



## Clinical trial results:

### A Phase 2b, Multicentre, Randomised, Double-blind, Placebo-controlled, and Open-label Comparator Study of Cotadutide in Participants Who Have Chronic Kidney Disease with Type 2 Diabetes.

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-000255-12 |
| Trial protocol           | GB DE          |
| Global end of trial date | 08 March 2022  |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v2 (current)  |
| This version publication date  | 21 March 2025 |
| First version publication date | 20 March 2023 |
| Version creation reason        |               |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | D5676C00001 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04515849 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | AstraZeneca   |
| Sponsor organisation address | Granta Park, Cambridge, United Kingdom, CB21 6GH                                      |
| Public contact               | Global Clinical Lead, AstraZeneca, +1 18772409479, information.center@astrazeneca.com |
| Scientific contact           | Global Clinical Lead, AstraZeneca, +1 18772409479, information.center@astrazeneca.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 21 June 2022  |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 08 March 2022 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 08 March 2022 |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

This Phase 2b study is designed to evaluate the efficacy, safety, tolerability, and pharmacokinetic (PK) profile of cotadutide at different dose levels in participants who have CKD with T2DM.

Protection of trial subjects:

In the study, fasting was minimised and continuous glucose monitoring (CGM) was used instead of more invasive glucose measures to reduce participant discomfort.

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 31 August 2020 |
| Long term follow-up planned                               | No             |
| Independent data monitoring committee (IDMC) involvement? | Yes            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Japan: 26         |
| Country: Number of subjects enrolled | Spain: 61         |
| Country: Number of subjects enrolled | Germany: 34       |
| Country: Number of subjects enrolled | Poland: 16        |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | Canada: 59        |
| Country: Number of subjects enrolled | New Zealand: 31   |
| Country: Number of subjects enrolled | Australia: 18     |
| Worldwide total number of subjects   | 248               |
| EEA total number of subjects         | 111               |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |
| Children (2-11 years)                     | 0 |

|                           |     |
|---------------------------|-----|
| Adolescents (12-17 years) | 0   |
| Adults (18-64 years)      | 77  |
| From 65 to 84 years       | 171 |
| 85 years and over         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at 79 participating sites in Canada, Australia, New Zealand, Japan, Germany, Poland, Spain and United Kingdom. First subject enrolled 31st August 2020. Last subject last visit: 28th June 2021.

### Pre-assignment

Screening details:

This is a parallel treatment, double-blind study with 5 arms. The study had a 14-day run-in period during which participants will be given advice on diet and exercise and asked to wear a CGM sensor, followed by a 26-week treatment period and 28-day follow-up period.

### Period 1

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

### Arms

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes               |
| <b>Arm title</b>             | Cotadutide 100 ug |

Arm description:

Participants randomised to Cotadutide 100 ug daily

|  |  |
|--|--|
| Arm type                               | Experimental                             |
| Investigational medicinal product name | Cotadutide 100 ug                        |
| Investigational medicinal product code | MEDI0382                                 |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled pen |
| Routes of administration               | Subcutaneous use                         |

Dosage and administration details:

100 ug, subcutaneous

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Cotadutide 300 ug |
|------------------|-------------------|

Arm description:

Participants randomised to Cotadutide 300 ug daily

|  |  |
|--|--|
| Arm type                               | Experimental                             |
| Investigational medicinal product name | Cotadutide 300 ug                        |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled pen |
| Routes of administration               | Subcutaneous use                         |

Dosage and administration details:

300 ug, Subcutaneous

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Cotadutide 600 ug |
|------------------|-------------------|

Arm description:

Participants randomised to Cotadutide 600 ug daily

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

|  |  |
|--|--|
| Investigational medicinal product name                                 | Cotadutide 600 ug                        |
| Investigational medicinal product code                                 |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection in pre-filled pen |
| Routes of administration   | Subcutaneous use                         |
| Dosage and administration details:<br>600 ug, subcutaneous             |  |
| <b>Arm title</b>   | Placebo                                  |
| Arm description:<br>Participants randomised to placebo daily           |  |
| Arm type   | Placebo                                  |
| Investigational medicinal product name                                 | Placebo                                  |
| Investigational medicinal product code                                 |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection in pre-filled pen |
| Routes of administration   | Subcutaneous use                         |
| Dosage and administration details:<br>subcutaneous                     |  |
| <b>Arm title</b>   | Semaglutide 1 mg                         |
| Arm description:<br>Participants randomised to active comparator daily |  |
| Arm type   | No intervention                          |
| No investigational medicinal product assigned in this arm              |  |

| <b>Number of subjects in period 1</b> | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug |
|---------------------------------------|-------------------|-------------------|-------------------|
| Started                               | 52                | 49                | 51                |
| Completed                             | 49                | 45                | 50                |
| Not completed                         | 3                 | 4                 | 1                 |
| Adverse event, serious fatal          | 2                 | -                 | -                 |
| Consent withdrawn by subject          | 1                 | 2                 | 1                 |
| Other: randomised by error            | -                 | 1                 | -                 |
| Adverse event, non-fatal              | -                 | -                 | -                 |
| Other: family emergency               | -                 | -                 | -                 |
| Protocol deviation                    | -                 | 1                 | -                 |

| <b>Number of subjects in period 1</b> | Placebo | Semaglutide 1 mg |
|---------------------------------------|---------|------------------|
| Started                               | 51      | 45               |
| Completed                             | 48      | 43               |
| Not completed                         | 3       | 2                |
| Adverse event, serious fatal          | -       | 1                |
| Consent withdrawn by subject          | -       | -                |
| Other: randomised by error            | -       | -                |
| Adverse event, non-fatal              | 1       | -                |

|                        |   |   |
|------------------------|---|---|
| Other:family emergency | 1 | - |
| Protocol deviation     | - | 1 |

## Baseline characteristics

### Reporting groups

|  |                   |
|--|-------------------|
| Reporting group title                              | Cotadutide 100 ug |
| Reporting group description:                       |                   |
| Participants randomised to Cotadutide 100 ug daily |                   |
| Reporting group title                              | Cotadutide 300 ug |
| Reporting group description:                       |                   |
| Participants randomised to Cotadutide 300 ug daily |                   |
| Reporting group title                              | Cotadutide 600 ug |
| Reporting group description:                       |                   |
| Participants randomised to Cotadutide 600 ug daily |                   |
| Reporting group title                              | Placebo           |
| Reporting group description:                       |                   |
| Participants randomised to placebo daily           |                   |
| Reporting group title                              | Semaglutide 1 mg  |
| Reporting group description:                       |                   |
| Participants randomised to active comparator daily |                   |

| Reporting group values                             | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug |
|--|-------------------|-------------------|-------------------|
| Number of subjects                                 | 52                | 49                | 51                |
| Age categorical                                    |                   |                   |                   |
| Units: Subjects                                    |                   |                   |                   |
| In utero   | 0                 | 0                 | 0                 |
| Preterm newborn infants (gestational age < 37 wks) | 0                 | 0                 | 0                 |
| Newborns (0-27 days)                               | 0                 | 0                 | 0                 |
| Infants and toddlers (28 days-23 months)           | 0                 | 0                 | 0                 |
| Children (2-11 years)                              | 0                 | 0                 | 0                 |
| Adolescents (12-17 years)                          | 0                 | 0                 | 0                 |
| Adults (18-64 years)                               | 17                | 13                | 23                |
| From 65-84 years                                   | 35                | 36                | 28                |
| 85 years and over                                  | 0                 | 0                 | 0                 |
| Age Continuous                                     |                   |                   |                   |
| Units: Years                                       |                   |                   |                   |
| arithmetic mean                                    | 67.2              | 65.7              | 66.1              |
| standard deviation                                 | ± 7.3             | ± 8.8             | ± 7.4             |
| Sex: Female, Male                                  |                   |                   |                   |
| Units: Participants                                |                   |                   |                   |
| Female   | 9                 | 3                 | 10                |
| Male   | 43                | 46                | 41                |
| Race (NIH/OMB)                                     |                   |                   |                   |
| Units: Subjects                                    |                   |                   |                   |
| AMERICAN INDIAN OR ALASKA NATIVE                   | 0                 | 0                 | 0                 |
| ASIAN  | 10                | 10                | 13                |
| BLACK OR AFRICAN AMERICAN                          | 2                 | 0                 | 0                 |
| NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER          | 2                 | 0                 | 1                 |

|       |    |    |    |
|-------|----|----|----|
| OTHER | 0  | 3  | 1  |
| WHITE | 38 | 36 | 36 |

| Reporting group values                                | Placebo | Semaglutide 1 mg | Total |
|---|---------|------------------|-------|
| Number of subjects                                    | 51      | 45               | 248   |
| Age categorical<br>Units: Subjects                    |         |                  |       |
| In utero  | 0       | 0                | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0       | 0                | 0     |
| Newborns (0-27 days)                                  | 0       | 0                | 0     |
| Infants and toddlers (28 days-23 months)              | 0       | 0                | 0     |
| Children (2-11 years)                                 | 0       | 0                | 0     |
| Adolescents (12-17 years)                             | 0       | 0                | 0     |
| Adults (18-64 years)                                  | 10      | 14               | 77    |
| From 65-84 years                                      | 41      | 31               | 171   |
| 85 years and over                                     | 0       | 0                | 0     |
| Age Continuous<br>Units: Years                        |         |                  |       |
| arithmetic mean                                       | 69.5    | 67.0             |       |
| standard deviation                                    | ± 7.3   | ± 7.8            | -     |
| Sex: Female, Male<br>Units: Participants              |         |                  |       |
| Female  | 13      | 12               | 47    |
| Male  | 38      | 33               | 201   |
| Race (NIH/OMB)<br>Units: Subjects                     |         |                  |       |
| AMERICAN INDIAN OR ALASKA NATIVE                      | 0       | 0                | 0     |
| ASIAN   | 10      | 2                | 45    |
| BLACK OR AFRICAN AMERICAN                             | 1       | 2                | 5     |
| NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER             | 1       | 0                | 4     |
| OTHER   | 0       | 0                | 4     |
| WHITE   | 39      | 41               | 190   |

### Subject analysis sets

|                                   |                    |
|-----------------------------------|--------------------|
| Subject analysis set title        | ITT                |
| Subject analysis set type         | Intention-to-treat |
| Subject analysis set description: |                    |
| Intent to treat                   |                    |

| Reporting group values                                | ITT |  |  |
|---|-----|--|--|
| Number of subjects                                    | 248 |  |  |
| Age categorical<br>Units: Subjects                    |     |  |  |
| In utero  | 0   |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 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)                      | 171   |  |  |
| From 65-84 years                          | 77    |  |  |
| 85 years and over                         | 0     |  |  |
| Age Continuous                            |       |  |  |
| Units: Years                              |       |  |  |
| arithmetic mean                           | 67.1  |  |  |
| standard deviation                        | ± 7.8 |  |  |
| Sex: Female, Male                         |       |  |  |
| Units: Participants                       |       |  |  |
| Female                                    |       |  |  |
| Male                                      |       |  |  |
| Race (NIH/OMB)                            |       |  |  |
| Units: Subjects                           |       |  |  |
| AMERICAN INDIAN OR ALASKA NATIVE          |       |  |  |
| ASIAN                                     |       |  |  |
| BLACK OR AFRICAN AMERICAN                 |       |  |  |
| NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER |       |  |  |
| OTHER                                     |       |  |  |
| WHITE                                     |       |  |  |

## End points

### End points reporting groups

|  |                    |
|--|--------------------|
| Reporting group title                              | Cotadutide 100 ug  |
| Reporting group description:                       |                    |
| Participants randomised to Cotadutide 100 ug daily |                    |
| Reporting group title                              | Cotadutide 300 ug  |
| Reporting group description:                       |                    |
| Participants randomised to Cotadutide 300 ug daily |                    |
| Reporting group title                              | Cotadutide 600 ug  |
| Reporting group description:                       |                    |
| Participants randomised to Cotadutide 600 ug daily |                    |
| Reporting group title                              | Placebo            |
| Reporting group description:                       |                    |
| Participants randomised to placebo daily           |                    |
| Reporting group title                              | Semaglutide 1 mg   |
| Reporting group description:                       |                    |
| Participants randomised to active comparator daily |                    |
| Subject analysis set title                         | ITT                |
| Subject analysis set type                          | Intention-to-treat |
| Subject analysis set description:                  |                    |
| Intent to treat                                    |                    |

### Primary: Percentage change in UACR of cotadutide at different dose levels compared to placebo after 14 weeks

|  |   |
|--|---|
| End point title  | Percentage change in UACR of cotadutide at different dose levels compared to placebo after 14 weeks <sup>[1][2]</sup> |
| End point description:   |   |
| Percentage change in UACR of cotadutide at different dose levels compared to placebo after 14 weeks. Efficacy endpoints for cotadutide vs. semaglutide are exploratory and are therefore excluded. |   |
| End point type   | Primary   |
| End point timeframe:   |   |
| Baseline to the end of 14 weeks of dosing  |   |

#### Notes:

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

Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                             | Cotadutide 100 ug        | Cotadutide 300 ug         | Cotadutide 600 ug         | Placebo                |
|--|--------------------------|---------------------------|---------------------------|------------------------|
| Subject group type                           | Reporting group          | Reporting group           | Reporting group           | Reporting group        |
| Number of subjects analysed                  | 49                       | 43                        | 37                        | 43                     |
| Units: UACR ratio                            |                          |                           |                           |                        |
| least squares mean (confidence interval 95%) | -10.96 (-29.60 to 12.61) | -40.47 (-53.00 to -24.60) | -44.60 (-56.21 to -29.91) | 4.60 (-18.02 to 33.46) |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage change in UACR of cotadutide at different dose levels compared to placebo after 26 weeks

|                 |  |
|-----------------|--|
| End point title | Percentage change in UACR of cotadutide at different dose levels compared to placebo after 26 weeks <sup>[3]</sup> |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                             | Cotadutide 100 ug        | Cotadutide 300 ug        | Cotadutide 600 ug         | Placebo                 |
|--|--------------------------|--------------------------|---------------------------|-------------------------|
| Subject group type                           | Reporting group          | Reporting group          | Reporting group           | Reporting group         |
| Number of subjects analysed                  | 49                       | 46                       | 48                        | 49                      |
| Units: UACR ratio                            |                          |                          |                           |                         |
| least squares mean (confidence interval 95%) | -17.85 (-45.47 to 23.78) | -38.68 (-59.61 to -6.88) | -57.87 (-73.33 to -33.34) | 11.79 (-27.85 to 73.22) |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent change in body weight of cotadutide at different dose levels versus placebo from baseline to end of 14 weeks of dosing

|                 |   |
|-----------------|---|
| End point title | Percent change in body weight of cotadutide at different dose levels versus placebo from baseline to end of 14 weeks of dosing <sup>[4]</sup> |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline to end of 14 weeks of dosing

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                    | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo         |
|-------------------------------------|-------------------|-------------------|-------------------|-----------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group |
| Number of subjects analysed         | 37                | 32                | 27                | 35              |
| Units: Absolute value               |                   |                   |                   |                 |
| least squares mean (standard error) | -2.84 (± 0.65)    | -4.15 (± 0.68)    | -5.40 (± 0.73)    | -1.61 (± 0.66)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage change in body weight of cotadutide at different dose levels versus placebo from baseline to end of 26 weeks of dosing

|                 |  |
|-----------------|--|
| End point title | Percentage change in body weight of cotadutide at different dose levels versus placebo from baseline to end of 26 weeks of dosing <sup>[5]</sup> |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                    | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo         |
|-------------------------------------|-------------------|-------------------|-------------------|-----------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group |
| Number of subjects analysed         | 37                | 33                | 27                | 35              |
| Units: Absolute value               |                   |                   |                   |                 |
| least squares mean (standard error) | -2.60 (± 0.89)    | -5.45 (± 0.92)    | -7.35 (± 0.99)    | -2.23 (± 0.90)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent change in HbA1c of cotadutide at different dose levels versus placebo from baseline to the end of 14 of dosing

|                 |   |
|-----------------|---|
| End point title | Percent change in HbA1c of cotadutide at different dose levels versus placebo from baseline to the end of 14 of dosing <sup>[6]</sup> |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline to end of 14 weeks of dosing

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                    | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo         |
|-------------------------------------|-------------------|-------------------|-------------------|-----------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group |
| Number of subjects analysed         | 49                | 45                | 48                | 39              |
| Units: Percent change               |                   |                   |                   |                 |
| least squares mean (standard error) | -0.76 (± 0.12)    | -0.82 (± 0.12)    | -0.65 (± 0.12)    | -0.08 (± 0.12)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent change in HbA1c of cotadutide at different dose levels versus placebo from baseline to the end of 26 of dosing

|                 |   |
|-----------------|---|
| End point title | Percent change in HbA1c of cotadutide at different dose levels versus placebo from baseline to the end of 26 of dosing <sup>[7]</sup> |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                    | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo         |
|-------------------------------------|-------------------|-------------------|-------------------|-----------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group |
| Number of subjects analysed         | 49                | 46                | 48                | 39              |
| Units: Percent change               |                   |                   |                   |                 |
| least squares mean (standard error) | -0.92 (± 0.11)    | -0.92 (± 0.11)    | -0.89 (± 0.11)    | -0.25 (± 0.11)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in fasting glucose of cotadutide at different dose levels from baseline versus placebo after 26 weeks of dosing

|                 |   |
|-----------------|---|
| End point title | Change in fasting glucose of cotadutide at different dose levels from baseline versus placebo after 26 weeks of dosing <sup>[8]</sup> |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                    | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo         |
|-------------------------------------|-------------------|-------------------|-------------------|-----------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group |
| Number of subjects analysed         | 45                | 43                | 39                | 45              |
| Units: mmol/L                       |                   |                   |                   |                 |
| least squares mean (standard error) | -1.78 (± 0.36)    | -1.76 (± 0.37)    | -1.57 (± 0.39)    | -0.72 (± 0.37)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in fasting glucose of cotadutide at different dose levels from baseline versus placebo after 14 weeks of dosing

|                 |   |
|-----------------|---|
| End point title | Change in fasting glucose of cotadutide at different dose levels from baseline versus placebo after 14 weeks of dosing <sup>[9]</sup> |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline to end of 14 weeks of dosing

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                    | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo         |
|-------------------------------------|-------------------|-------------------|-------------------|-----------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group |
| Number of subjects analysed         | 42                | 45                | 48                | 49              |
| Units: mmol/L                       |                   |                   |                   |                 |
| least squares mean (standard error) | -1.35 (± 0.37)    | -1.57 (± 0.35)    | -1.69 (± 0.40)    | -0.54 (± 0.37)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in 10-day average glucose levels of cotadutide at different dose levels versus placebo from baseline to end of 26 weeks of dosing

|                 |  |
|-----------------|--|
| End point title | Change in 10-day average glucose levels of cotadutide at different dose levels versus placebo from baseline to end of 26 weeks of dosing <sup>[10]</sup> |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                    | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo          |
|-------------------------------------|-------------------|-------------------|-------------------|------------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group  |
| Number of subjects analysed         | 25                | 18                | 22                | 30               |
| Units: Percent change               |                   |                   |                   |                  |
| least squares mean (standard error) | -1.735 (± 0.307)  | -1.446 (± 0.334)  | -1.118 (± 0.321)  | -0.273 (± 0.290) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in percentage time spent in hyperglycaemia over 10 days of cotadutide at different dose levels compared to placebo after 14 weeks of dosing

|                 |  |
|-----------------|--|
| End point title | Change in percentage time spent in hyperglycaemia over 10 days of cotadutide at different dose levels compared to placebo after 14 weeks of dosing <sup>[11]</sup> |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline to 14 weeks of dosing

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                    | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo         |
|-------------------------------------|-------------------|-------------------|-------------------|-----------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group |
| Number of subjects analysed         | 30                | 25                | 26                | 30              |
| Units: Percent Change               |                   |                   |                   |                 |
| least squares mean (standard error) | -13.87 (± 3.35)   | -15.79 (± 3.55)   | -13.90 (± 3.52)   | -4.09 (± 3.27)  |

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Change in 10-day average glucose levels of cotadutide at different dose levels versus placebo from baseline to end of 14 weeks of dosing**

---

|                 |  |
|-----------------|--|
| End point title | Change in 10-day average glucose levels of cotadutide at different dose levels versus placebo from baseline to end of 14 weeks of dosing <sup>[12]</sup> |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline to end of 14 weeks of dosing

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

| End point values                    | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo          |
|-------------------------------------|-------------------|-------------------|-------------------|------------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group  |
| Number of subjects analysed         | 30                | 25                | 26                | 30               |
| Units: Percent change               |                   |                   |                   |                  |
| least squares mean (standard error) | -1.556 (± 0.320)  | -1.478 (± 0.337)  | -1.269 (± 0.334)  | -0.440 (± 0.311) |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Change in percentage time spent in hyperglycaemia over 10 days of cotadutide at different dose levels compared to placebo after 26 weeks of dosing**

---

|                 |  |
|-----------------|--|
| End point title | Change in percentage time spent in hyperglycaemia over 10 days of cotadutide at different dose levels compared to placebo after 26 weeks of dosing <sup>[13]</sup> |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline to 26 weeks of dosing

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: In this study, the efficacy endpoints vs. semaglutide are exploratory and were therefore excluded



| <b>End point values</b>             | Cotadutide 100 ug | Cotadutide 300 ug | Cotadutide 600 ug | Placebo         |
|-------------------------------------|-------------------|-------------------|-------------------|-----------------|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group   | Reporting group |
| Number of subjects analysed         | 25                | 18                | 22                | 27              |
| Units: Percent change               |                   |                   |                   |                 |
| least squares mean (standard error) | -18.06 (± 3.33)   | -15.38 (± 3.76)   | -11.91 (± 3.51)   | -3.00 (± 3.17)  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until last study visit

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Cotadutide 300 ug |
|-----------------------|-------------------|

Reporting group description: -

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

Reporting group description: -

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Semaglutide 1 mg |
|-----------------------|------------------|

Reporting group description: -

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Cotadutide 600 ug |
|-----------------------|-------------------|

Reporting group description: -

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Cotadutide 100 ug |
|-----------------------|-------------------|

Reporting group description: -

| <b>Serious adverse events</b>                                       | Cotadutide 300 ug | Placebo        | Semaglutide 1 mg |
|---|-------------------|----------------|------------------|
| Total subjects affected by serious adverse events                   |                   |                |                  |
| subjects affected / exposed   | 5 / 48 (10.42%)   | 5 / 51 (9.80%) | 4 / 45 (8.89%)   |
| number of deaths (all causes)                                       | 0                 | 0              | 0                |
| number of deaths resulting from adverse events                      | 0                 | 0              | 0                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                |                  |
| Adenocarcinoma  |                   |                |                  |
| subjects affected / exposed   | 0 / 48 (0.00%)    | 0 / 51 (0.00%) | 0 / 45 (0.00%)   |
| 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 / 48 (0.00%)    | 0 / 51 (0.00%) | 0 / 45 (0.00%)   |
| 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                     | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (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 |                |                |                |
| Hypoxia   |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary mass                                  |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary oedema                                |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |                |                |                |
| Suspected suicide                               |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Adjustment disorder with anxiety                |                |                |                |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (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  |                |                |                |
| Humerus fracture                                |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| 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                               |                |                |                |
| Coronary artery disease                         |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Angina pectoris                                 |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Acute myocardial infarction                     |                |                |                |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (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          |
| Nervous system disorders                        |                |                |                |
| Ischaemic stroke                                |                |                |                |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Vomiting  |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Obstructive pancreatitis                        |                |                |                |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (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          |
| Constipation                                    |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Renal and urinary disorders                     |                |                |                |
| Acute kidney injury                             |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (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                                   |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (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 |                |                |                |
| Groin pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (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 / 48 (0.00%) | 1 / 51 (1.96%) | 1 / 45 (2.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vestibular neuronitis                           |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| COVID-19  |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (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              |                |                |                |
| Ketosis   |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypoglycaemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| 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>                                       | Cotadutide 600 ug | Cotadutide 100 ug |  |
|---|-------------------|-------------------|--|
| Total subjects affected by serious adverse events                   |                   |                   |  |
| subjects affected / exposed   | 5 / 48 (10.42%)   | 5 / 55 (9.09%)    |  |
| number of deaths (all causes)                                       | 0                 | 2                 |  |
| number of deaths resulting from adverse events                      | 0                 | 2                 |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                   |  |
| Adenocarcinoma  |                   |                   |  |
| subjects affected / exposed   | 1 / 48 (2.08%)    | 0 / 55 (0.00%)    |  |
| occurrences causally related to treatment / all                     | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             |  |
| Vascular disorders  |                   |                   |  |
| Hypertension  |                   |                   |  |
| subjects affected / exposed   | 0 / 48 (0.00%)    | 1 / 55 (1.82%)    |  |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             |  |
| General disorders and administration site conditions                |                   |                   |  |
| Chest pain  |                   |                   |  |
| subjects affected / exposed   | 0 / 48 (0.00%)    | 0 / 55 (0.00%)    |  |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             |  |
| Respiratory, thoracic and mediastinal disorders                     |                   |                   |  |
| Hypoxia   |                   |                   |  |
| subjects affected / exposed   | 0 / 48 (0.00%)    | 0 / 55 (0.00%)    |  |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             |  |
| Pulmonary embolism  |                   |                   |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pulmonary mass                                  |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pulmonary oedema                                |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                           |                |                |  |
| Suspected suicide                               |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Adjustment disorder with anxiety                |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                |                |  |
| Humerus fracture                                |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac disorders                               |                |                |  |
| Coronary artery disease                         |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Angina pectoris                                 |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

|  |                                  |                                  |  |
|--|----------------------------------|----------------------------------|--|
| Acute myocardial infarction<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                        | 0 / 48 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 55 (1.82%)<br>0 / 1<br>0 / 1 |  |
| Nervous system disorders<br>Ischaemic stroke<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all       | 0 / 48 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 55 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Gastrointestinal disorders<br>Vomiting<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all             | 0 / 48 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 55 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Obstructive pancreatitis<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                           | 0 / 48 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 55 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Constipation<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                       | 0 / 48 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 55 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Renal and urinary disorders<br>Acute kidney injury<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 48 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 55 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Renal failure<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                      | 0 / 48 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 55 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Musculoskeletal and connective tissue<br>disorders<br>Groin pain   |                                  |                                  |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| <b>Infections and infestations</b>              |                |                |  |
| Diverticulitis                                  |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia                                       |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vestibular neuronitis                           |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| COVID-19  |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| <b>Metabolism and nutrition disorders</b>       |                |                |  |
| Ketosis   |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hypoglycaemia                                   |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                                   | Cotadutide 300 ug | Placebo          | Semaglutide 1 mg |
|---|-------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events               |                   |                  |                  |
| subjects affected / exposed   | 38 / 48 (79.17%)  | 38 / 51 (74.51%) | 39 / 45 (86.67%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                  |                  |
| Seborrhoeic keratosis   |                   |                  |                  |
| subjects affected / exposed   | 0 / 48 (0.00%)    | 0 / 51 (0.00%)   | 0 / 45 (0.00%)   |
| occurrences (all)   | 0                 | 0                | 0                |
| Haemangioma of liver  |                   |                  |                  |
| subjects affected / exposed   | 1 / 48 (2.08%)    | 0 / 51 (0.00%)   | 0 / 45 (0.00%)   |
| occurrences (all)   | 1                 | 0                | 0                |
| Adrenal neoplasm  |                   |                  |                  |
| subjects affected / exposed   | 1 / 48 (2.08%)    | 0 / 51 (0.00%)   | 0 / 45 (0.00%)   |
| occurrences (all)   | 1                 | 0                | 0                |
| B-cell lymphoma stage III   |                   |                  |                  |
| subjects affected / exposed   | 0 / 48 (0.00%)    | 0 / 51 (0.00%)   | 1 / 45 (2.22%)   |
| occurrences (all)   | 0                 | 0                | 1                |
| Vascular disorders  |                   |                  |                  |
| Aortic stenosis   |                   |                  |                  |
| subjects affected / exposed   | 0 / 48 (0.00%)    | 0 / 51 (0.00%)   | 1 / 45 (2.22%)   |
| occurrences (all)   | 0                 | 0                | 1                |
| Haematoma   |                   |                  |                  |
| subjects affected / exposed   | 1 / 48 (2.08%)    | 0 / 51 (0.00%)   | 0 / 45 (0.00%)   |
| occurrences (all)   | 1                 | 0                | 0                |
| Hot flush   |                   |                  |                  |
| subjects affected / exposed   | 1 / 48 (2.08%)    | 0 / 51 (0.00%)   | 0 / 45 (0.00%)   |
| occurrences (all)   | 1                 | 0                | 0                |
| Hypertension  |                   |                  |                  |
| subjects affected / exposed   | 0 / 48 (0.00%)    | 1 / 51 (1.96%)   | 0 / 45 (0.00%)   |
| occurrences (all)   | 0                 | 1                | 0                |
| Hypotension   |                   |                  |                  |
| subjects affected / exposed   | 1 / 48 (2.08%)    | 0 / 51 (0.00%)   | 5 / 45 (11.11%)  |
| occurrences (all)   | 1                 | 0                | 5                |
| Surgical and medical procedures                                     |                   |                  |                  |
| Skin neoplasm excision  |                   |                  |                  |
| subjects affected / exposed   | 0 / 48 (0.00%)    | 1 / 51 (1.96%)   | 0 / 45 (0.00%)   |
| occurrences (all)   | 0                 | 1                | 0                |
| Meniscus removal  |                   |                  |                  |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                          | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                    | 1              | 0              | 0              |
| Tooth extraction                                     |                |                |                |
| subjects affected / exposed                          | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| General disorders and administration site conditions |                |                |                |
| Injection site erythema                              |                |                |                |
| subjects affected / exposed                          | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                    | 1              | 0              | 0              |
| Injection site induration                            |                |                |                |
| subjects affected / exposed                          | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                    | 1              | 0              | 0              |
| Injection site pain                                  |                |                |                |
| subjects affected / exposed                          | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                    | 1              | 0              | 0              |
| Injection site pruritus                              |                |                |                |
| subjects affected / exposed                          | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                    | 1              | 0              | 0              |
| Asthenia   |                |                |                |
| subjects affected / exposed                          | 2 / 48 (4.17%) | 0 / 51 (0.00%) | 2 / 45 (4.44%) |
| occurrences (all)                                    | 2              | 0              | 2              |
| Chest pain   |                |                |                |
| subjects affected / exposed                          | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                                    | 0              | 1              | 0              |
| Early satiety  |                |                |                |
| subjects affected / exposed                          | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Fatigue  |                |                |                |
| subjects affected / exposed                          | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 1 / 45 (2.22%) |
| occurrences (all)                                    | 0              | 1              | 1              |
| Injection site bruising                              |                |                |                |
| subjects affected / exposed                          | 1 / 48 (2.08%) | 2 / 51 (3.92%) | 0 / 45 (0.00%) |
| occurrences (all)                                    | 1              | 2              | 0              |
| Injection site reaction                              |                |                |                |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Malaise<br>subjects affected / exposed<br>occurrences (all)   | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Vaccination site pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 48 (2.08%)<br>2 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Oedema<br>subjects affected / exposed<br>occurrences (all)  | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)   | 1 / 48 (2.08%)<br>1 | 1 / 51 (1.96%)<br>1 | 1 / 45 (2.22%)<br>1 |
| Pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)   | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Puncture site haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 3 / 51 (5.88%)<br>3 | 1 / 45 (2.22%)<br>1 |
| Reproductive system and breast disorders<br>Breast tenderness<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 1 / 48 (2.08%)<br>1 | 2 / 51 (3.92%)<br>2 | 0 / 45 (0.00%)<br>0 |
| Allergic cough  |                     |                     |                     |

|                                       |                |                |                |
|---------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed           | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Atelectasis                           |                |                |                |
| subjects affected / exposed           | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0              |
| Bronchiectasis                        |                |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Chronic obstructive pulmonary disease |                |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Cough                                 |                |                |                |
| subjects affected / exposed           | 1 / 48 (2.08%) | 3 / 51 (5.88%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 1              | 3              | 0              |
| Dyspnoea exertional                   |                |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Epistaxis                             |                |                |                |
| subjects affected / exposed           | 2 / 48 (4.17%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 3              | 0              | 0              |
| Nasal congestion                      |                |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Oropharyngeal pain                    |                |                |                |
| subjects affected / exposed           | 1 / 48 (2.08%) | 2 / 51 (3.92%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 1              | 2              | 0              |
| Pulmonary congestion                  |                |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Rales                                 |                |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Rhinorrhoea                           |                |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Sinus congestion<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Sneezing<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 48 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Pulmonary mass<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 48 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Psychiatric disorders<br>Depressed mood<br>subjects affected / exposed<br>occurrences (all)    | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Cardiovascular somatic symptom<br>disorder<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Irritability<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Depression<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 1 / 45 (2.22%)<br>1 |
| Investigations<br>Amylase increased<br>subjects affected / exposed<br>occurrences (all)        | 1 / 48 (2.08%)<br>1 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Blood calcium increased<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Blood bicarbonate increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Blood bicarbonate decreased  |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Blood creatinine increased  |                |                |                |
| subjects affected / exposed | 2 / 48 (4.17%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 2              | 0              | 0              |
| Blood glucose increased     |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Blood pressure increased    |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Blood pressure decreased    |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Blood potassium increased   |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 1              | 0              | 1              |
| Blood sodium increased      |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Cardiac murmur              |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Ejection fraction decreased |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Electrocardiogram change    |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pulse absent                |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 0              | 1              |
| Lipase increased            |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Occult blood positive       |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Pedal pulse decreased                          |                |                |                |
| subjects affected / exposed                    | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Pulmonary arterial pressure increased          |                |                |                |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Glomerular filtration rate decreased           |                |                |                |
| subjects affected / exposed                    | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 2 / 45 (4.44%) |
| occurrences (all)                              | 1              | 0              | 2              |
| Urine output increased                         |                |                |                |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Ventricular internal diameter                  |                |                |                |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Weight decreased                               |                |                |                |
| subjects affected / exposed                    | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                              | 1              | 0              | 1              |
| Electrocardiogram QT prolonged                 |                |                |                |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Animal bite                                    |                |                |                |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Rib fracture                                   |                |                |                |
| subjects affected / exposed                    | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Procedural pain                                |                |                |                |
| subjects affected / exposed                    | 2 / 48 (4.17%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                              | 2              | 0              | 0              |
| Muscle strain                                  |                |                |                |



|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Limb injury                 |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Ligament sprain             |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Ligament rupture            |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Heat stroke                 |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 0              | 1              |
| Heat illness                |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 6              | 0              | 0              |
| Fall                        |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Epicondylitis               |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Costal cartilage fracture   |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Contusion                   |                |                |                |
| subjects affected / exposed | 2 / 48 (4.17%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 3              | 1              | 0              |
| Arthropod bite              |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 0              | 1              |
| Wrist fracture              |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 0              | 1              |
| Vaccination complication    |                |                |                |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Tibia fracture                      |                |                |                |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Skin wound                          |                |                |                |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Skin pressure mark                  |                |                |                |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Skin laceration                     |                |                |                |
| subjects affected / exposed         | 1 / 48 (2.08%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                   | 1              | 1              | 0              |
| Skin abrasion                       |                |                |                |
| subjects affected / exposed         | 1 / 48 (2.08%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                   | 1              | 1              | 0              |
| Thoracic vertebral fracture         |                |                |                |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Cardiac disorders                   |                |                |                |
| Angina pectoris                     |                |                |                |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Angina unstable                     |                |                |                |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Mitral valve incompetence           |                |                |                |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Atrial flutter                      |                |                |                |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Atrioventricular block first degree |                |                |                |
| subjects affected / exposed         | 2 / 48 (4.17%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                   | 4              | 0              | 0              |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Atrioventricular block second degree<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Cardiac septal hypertrophy<br>subjects affected / exposed<br>occurrences (all)           | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Conduction disorder<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 48 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 48 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Pericardial effusion<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Ventricular tachycardia<br>subjects affected / exposed<br>occurrences (all)              | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Nervous system disorders   |                     |                     |                     |
| Lethargy<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Akinesia<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 1 / 45 (2.22%)<br>1 |
| Cognitive disorder   |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 0              | 1              |
| Dizziness                   |                |                |                |
| subjects affected / exposed | 4 / 48 (8.33%) | 1 / 51 (1.96%) | 1 / 45 (2.22%) |
| occurrences (all)           | 4              | 1              | 1              |
| Dizziness postural          |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Headache                    |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 51 (1.96%) | 2 / 45 (4.44%) |
| occurrences (all)           | 1              | 2              | 2              |
| Ischaemic stroke            |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Migraine                    |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Myelopathy                  |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Neuralgia                   |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Neuropathy peripheral       |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Polyneuropathy              |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Presyncope                  |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Sciatica                    |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Syncope                     |                |                |                |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed          | 1 / 48 (2.08%) | 1 / 51 (1.96%) | 1 / 45 (2.22%) |
| occurrences (all)                    | 1              | 1              | 1              |
| Restless legs syndrome               |                |                |                |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0              |
| Blood and lymphatic system disorders |                |                |                |
| Anaemia                              |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood loss anaemia                   |                |                |                |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0              |
| Ear and labyrinth disorders          |                |                |                |
| Vertigo                              |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Eye disorders                        |                |                |                |
| Eye haemorrhage                      |                |                |                |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0              |
| Cataract                             |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Conjunctival haemorrhage             |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0              |
| Diabetic retinopathy                 |                |                |                |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0              |
| Eye pain                             |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Glaucoma                             |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0              |
| Macular oedema                       |                |                |                |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 48 (2.08%)  | 0 / 51 (0.00%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Retinal haemorrhage         |                 |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%)  | 0 / 51 (0.00%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Vitreous detachment         |                 |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%)  | 0 / 51 (0.00%) | 1 / 45 (2.22%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Vitreous floaters           |                 |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%)  | 0 / 51 (0.00%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Gastrointestinal disorders  |                 |                |                 |
| Abdominal distension        |                 |                |                 |
| subjects affected / exposed | 1 / 48 (2.08%)  | 0 / 51 (0.00%) | 1 / 45 (2.22%)  |
| occurrences (all)           | 1               | 0              | 1               |
| Abdominal discomfort        |                 |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%)  | 0 / 51 (0.00%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Abdominal pain              |                 |                |                 |
| subjects affected / exposed | 1 / 48 (2.08%)  | 1 / 51 (1.96%) | 1 / 45 (2.22%)  |
| occurrences (all)           | 1               | 1              | 1               |
| Abdominal pain upper        |                 |                |                 |
| subjects affected / exposed | 2 / 48 (4.17%)  | 0 / 51 (0.00%) | 1 / 45 (2.22%)  |
| occurrences (all)           | 2               | 0              | 1               |
| Chronic gastritis           |                 |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%)  | 0 / 51 (0.00%) | 1 / 45 (2.22%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Constipation                |                 |                |                 |
| subjects affected / exposed | 2 / 48 (4.17%)  | 2 / 51 (3.92%) | 3 / 45 (6.67%)  |
| occurrences (all)           | 3               | 3              | 4               |
| Diarrhoea                   |                 |                |                 |
| subjects affected / exposed | 7 / 48 (14.58%) | 4 / 51 (7.84%) | 7 / 45 (15.56%) |
| occurrences (all)           | 10              | 8              | 9               |
| Dyspepsia                   |                 |                |                 |
| subjects affected / exposed | 4 / 48 (8.33%)  | 0 / 51 (0.00%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 5               | 0              | 0               |

|                                  |                 |                |                  |
|----------------------------------|-----------------|----------------|------------------|
| Nausea                           |                 |                |                  |
| subjects affected / exposed      | 7 / 48 (14.58%) | 5 / 51 (9.80%) | 12 / 45 (26.67%) |
| occurrences (all)                | 9               | 5              | 23               |
| Faeces hard                      |                 |                |                  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 0 / 51 (0.00%) | 1 / 45 (2.22%)   |
| occurrences (all)                | 0               | 0              | 1                |
| Flatulence                       |                 |                |                  |
| subjects affected / exposed      | 2 / 48 (4.17%)  | 1 / 51 (1.96%) | 0 / 45 (0.00%)   |
| occurrences (all)                | 2               | 1              | 0                |
| Gastrointestinal disorder        |                 |                |                  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 0 / 51 (0.00%) | 0 / 45 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0                |
| Gastrooesophageal reflux disease |                 |                |                  |
| subjects affected / exposed      | 2 / 48 (4.17%)  | 0 / 51 (0.00%) | 3 / 45 (6.67%)   |
| occurrences (all)                | 2               | 0              | 4                |
| Haemorrhoids                     |                 |                |                  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 0 / 51 (0.00%) | 0 / 45 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0                |
| Large intestine polyp            |                 |                |                  |
| subjects affected / exposed      | 1 / 48 (2.08%)  | 0 / 51 (0.00%) | 0 / 45 (0.00%)   |
| occurrences (all)                | 1               | 0              | 0                |
| Eructation                       |                 |                |                  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 1 / 51 (1.96%) | 1 / 45 (2.22%)   |
| occurrences (all)                | 0               | 1              | 1                |
| Oral lichen planus               |                 |                |                  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 1 / 51 (1.96%) | 0 / 45 (0.00%)   |
| occurrences (all)                | 0               | 1              | 0                |
| Toothache                        |                 |                |                  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 0 / 51 (0.00%) | 0 / 45 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0                |
| Vomiting                         |                 |                |                  |
| subjects affected / exposed      | 3 / 48 (6.25%)  | 2 / 51 (3.92%) | 7 / 45 (15.56%)  |
| occurrences (all)                | 4               | 2              | 9                |
| Hepatobiliary disorders          |                 |                |                  |
| Hepatomegaly                     |                 |                |                  |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Hepatic cirrhosis                      |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Dermatitis                             |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Actinic keratosis                      |                |                |                |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Blister                                |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dermal cyst                            |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Dermatitis contact                     |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Diabetic foot                          |                |                |                |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Dry skin                               |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Eczema                                 |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Hyperhidrosis                          |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Lichenification                        |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |



|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Macule                      |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Night sweats                |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pruritus                    |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash                        |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Scab                        |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 0              | 1              |
| Skin exfoliation            |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Skin lesion                 |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin ulcer                  |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 3              | 0              | 0              |
| Renal and urinary disorders |                |                |                |
| Nocturia                    |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pollakiuria                 |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Polyuria                    |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Urinary hesitation          |                |                |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Urinary incontinence<br>subjects affected / exposed<br>occurrences (all)   | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Renal mass<br>subjects affected / exposed<br>occurrences (all)   | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Endocrine disorders<br>Thyroid mass<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 1 / 45 (2.22%)<br>1 |
| Musculoskeletal and connective tissue disorders<br>Pain in jaw<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 0 / 45 (0.00%)<br>0 |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0 | 3 / 51 (5.88%)<br>3 | 1 / 45 (2.22%)<br>1 |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 48 (2.08%)<br>1 | 1 / 51 (1.96%)<br>1 | 2 / 45 (4.44%)<br>4 |
| Musculoskeletal discomfort<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Musculoskeletal chest pain<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 48 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 1 / 45 (2.22%)<br>1 |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)  | 1 / 48 (2.08%)<br>1 | 0 / 51 (0.00%)<br>0 | 1 / 45 (2.22%)<br>1 |
| Joint contracture<br>subjects affected / exposed<br>occurrences (all)  | 2 / 48 (4.17%)<br>2 | 0 / 51 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |
| Flank pain   |                     |                     |                     |

|                                   |                |                |                |
|-----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed       | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 2              | 0              | 0              |
| Back pain                         |                |                |                |
| subjects affected / exposed       | 2 / 48 (4.17%) | 4 / 51 (7.84%) | 2 / 45 (4.44%) |
| occurrences (all)                 | 2              | 4              | 2              |
| Arthritis                         |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Arthralgia                        |                |                |                |
| subjects affected / exposed       | 1 / 48 (2.08%) | 3 / 51 (5.88%) | 1 / 45 (2.22%) |
| occurrences (all)                 | 1              | 3              | 2              |
| Joint swelling                    |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Tenosynovitis                     |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Spinal pain                       |                |                |                |
| subjects affected / exposed       | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0              |
| Infections and infestations       |                |                |                |
| Bronchitis                        |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Onychomycosis                     |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Nasopharyngitis                   |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 3 / 51 (5.88%) | 3 / 45 (6.67%) |
| occurrences (all)                 | 0              | 3              | 3              |
| Lower respiratory tract infection |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Localised infection               |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Giardiasis                              |                |                |                |
| subjects affected / exposed             | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Gastroenteritis                         |                |                |                |
| subjects affected / exposed             | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                       | 1              | 0              | 1              |
| Fungal skin infection                   |                |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                       | 0              | 0              | 1              |
| Eye infection                           |                |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Cystitis                                |                |                |                |
| subjects affected / exposed             | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Conjunctivitis                          |                |                |                |
| subjects affected / exposed             | 1 / 48 (2.08%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                       | 2              | 1              | 0              |
| Cellulitis                              |                |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Paronychia                              |                |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                       | 0              | 0              | 1              |
| Viral upper respiratory tract infection |                |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                       | 0              | 0              | 1              |
| Vestibular neuronitis                   |                |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Urinary tract infection                 |                |                |                |
| subjects affected / exposed             | 3 / 48 (6.25%) | 1 / 51 (1.96%) | 2 / 45 (4.44%) |
| occurrences (all)                       | 3              | 2              | 2              |
| Upper respiratory tract infection       |                |                |                |
| subjects affected / exposed             | 1 / 48 (2.08%) | 1 / 51 (1.96%) | 0 / 45 (0.00%) |
| occurrences (all)                       | 1              | 1              | 0              |

|   |                         |                         |                      |
|---|-------------------------|-------------------------|----------------------|
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 48 (0.00%)<br>0     | 1 / 51 (1.96%)<br>1     | 0 / 45 (0.00%)<br>0  |
| Vulvovaginal candidiasis<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 48 (0.00%)<br>0     | 0 / 51 (0.00%)<br>0     | 0 / 45 (0.00%)<br>0  |
| Tinea infection<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 48 (0.00%)<br>0     | 0 / 51 (0.00%)<br>0     | 0 / 45 (0.00%)<br>0  |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0     | 0 / 51 (0.00%)<br>0     | 1 / 45 (2.22%)<br>1  |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 48 (2.08%)<br>1     | 0 / 51 (0.00%)<br>0     | 0 / 45 (0.00%)<br>0  |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0     | 1 / 51 (1.96%)<br>1     | 0 / 45 (0.00%)<br>0  |
| Periodontitis<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 48 (2.08%)<br>1     | 0 / 51 (0.00%)<br>0     | 0 / 45 (0.00%)<br>0  |
| Tonsillitis<br>subjects affected / exposed<br>occurrences (all)   | 1 / 48 (2.08%)<br>1     | 0 / 51 (0.00%)<br>0     | 0 / 45 (0.00%)<br>0  |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)  | 1 / 48 (2.08%)<br>1     | 2 / 51 (3.92%)<br>2     | 2 / 45 (4.44%)<br>2  |
| Asymptomatic COVID-19<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 48 (0.00%)<br>0     | 0 / 51 (0.00%)<br>0     | 0 / 45 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all) | 16 / 48 (33.33%)<br>106 | 13 / 51 (25.49%)<br>148 | 4 / 45 (8.89%)<br>28 |
| Hypervolaemia   |                         |                         |                      |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 0              | 2              | 0               |
| Hyperuricaemia              |                |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Hypernatraemia              |                |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Hyperkalaemia               |                |                |                 |
| subjects affected / exposed | 1 / 48 (2.08%) | 2 / 51 (3.92%) | 3 / 45 (6.67%)  |
| occurrences (all)           | 1              | 2              | 3               |
| Hyperglycaemia              |                |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Hypercalcaemia              |                |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 51 (1.96%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Gout                        |                |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Electrolyte imbalance       |                |                |                 |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 51 (0.00%) | 0 / 45 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Decreased appetite          |                |                |                 |
| subjects affected / exposed | 3 / 48 (6.25%) | 1 / 51 (1.96%) | 8 / 45 (17.78%) |
| occurrences (all)           | 3              | 1              | 8               |
| Hypophagia                  |                |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Iron deficiency             |                |                |                 |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 51 (0.00%) | 1 / 45 (2.22%)  |
| occurrences (all)           | 0              | 0              | 1               |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| <b>Non-serious adverse events</b>                     | Cotadutide 600 ug | Cotadutide 100 ug |  |
| Total subjects affected by non-serious adverse events |                   |                   |  |
| subjects affected / exposed                           | 38 / 48 (79.17%)  | 43 / 55 (78.18%)  |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |  |
| Seborrhoeic keratosis   |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)   | 0              | 1              |  |
| Haemangioma of liver  |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)   | 0              | 0              |  |
| Adrenal neoplasm  |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)   | 0              | 0              |  |
| B-cell lymphoma stage III   |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)   | 0              | 0              |  |
| Vascular disorders  |                |                |  |
| Aortic stenosis   |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)   | 0              | 0              |  |
| Haematoma   |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)   | 0              | 0              |  |
| Hot flush   |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)   | 0              | 0              |  |
| Hypertension  |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)   | 0              | 1              |  |
| Hypotension   |                |                |  |
| subjects affected / exposed   | 3 / 48 (6.25%) | 0 / 55 (0.00%) |  |
| occurrences (all)   | 4              | 0              |  |
| Surgical and medical procedures                                     |                |                |  |
| Skin neoplasm excision  |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)   | 0              | 0              |  |
| Meniscus removal  |                |                |  |
| subjects affected / exposed   | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)   | 0              | 0              |  |

|   |                     |                     |  |
|---|---------------------|---------------------|--|
| Tooth extraction<br>subjects affected / exposed<br>occurrences (all)          | 0 / 48 (0.00%)<br>0 | 1 / 55 (1.82%)<br>1 |  |
| General disorders and administration site conditions                          |                     |                     |  |
| Injection site erythema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 1 / 55 (1.82%)<br>1 |  |
| Injection site induration<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Injection site pain<br>subjects affected / exposed<br>occurrences (all)       | 1 / 48 (2.08%)<br>1 | 1 / 55 (1.82%)<br>1 |  |
| Injection site pruritus<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 1 / 55 (1.82%)<br>1 |  |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)                | 0 / 48 (0.00%)<br>0 | 1 / 55 (1.82%)<br>1 |  |
| Early satiety<br>subjects affected / exposed<br>occurrences (all)             | 2 / 48 (4.17%)<br>2 | 0 / 55 (0.00%)<br>0 |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 48 (2.08%)<br>1 | 3 / 55 (5.45%)<br>3 |  |
| Injection site bruising<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Injection site reaction<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 2 / 55 (3.64%)<br>2 |  |
| Malaise   |                     |                     |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Vaccination site pain                           |                |                |  |
| subjects affected / exposed                     | 2 / 48 (4.17%) | 0 / 55 (0.00%) |  |
| occurrences (all)                               | 2              | 0              |  |
| Oedema  |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Oedema peripheral                               |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 2 / 55 (3.64%) |  |
| occurrences (all)                               | 0              | 2              |  |
| Pain  |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Peripheral swelling                             |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Puncture site haemorrhage                       |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Pyrexia   |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Reproductive system and breast disorders        |                |                |  |
| Breast tenderness                               |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Dyspnoea  |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Allergic cough                                  |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Atelectasis                                     |                |                |  |

|                                       |                |                |
|---------------------------------------|----------------|----------------|
| subjects affected / exposed           | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Bronchiectasis                        |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Chronic obstructive pulmonary disease |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)                     | 0              | 2              |
| Cough                                 |                |                |
| subjects affected / exposed           | 2 / 48 (4.17%) | 0 / 55 (0.00%) |
| occurrences (all)                     | 2              | 0              |
| Dyspnoea exertional                   |                |                |
| subjects affected / exposed           | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)                     | 1              | 0              |
| Epistaxis                             |                |                |
| subjects affected / exposed           | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)                     | 1              | 0              |
| Nasal congestion                      |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Oropharyngeal pain                    |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)                     | 0              | 1              |
| Pulmonary congestion                  |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Rales                                 |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Rhinorrhoea                           |                |                |
| subjects affected / exposed           | 1 / 48 (2.08%) | 1 / 55 (1.82%) |
| occurrences (all)                     | 1              | 1              |
| Sinus congestion                      |                |                |
| subjects affected / exposed           | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)                     | 0              | 1              |

|   |                     |                     |  |
|---|---------------------|---------------------|--|
| Sneezing<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Pulmonary mass<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Psychiatric disorders   |                     |                     |  |
| Depressed mood<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Cardiovascular somatic symptom disorder<br>subjects affected / exposed<br>occurrences (all) | 1 / 48 (2.08%)<br>1 | 0 / 55 (0.00%)<br>0 |  |
| Irritability<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 48 (2.08%)<br>1 | 0 / 55 (0.00%)<br>0 |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 48 (0.00%)<br>0 | 2 / 55 (3.64%)<br>2 |  |
| Depression<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Investigations  |                     |                     |  |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Blood calcium increased<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 48 (2.08%)<br>1 | 0 / 55 (0.00%)<br>0 |  |
| Blood bicarbonate increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 48 (0.00%)<br>0 | 1 / 55 (1.82%)<br>1 |  |
| Blood bicarbonate decreased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 48 (2.08%)<br>3 | 0 / 55 (0.00%)<br>0 |  |
| Blood creatinine increased  |                     |                     |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Blood glucose increased     |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Blood pressure increased    |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Blood pressure decreased    |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Blood potassium increased   |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)           | 0              | 1              |
| Blood sodium increased      |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Cardiac murmur              |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ejection fraction decreased |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Electrocardiogram change    |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Pulse absent                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Lipase increased            |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Occult blood positive       |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Pedal pulse decreased       |                |                |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                              | 0              | 0              |  |
| Pulmonary arterial pressure increased          |                |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                              | 0              | 0              |  |
| Glomerular filtration rate decreased           |                |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                              | 0              | 0              |  |
| Urine output increased                         |                |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                              | 0              | 1              |  |
| Ventricular internal diameter                  |                |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                              | 0              | 0              |  |
| Weight decreased                               |                |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                              | 0              | 0              |  |
| Electrocardiogram QT prolonged                 |                |                |  |
| subjects affected / exposed                    | 1 / 48 (2.08%) | 1 / 55 (1.82%) |  |
| occurrences (all)                              | 3              | 1              |  |
| Injury, poisoning and procedural complications |                |                |  |
| Animal bite                                    |                |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                              | 0              | 0              |  |
| Rib fracture                                   |                |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                              | 0              | 0              |  |
| Procedural pain                                |                |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                              | 0              | 0              |  |
| Muscle strain                                  |                |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                              | 0              | 0              |  |
| Limb injury                                    |                |                |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)           | 0              | 1              |
| Ligament sprain             |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ligament rupture            |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)           | 0              | 1              |
| Heat stroke                 |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Heat illness                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Fall                        |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Epicondylitis               |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Costal cartilage fracture   |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)           | 0              | 1              |
| Contusion                   |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Arthropod bite              |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Wrist fracture              |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Vaccination complication    |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Tibia fracture              |                |                |

|                                      |                |                |  |
|--------------------------------------|----------------|----------------|--|
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Skin wound                           |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Skin pressure mark                   |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Skin laceration                      |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Skin abrasion                        |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Thoracic vertebral fracture          |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Cardiac disorders                    |                |                |  |
| Angina pectoris                      |                |                |  |
| subjects affected / exposed          | 2 / 48 (4.17%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 2              | 0              |  |
| Angina unstable                      |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Mitral valve incompetence            |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Atrial flutter                       |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Atrioventricular block first degree  |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Atrioventricular block second degree |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                    | 0              | 1              |  |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| Cardiac septal hypertrophy<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Conduction disorder<br>subjects affected / exposed<br>occurrences (all)        | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)        | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)               | 1 / 48 (2.08%)<br>1 | 1 / 55 (1.82%)<br>1 |  |
| Pericardial effusion<br>subjects affected / exposed<br>occurrences (all)       | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all)          | 1 / 48 (2.08%)<br>1 | 0 / 55 (0.00%)<br>0 |  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 48 (2.08%)<br>1 | 0 / 55 (0.00%)<br>0 |  |
| Ventricular tachycardia<br>subjects affected / exposed<br>occurrences (all)    | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Nervous system disorders   |                     |                     |  |
| Lethargy<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Akinesia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Cognitive disorder<br>subjects affected / exposed<br>occurrences (all)         | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Dizziness  |                     |                     |  |



|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 2 / 48 (4.17%) | 1 / 55 (1.82%) |
| occurrences (all)           | 2              | 1              |
| Dizziness postural          |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)           | 0              | 1              |
| Headache                    |                |                |
| subjects affected / exposed | 3 / 48 (6.25%) | 1 / 55 (1.82%) |
| occurrences (all)           | 5              | 1              |
| Ischaemic stroke            |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)           | 0              | 1              |
| Migraine                    |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Myelopathy                  |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Neuralgia                   |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Neuropathy peripheral       |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Polyneuropathy              |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Presyncope                  |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Sciatica                    |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)           | 0              | 1              |
| Syncope                     |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Restless legs syndrome      |                |                |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Blood and lymphatic system disorders             |                     |                     |  |
| Anaemia  |                     |                     |  |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 2 / 55 (3.64%)      |  |
| occurrences (all)                                | 0                   | 2                   |  |
| Blood loss anaemia                               |                     |                     |  |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 55 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| Ear and labyrinth disorders                      |                     |                     |  |
| Vertigo  |                     |                     |  |
| subjects affected / exposed                      | 1 / 48 (2.08%)      | 0 / 55 (0.00%)      |  |
| occurrences (all)                                | 1                   | 0                   |  |
| Eye disorders                                    |                     |                     |  |
| Eye haemorrhage                                  |                     |                     |  |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 55 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| Cataract   |                     |                     |  |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 55 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| Conjunctival haemorrhage                         |                     |                     |  |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 55 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| Diabetic retinopathy                             |                     |                     |  |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 1 / 55 (1.82%)      |  |
| occurrences (all)                                | 0                   | 1                   |  |
| Eye pain   |                     |                     |  |
| subjects affected / exposed                      | 1 / 48 (2.08%)      | 0 / 55 (0.00%)      |  |
| occurrences (all)                                | 1                   | 0                   |  |
| Glaucoma   |                     |                     |  |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 55 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| Macular oedema                                   |                     |                     |  |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 55 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| Retinal haemorrhage                              |                     |                     |  |

|                             |                  |                 |  |
|-----------------------------|------------------|-----------------|--|
| subjects affected / exposed | 1 / 48 (2.08%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)           | 1                | 0               |  |
| Vitreous detachment         |                  |                 |  |
| subjects affected / exposed | 0 / 48 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)           | 0                | 0               |  |
| Vitreous floaters           |                  |                 |  |
| subjects affected / exposed | 0 / 48 (0.00%)   | 1 / 55 (1.82%)  |  |
| occurrences (all)           | 0                | 1               |  |
| Gastrointestinal disorders  |                  |                 |  |
| Abdominal distension        |                  |                 |  |
| subjects affected / exposed | 1 / 48 (2.08%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)           | 1                | 0               |  |
| Abdominal discomfort        |                  |                 |  |
| subjects affected / exposed | 0 / 48 (0.00%)   | 1 / 55 (1.82%)  |  |
| occurrences (all)           | 0                | 1               |  |
| Abdominal pain              |                  |                 |  |
| subjects affected / exposed | 2 / 48 (4.17%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)           | 2                | 0               |  |
| Abdominal pain upper        |                  |                 |  |
| subjects affected / exposed | 2 / 48 (4.17%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)           | 2                | 0               |  |
| Chronic gastritis           |                  |                 |  |
| subjects affected / exposed | 0 / 48 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)           | 0                | 0               |  |
| Constipation                |                  |                 |  |
| subjects affected / exposed | 5 / 48 (10.42%)  | 7 / 55 (12.73%) |  |
| occurrences (all)           | 7                | 7               |  |
| Diarrhoea                   |                  |                 |  |
| subjects affected / exposed | 6 / 48 (12.50%)  | 5 / 55 (9.09%)  |  |
| occurrences (all)           | 9                | 5               |  |
| Dyspepsia                   |                  |                 |  |
| subjects affected / exposed | 0 / 48 (0.00%)   | 1 / 55 (1.82%)  |  |
| occurrences (all)           | 0                | 1               |  |
| Nausea                      |                  |                 |  |
| subjects affected / exposed | 14 / 48 (29.17%) | 6 / 55 (10.91%) |  |
| occurrences (all)           | 18               | 7               |  |

|                                  |                 |                |  |
|----------------------------------|-----------------|----------------|--|
| Faeces hard                      |                 |                |  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 0 / 55 (0.00%) |  |
| occurrences (all)                | 0               | 0              |  |
| Flatulence                       |                 |                |  |
| subjects affected / exposed      | 2 / 48 (4.17%)  | 1 / 55 (1.82%) |  |
| occurrences (all)                | 2               | 1              |  |
| Gastrointestinal disorder        |                 |                |  |
| subjects affected / exposed      | 1 / 48 (2.08%)  | 0 / 55 (0.00%) |  |
| occurrences (all)                | 1               | 0              |  |
| Gastrooesophageal reflux disease |                 |                |  |
| subjects affected / exposed      | 3 / 48 (6.25%)  | 1 / 55 (1.82%) |  |
| occurrences (all)                | 3               | 1              |  |
| Haemorrhoids                     |                 |                |  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 1 / 55 (1.82%) |  |
| occurrences (all)                | 0               | 1              |  |
| Large intestine polyp            |                 |                |  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 1 / 55 (1.82%) |  |
| occurrences (all)                | 0               | 1              |  |
| Eructation                       |                 |                |  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 0 / 55 (0.00%) |  |
| occurrences (all)                | 0               | 0              |  |
| Oral lichen planus               |                 |                |  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 0 / 55 (0.00%) |  |
| occurrences (all)                | 0               | 0              |  |
| Toothache                        |                 |                |  |
| subjects affected / exposed      | 2 / 48 (4.17%)  | 2 / 55 (3.64%) |  |
| occurrences (all)                | 2               | 2              |  |
| Vomiting                         |                 |                |  |
| subjects affected / exposed      | 7 / 48 (14.58%) | 2 / 55 (3.64%) |  |
| occurrences (all)                | 12              | 2              |  |
| Hepatobiliary disorders          |                 |                |  |
| Hepatomegaly                     |                 |                |  |
| subjects affected / exposed      | 0 / 48 (0.00%)  | 1 / 55 (1.82%) |  |
| occurrences (all)                | 0               | 1              |  |
| Hepatic cirrhosis                |                 |                |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Skin and subcutaneous tissue disorders |                |                |  |
| Dermatitis                             |                |                |  |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 3              | 0              |  |
| Actinic keratosis                      |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Blister                                |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Dermal cyst                            |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Dermatitis contact                     |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Diabetic foot                          |                |                |  |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 1              | 0              |  |
| Dry skin                               |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Eczema                                 |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Hyperhidrosis                          |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Lichenification                        |                |                |  |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 1              | 0              |  |
| Macule                                 |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| Night sweats                |                |                |  |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Pruritus                    |                |                |  |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Rash                        |                |                |  |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 1              | 1              |  |
| Scab                        |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Skin exfoliation            |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Skin lesion                 |                |                |  |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Skin ulcer                  |                |                |  |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Renal and urinary disorders |                |                |  |
| Nocturia                    |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 0              | 1              |  |
| Pollakiuria                 |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 0              | 1              |  |
| Polyuria                    |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 0              | 1              |  |
| Urinary hesitation          |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 0              | 1              |  |
| Urinary incontinence        |                |                |  |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Renal mass<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Endocrine disorders<br>Thyroid mass<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Musculoskeletal and connective tissue disorders<br>Pain in jaw<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0 | 1 / 55 (1.82%)<br>1 |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Musculoskeletal discomfort<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 48 (2.08%)<br>1 | 0 / 55 (0.00%)<br>0 |  |
| Musculoskeletal chest pain<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0 | 1 / 55 (1.82%)<br>1 |  |
| Joint contracture<br>subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Flank pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Back pain  |                     |                     |  |

|                                   |                |                |  |
|-----------------------------------|----------------|----------------|--|
| subjects affected / exposed       | 3 / 48 (6.25%) | 2 / 55 (3.64%) |  |
| occurrences (all)                 | 3              | 2              |  |
| Arthritis                         |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                 | 0              | 1              |  |
| Arthralgia                        |                |                |  |
| subjects affected / exposed       | 2 / 48 (4.17%) | 0 / 55 (0.00%) |  |
| occurrences (all)                 | 2              | 0              |  |
| Joint swelling                    |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                 | 0              | 0              |  |
| Tenosynovitis                     |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                 | 0              | 0              |  |
| Spinal pain                       |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                 | 0              | 0              |  |
| Infections and infestations       |                |                |  |
| Bronchitis                        |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                 | 0              | 0              |  |
| Onychomycosis                     |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                 | 0              | 0              |  |
| Nasopharyngitis                   |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 2 / 55 (3.64%) |  |
| occurrences (all)                 | 0              | 2              |  |
| Lower respiratory tract infection |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                 | 0              | 0              |  |
| Localised infection               |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                 | 0              | 1              |  |
| Giardiasis                        |                |                |  |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                 | 0              | 0              |  |



|   |                |                |
|---|----------------|----------------|
| Gastroenteritis                         |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                       | 0              | 0              |
| Fungal skin infection                   |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                       | 0              | 0              |
| Eye infection                           |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)                       | 0              | 1              |
| Cystitis                                |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                       | 0              | 0              |
| Conjunctivitis                          |                |                |
| subjects affected / exposed             | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)                       | 1              | 0              |
| Cellulitis                              |                |                |
| subjects affected / exposed             | 1 / 48 (2.08%) | 1 / 55 (1.82%) |
| occurrences (all)                       | 1              | 1              |
| Paronychia                              |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                       | 0              | 0              |
| Viral upper respiratory tract infection |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)                       | 0              | 1              |
| Vestibular neuronitis                   |                |                |
| subjects affected / exposed             | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)                       | 1              | 0              |
| Urinary tract infection                 |                |                |
| subjects affected / exposed             | 2 / 48 (4.17%) | 0 / 55 (0.00%) |
| occurrences (all)                       | 2              | 0              |
| Upper respiratory tract infection       |                |                |
| subjects affected / exposed             | 0 / 48 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)                       | 0              | 0              |
| Tooth abscess                           |                |                |
| subjects affected / exposed             | 1 / 48 (2.08%) | 0 / 55 (0.00%) |
| occurrences (all)                       | 1              | 0              |

|                                    |                  |                  |  |
|------------------------------------|------------------|------------------|--|
| Vulvovaginal candidiasis           |                  |                  |  |
| subjects affected / exposed        | 0 / 48 (0.00%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)                  | 0                | 1                |  |
| Tinea infection                    |                  |                  |  |
| subjects affected / exposed        | 0 / 48 (0.00%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)                  | 0                | 1                |  |
| Sinusitis                          |                  |                  |  |
| subjects affected / exposed        | 0 / 48 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                  | 0                | 0                |  |
| Rhinitis                           |                  |                  |  |
| subjects affected / exposed        | 0 / 48 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                  | 0                | 0                |  |
| Pneumonia                          |                  |                  |  |
| subjects affected / exposed        | 0 / 48 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                  | 0                | 0                |  |
| Periodontitis                      |                  |                  |  |
| subjects affected / exposed        | 0 / 48 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                  | 0                | 0                |  |
| Tonsillitis                        |                  |                  |  |
| subjects affected / exposed        | 0 / 48 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                  | 0                | 0                |  |
| COVID-19                           |                  |                  |  |
| subjects affected / exposed        | 1 / 48 (2.08%)   | 2 / 55 (3.64%)   |  |
| occurrences (all)                  | 1                | 2                |  |
| Asymptomatic COVID-19              |                  |                  |  |
| subjects affected / exposed        | 0 / 48 (0.00%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)                  | 0                | 1                |  |
| Metabolism and nutrition disorders |                  |                  |  |
| Hypoglycaemia                      |                  |                  |  |
| subjects affected / exposed        | 13 / 48 (27.08%) | 13 / 55 (23.64%) |  |
| occurrences (all)                  | 83               | 88               |  |
| Hypervolaemia                      |                  |                  |  |
| subjects affected / exposed        | 0 / 48 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                  | 0                | 0                |  |
| Hyperuricaemia                     |                  |                  |  |

|                             |                 |                |  |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 48 (0.00%)  | 1 / 55 (1.82%) |  |
| occurrences (all)           | 0               | 1              |  |
| Hypernatraemia              |                 |                |  |
| subjects affected / exposed | 1 / 48 (2.08%)  | 1 / 55 (1.82%) |  |
| occurrences (all)           | 1               | 1              |  |
| Hyperkalaemia               |                 |                |  |
| subjects affected / exposed | 1 / 48 (2.08%)  | 1 / 55 (1.82%) |  |
| occurrences (all)           | 1               | 1              |  |
| Hyperglycaemia              |                 |                |  |
| subjects affected / exposed | 1 / 48 (2.08%)  | 2 / 55 (3.64%) |  |
| occurrences (all)           | 1               | 2              |  |
| Hypercalcaemia              |                 |                |  |
| subjects affected / exposed | 0 / 48 (0.00%)  | 0 / 55 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Gout                        |                 |                |  |
| subjects affected / exposed | 1 / 48 (2.08%)  | 2 / 55 (3.64%) |  |
| occurrences (all)           | 1               | 2              |  |
| Electrolyte imbalance       |                 |                |  |
| subjects affected / exposed | 0 / 48 (0.00%)  | 0 / 55 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Decreased appetite          |                 |                |  |
| subjects affected / exposed | 5 / 48 (10.42%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 5               | 0              |  |
| Hypophagia                  |                 |                |  |
| subjects affected / exposed | 0 / 48 (0.00%)  | 0 / 55 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Iron deficiency             |                 |                |  |
| subjects affected / exposed | 1 / 48 (2.08%)  | 0 / 55 (0.00%) |  |
| occurrences (all)           | 1               | 0              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 29 June 2020    | This global amendment contains revisions to the original global protocol dated (01Apr2020) to remove Cohort 2, which is no longer needed due to completion of Study D5671C00003 earlier than originally planned. Other minor revisions such as clarifications and correction of typos were made. This amendment is considered to be non-substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union because it neither significantly impacts the safety or physical/mental integrity of participants nor the scientific value of the study.                                       |
| 04 January 2021 | This global amendment contains revisions to Amendment 1 of the global protocol dated (29Jun2020) to add time windows for specific visits to make the study more accessible to participants during the current coronavirus disease (COVID-19) pandemic. Other minor revisions such as clarifications and correction of typos were made. This amendment is considered to be non-substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union because it neither significantly impacts the safety or physical/mental integrity of participants nor the scientific value of the study. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/39218393>