |  |  |
| occurrences (all)           | 9               |  |  |
| Humerus Fracture            |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Joint Sprain                |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Limb Injury                 |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Muscle Strain               |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Open Wound                  |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Procedural Pain             |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Radius Fracture             |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Rib Fracture                |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Skin Laceration             |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Skull Fractured Base        |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Spinal Compression Fracture |                 |  |  |

|                                            |                 |  |  |
|--------------------------------------------|-----------------|--|--|
| subjects affected / exposed                | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                          | 0               |  |  |
| Spinal Fracture                            |                 |  |  |
| subjects affected / exposed                | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                          | 0               |  |  |
| Subdural Haematoma                         |                 |  |  |
| subjects affected / exposed                | 1 / 32 (3.13%)  |  |  |
| occurrences (all)                          | 1               |  |  |
| Thoracic Vertebral Fracture                |                 |  |  |
| subjects affected / exposed                | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                          | 0               |  |  |
| Tooth Fracture                             |                 |  |  |
| subjects affected / exposed                | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                          | 0               |  |  |
| Vertebral Injury                           |                 |  |  |
| subjects affected / exposed                | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                          | 0               |  |  |
| Laceration                                 |                 |  |  |
| subjects affected / exposed                | 1 / 32 (3.13%)  |  |  |
| occurrences (all)                          | 3               |  |  |
| Ligament sprain                            |                 |  |  |
| subjects affected / exposed                | 4 / 32 (12.50%) |  |  |
| occurrences (all)                          | 4               |  |  |
| Congenital, familial and genetic disorders |                 |  |  |
| Congenital Diaphragmatic Hernia            |                 |  |  |
| subjects affected / exposed                | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                          | 0               |  |  |
| Cardiac disorders                          |                 |  |  |
| Arrhythmia                                 |                 |  |  |
| subjects affected / exposed                | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                          | 0               |  |  |
| Atrial Flutter                             |                 |  |  |
| subjects affected / exposed                | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                          | 0               |  |  |
| Mitral Valve Prolapse                      |                 |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Palpitations                |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Tachycardia                 |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Nervous system disorders    |                |  |  |
| Cervicobrachial Syndrome    |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Headache                    |                |  |  |
| subjects affected / exposed | 3 / 32 (9.38%) |  |  |
| occurrences (all)           | 4              |  |  |
| Memory Impairment           |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Migraine                    |                |  |  |
| subjects affected / exposed | 1 / 32 (3.13%) |  |  |
| occurrences (all)           | 1              |  |  |
| Paraesthesia                |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Sciatica                    |                |  |  |
| subjects affected / exposed | 1 / 32 (3.13%) |  |  |
| occurrences (all)           | 3              |  |  |
| Somnolence                  |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Tension Headache            |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Tremor                      |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |

|                                                                                             |                     |  |  |
|---------------------------------------------------------------------------------------------|---------------------|--|--|
| Trigeminal Neuralgia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 32 (0.00%)<br>0 |  |  |
| Upper Motor Neuron Lesion<br>subjects affected / exposed<br>occurrences (all)               | 0 / 32 (0.00%)<br>0 |  |  |
| Carpal tunnel syndrome<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 32 (0.00%)<br>0 |  |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                               | 2 / 32 (6.25%)<br>2 |  |  |
| Parkinson's disease<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 32 (0.00%)<br>0 |  |  |
| Ear and labyrinth disorders<br>Deafness<br>subjects affected / exposed<br>occurrences (all) | 1 / 32 (3.13%)<br>1 |  |  |
| Tinnitus<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 32 (0.00%)<br>0 |  |  |
| Tympanosclerosis<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 32 (0.00%)<br>0 |  |  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 32 (3.13%)<br>1 |  |  |
| Vertigo Positional<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 32 (0.00%)<br>0 |  |  |
| Eye disorders<br>Cataract<br>subjects affected / exposed<br>occurrences (all)               | 1 / 32 (3.13%)<br>1 |  |  |
| Conjunctivitis                                                                              |                     |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 32 (3.13%) |  |  |
| occurrences (all)           | 1              |  |  |
| Conjunctivitis Allergic     |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Eye Pruritus                |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Macular Degeneration        |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Retinal Tear                |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Gastrointestinal disorders  |                |  |  |
| Abdominal Pain Upper        |                |  |  |
| subjects affected / exposed | 3 / 32 (9.38%) |  |  |
| occurrences (all)           | 4              |  |  |
| Abdominal Pain              |                |  |  |
| subjects affected / exposed | 2 / 32 (6.25%) |  |  |
| occurrences (all)           | 3              |  |  |
| Anal Fissure                |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Aphthous Stomatitis         |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Colitis                     |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Constipation                |                |  |  |
| subjects affected / exposed | 1 / 32 (3.13%) |  |  |
| occurrences (all)           | 1              |  |  |
| Diarrhoea                   |                |  |  |
| subjects affected / exposed | 2 / 32 (6.25%) |  |  |
| occurrences (all)           | 2              |  |  |

|                                  |                |  |  |
|----------------------------------|----------------|--|--|
| Dry Mouth                        |                |  |  |
| subjects affected / exposed      | 1 / 32 (3.13%) |  |  |
| occurrences (all)                | 1              |  |  |
| Duodenal Ulcer                   |                |  |  |
| subjects affected / exposed      | 0 / 32 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Dyspepsia                        |                |  |  |
| subjects affected / exposed      | 3 / 32 (9.38%) |  |  |
| occurrences (all)                | 3              |  |  |
| Faecal Incontinence              |                |  |  |
| subjects affected / exposed      | 0 / 32 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Flatulence                       |                |  |  |
| subjects affected / exposed      | 0 / 32 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Gastric Disorder                 |                |  |  |
| subjects affected / exposed      | 0 / 32 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Gastric Polyps                   |                |  |  |
| subjects affected / exposed      | 0 / 32 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Gastric Ulcer                    |                |  |  |
| subjects affected / exposed      | 0 / 32 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Gastritis                        |                |  |  |
| subjects affected / exposed      | 0 / 32 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Gastrointestinal Disorder        |                |  |  |
| subjects affected / exposed      | 0 / 32 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Gastrooesophageal Reflux Disease |                |  |  |
| subjects affected / exposed      | 2 / 32 (6.25%) |  |  |
| occurrences (all)                | 2              |  |  |
| Gingival Swelling                |                |  |  |
| subjects affected / exposed      | 0 / 32 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |

|                                    |                |  |  |
|------------------------------------|----------------|--|--|
| Gingivitis                         |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Hiatus Hernia                      |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Inguinal Hernia                    |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Irritable Bowel Syndrome           |                |  |  |
| subjects affected / exposed        | 1 / 32 (3.13%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Mouth Ulceration                   |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Nausea                             |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Oesophagitis                       |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Rectal Haemorrhage                 |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Reflux Oesophagitis                |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Toothache                          |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Upper Gastrointestinal Haemorrhage |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Vomiting                           |                |  |  |
| subjects affected / exposed        | 0 / 32 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |

|                                        |                |  |  |
|----------------------------------------|----------------|--|--|
| Dental caries                          |                |  |  |
| subjects affected / exposed            | 2 / 32 (6.25%) |  |  |
| occurrences (all)                      | 2              |  |  |
| Skin and subcutaneous tissue disorders |                |  |  |
| Actinic Keratosis                      |                |  |  |
| subjects affected / exposed            | 3 / 32 (9.38%) |  |  |
| occurrences (all)                      | 4              |  |  |
| Dermatitis Atopic                      |                |  |  |
| subjects affected / exposed            | 1 / 32 (3.13%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Ecchymosis                             |                |  |  |
| subjects affected / exposed            | 1 / 32 (3.13%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Granuloma Annulare                     |                |  |  |
| subjects affected / exposed            | 0 / 32 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Hyperkeratosis                         |                |  |  |
| subjects affected / exposed            | 1 / 32 (3.13%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Hypertrichosis                         |                |  |  |
| subjects affected / exposed            | 0 / 32 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Lichen Planus                          |                |  |  |
| subjects affected / exposed            | 0 / 32 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Neurodermatitis                        |                |  |  |
| subjects affected / exposed            | 0 / 32 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Pruritus                               |                |  |  |
| subjects affected / exposed            | 0 / 32 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Psoriasis                              |                |  |  |
| subjects affected / exposed            | 0 / 32 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Rash                                   |                |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Rash Erythematous           |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Rash Papular                |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Sebaceous Hyperplasia       |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Skin Irritation             |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Skin Lesion                 |                |  |  |
| subjects affected / exposed | 1 / 32 (3.13%) |  |  |
| occurrences (all)           | 1              |  |  |
| Urticaria                   |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Alopecia                    |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Dermal cyst                 |                |  |  |
| subjects affected / exposed | 2 / 32 (6.25%) |  |  |
| occurrences (all)           | 2              |  |  |
| Dermatitis                  |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Dry skin                    |                |  |  |
| subjects affected / exposed | 0 / 32 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Renal and urinary disorders |                |  |  |
| Dysuria                     |                |  |  |
| subjects affected / exposed | 1 / 32 (3.13%) |  |  |
| occurrences (all)           | 1              |  |  |

|                                                                             |                     |  |  |
|-----------------------------------------------------------------------------|---------------------|--|--|
| Micturition Urgency<br>subjects affected / exposed<br>occurrences (all)     | 0 / 32 (0.00%)<br>0 |  |  |
| Endocrine disorders                                                         |                     |  |  |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)          | 0 / 32 (0.00%)<br>0 |  |  |
| Thyroiditis Chronic<br>subjects affected / exposed<br>occurrences (all)     | 0 / 32 (0.00%)<br>0 |  |  |
| Musculoskeletal and connective tissue disorders                             |                     |  |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 32 (0.00%)<br>0 |  |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)              | 3 / 32 (9.38%)<br>3 |  |  |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)               | 2 / 32 (6.25%)<br>2 |  |  |
| Bone Pain<br>subjects affected / exposed<br>occurrences (all)               | 0 / 32 (0.00%)<br>0 |  |  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)                | 2 / 32 (6.25%)<br>2 |  |  |
| Costochondritis<br>subjects affected / exposed<br>occurrences (all)         | 1 / 32 (3.13%)<br>1 |  |  |
| Dupuytren's Contracture<br>subjects affected / exposed<br>occurrences (all) | 0 / 32 (0.00%)<br>0 |  |  |
| Foot Deformity<br>subjects affected / exposed<br>occurrences (all)          | 1 / 32 (3.13%)<br>1 |  |  |
| Joint Stiffness                                                             |                     |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Monarthrititis              |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Muscle Contracture          |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Muscle Spasms               |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Muscular Weakness           |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Musculoskeletal Chest Pain  |                 |  |  |
| subjects affected / exposed | 3 / 32 (9.38%)  |  |  |
| occurrences (all)           | 3               |  |  |
| Musculoskeletal Discomfort  |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Musculoskeletal Pain        |                 |  |  |
| subjects affected / exposed | 4 / 32 (12.50%) |  |  |
| occurrences (all)           | 4               |  |  |
| Musculoskeletal Stiffness   |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Myalgia Intercostal         |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Neck Pain                   |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Osteoarthritis              |                 |  |  |
| subjects affected / exposed | 2 / 32 (6.25%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Osteochondrosis             |                 |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Osteosclerosis              |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Pain In Extremity           |                 |  |  |
| subjects affected / exposed | 7 / 32 (21.88%) |  |  |
| occurrences (all)           | 9               |  |  |
| Polyarthritis               |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Rotator Cuff Syndrome       |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Sacroiliitis                |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Synovial Cyst               |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Tendonitis                  |                 |  |  |
| subjects affected / exposed | 2 / 32 (6.25%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Torticollis                 |                 |  |  |
| subjects affected / exposed | 2 / 32 (6.25%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Fibromyalgia                |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 3               |  |  |
| Joint swelling              |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Spinal osteoarthritis       |                 |  |  |
| subjects affected / exposed | 2 / 32 (6.25%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Trigger finger              |                 |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Infections and infestations |                 |  |  |
| Bacterial Infection         |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Bronchitis                  |                 |  |  |
| subjects affected / exposed | 5 / 32 (15.63%) |  |  |
| occurrences (all)           | 5               |  |  |
| Cellulitis                  |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Chronic Sinusitis           |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Cystitis                    |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Ear Infection               |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Fungal Infection            |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Furuncle                    |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Gastroenteritis             |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Gastroenteritis Viral       |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Gastrointestinal Infection  |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| Herpes Zoster               |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Influenza                   |                 |  |  |
| subjects affected / exposed | 5 / 32 (15.63%) |  |  |
| occurrences (all)           | 7               |  |  |
| Nail Bed Infection Fungal   |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Nasal Abscess               |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Nasopharyngitis             |                 |  |  |
| subjects affected / exposed | 9 / 32 (28.13%) |  |  |
| occurrences (all)           | 20              |  |  |
| Onychomycosis               |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Oral Candidiasis            |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Oral Fungal Infection       |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Oral Herpes                 |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Otitis Media Acute          |                 |  |  |
| subjects affected / exposed | 0 / 32 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Pharyngitis                 |                 |  |  |
| subjects affected / exposed | 1 / 32 (3.13%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Pharyngitis Streptococcal   |                 |  |  |
| subjects affected / exposed | 3 / 32 (9.38%)  |  |  |
| occurrences (all)           | 4               |  |  |

|                                         |                 |  |  |
|-----------------------------------------|-----------------|--|--|
| Pneumonia                               |                 |  |  |
| subjects affected / exposed             | 3 / 32 (9.38%)  |  |  |
| occurrences (all)                       | 4               |  |  |
| Pyoderma                                |                 |  |  |
| subjects affected / exposed             | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                       | 0               |  |  |
| Respiratory Tract Infection             |                 |  |  |
| subjects affected / exposed             | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                       | 0               |  |  |
| Respiratory Tract Infection Viral       |                 |  |  |
| subjects affected / exposed             | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                       | 0               |  |  |
| Rhinitis                                |                 |  |  |
| subjects affected / exposed             | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                       | 0               |  |  |
| Sinusitis                               |                 |  |  |
| subjects affected / exposed             | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                       | 0               |  |  |
| Tooth Abscess                           |                 |  |  |
| subjects affected / exposed             | 1 / 32 (3.13%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Tooth Infection                         |                 |  |  |
| subjects affected / exposed             | 1 / 32 (3.13%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Upper Respiratory Tract Infection       |                 |  |  |
| subjects affected / exposed             | 2 / 32 (6.25%)  |  |  |
| occurrences (all)                       | 2               |  |  |
| Urinary Tract Infection                 |                 |  |  |
| subjects affected / exposed             | 7 / 32 (21.88%) |  |  |
| occurrences (all)                       | 15              |  |  |
| Viral Infection                         |                 |  |  |
| subjects affected / exposed             | 1 / 32 (3.13%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Viral Upper Respiratory Tract Infection |                 |  |  |

|                                             |                 |  |  |
|---------------------------------------------|-----------------|--|--|
| subjects affected / exposed                 | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| Borrelia infection                          |                 |  |  |
| subjects affected / exposed                 | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| Eye infection                               |                 |  |  |
| subjects affected / exposed                 | 2 / 32 (6.25%)  |  |  |
| occurrences (all)                           | 2               |  |  |
| Lower respiratory tract infection           |                 |  |  |
| subjects affected / exposed                 | 2 / 32 (6.25%)  |  |  |
| occurrences (all)                           | 3               |  |  |
| Wound infection                             |                 |  |  |
| subjects affected / exposed                 | 2 / 32 (6.25%)  |  |  |
| occurrences (all)                           | 3               |  |  |
| Metabolism and nutrition disorders          |                 |  |  |
| Anorexia                                    |                 |  |  |
| subjects affected / exposed                 | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| Dyslipidaemia                               |                 |  |  |
| subjects affected / exposed                 | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| Hypercholesterolaemia                       |                 |  |  |
| subjects affected / exposed                 | 4 / 32 (12.50%) |  |  |
| occurrences (all)                           | 4               |  |  |
| Hyperlipidaemia                             |                 |  |  |
| subjects affected / exposed                 | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| Food intolerance                            |                 |  |  |
| alternative assessment type: Non-systematic |                 |  |  |
| subjects affected / exposed                 | 0 / 32 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                    |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 26 June 2006     | AM1. The primary reason for this amendment was a revision to the protocol synopsis, in particular the data analysis section.                                                                                                                                                                                                                                                                 |
| 22 May 2007      | EXT1/004-10. The primary reason for this amendment was to add a 12-month extension to the previous protocol (Protocol 004-01).                                                                                                                                                                                                                                                               |
| 22 June 2007     | AM2. The primary reason for this amendment was to add an 18-month interim analysis (Protocol 004-02).                                                                                                                                                                                                                                                                                        |
| 03 April 2008    | EXT1,AM1/004-11. The primary reason for this amendment was to add preliminary information on the predicted magnetic resonance imaging (MRI) findings suggestive of metaphyseal fibrosis in the ongoing growing monkey toxicology study at 10-fold preclinical/clinical margins, along with information on the absence of such findings at 12-fold preclinical/clinical margins in aged dogs. |
| 03 June 2008     | EXT2/004-20. The primary reason for this amendment was to add a 24-month extension to the previous protocol (Protocol 004-11).                                                                                                                                                                                                                                                               |
| 11 December 2008 | EXT2,AM1/004-21. The primary reason for this amendment was to add supplementary bone mineral density (BMD) scans at Visits 21 and 25 (Months 42 and 54) for additional efficacy measurements.                                                                                                                                                                                                |
| 17 February 2010 | EXT2,AM2/004-22. The primary reason for this amendment was to issue a revised definition of overdose for odanacatib to the following: Ingesting two or more tablets of study drug within a 5-day period.                                                                                                                                                                                     |
| 25 May 2010      | EXT3/004-30. The primary reason for this amendment was to add a 5-year extension to the previous protocol (Protocol 004-22).                                                                                                                                                                                                                                                                 |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported