



Clinical trial results:

A Randomized, Double-Blind, Parallel Arm Study of the Efficacy and Safety of Investigational Dulaglutide Doses When Added to Metformin in Patients with Type 2 Diabetes Mellitus Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2017-003490-33 |
| Trial protocol | SK GR AT HU PL ES IT RO |
| Global end of trial date | 10 October 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 13 June 2020 |
| First version publication date | 13 June 2020 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | H9X-MC-GBGL |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03495102 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 16877 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559, |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 10 October 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 October 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and safety of investigational doses of once weekly dulaglutide when added to metformin in participants with type 2 diabetes with inadequate blood sugar control.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 05 April 2018 |
| 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 | Argentina: 290 |
| Country: Number of subjects enrolled | Romania: 233 |
| Country: Number of subjects enrolled | Hungary: 73 |
| Country: Number of subjects enrolled | United States: 508 |
| Country: Number of subjects enrolled | Russian Federation: 29 |
| Country: Number of subjects enrolled | Spain: 58 |
| Country: Number of subjects enrolled | Greece: 100 |
| Country: Number of subjects enrolled | Canada: 35 |
| Country: Number of subjects enrolled | Austria: 13 |
| Country: Number of subjects enrolled | Taiwan: 15 |
| Country: Number of subjects enrolled | Poland: 167 |
| Country: Number of subjects enrolled | Mexico: 111 |
| Country: Number of subjects enrolled | Italy: 25 |
| Country: Number of subjects enrolled | Slovakia: 131 |
| Country: Number of subjects enrolled | Israel: 54 |
| Worldwide total number of subjects | 1842 |
| EEA total number of subjects | 800 |

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) | 1404 |
| From 65 to 84 years | 437 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

No Text Available

Period 1

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

Arms

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

| | |
|------------------|--------------------|
| Arm title | Dulaglutide 1.5 mg |
|------------------|--------------------|

Arm description:

Dulaglutide 1.5 mg administered subcutaneously (SC) once a week.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Dulaglutide |
| Investigational medicinal product code | |
| Other name | LY2189265 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered SC

| | |
|------------------|------------------|
| Arm title | Dulaglutide 3 mg |
|------------------|------------------|

Arm description:

Dulaglutide 3 mg administered SC once a week.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dulaglutide |
| Investigational medicinal product code | |
| Other name | LY2189265 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered SC

| | |
|------------------|--------------------|
| Arm title | Dulaglutide 4.5 mg |
|------------------|--------------------|

Arm description:

Dulaglutide 4.5 mg administered SC once a week.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dulaglutide |
| Investigational medicinal product code | |
| Other name | LY2189265 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

| Number of subjects in period 1 | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg |
|--|--------------------|------------------|--------------------|
| Started | 612 | 616 | 614 |
| Received at least one dose of study drug | 612 | 616 | 614 |
| Completed | 556 | 549 | 560 |
| Not completed | 56 | 67 | 54 |
| Adverse event, serious fatal | 3 | 4 | 4 |
| Site Closure | 3 | 1 | 2 |
| Physician decision | 2 | - | 2 |
| Consent withdrawn by subject | 25 | 36 | 18 |
| Primary Care Physician Recommendation | - | 1 | - |
| Adverse event, non-fatal | 5 | 7 | 10 |
| Non-compliance | 1 | - | - |
| Relocated to Another Country | - | 1 | - |
| Participant Duplicated at Another Site | - | - | 1 |
| Lost to follow-up | 15 | 16 | 17 |
| Participant was in Rehabilitation | 1 | - | - |
| Protocol deviation | 1 | 1 | - |

Baseline characteristics

Reporting groups

| | |
|--|--------------------|
| Reporting group title | Dulaglutide 1.5 mg |
| Reporting group description: Dulaglutide 1.5 mg administered subcutaneously (SC) once a week. | |
| Reporting group title | Dulaglutide 3 mg |
| Reporting group description: Dulaglutide 3 mg administered SC once a week. | |
| Reporting group title | Dulaglutide 4.5 mg |
| Reporting group description: Dulaglutide 4.5 mg administered SC once a week. | |

| Reporting group values | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg |
|------------------------|--------------------|------------------|--------------------|
| Number of subjects | 612 | 616 | 614 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-------|--------|--------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 57.8 | 56.9 | 56.6 |
| standard deviation | ± 9.7 | ± 10.2 | ± 10.2 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 314 | 288 | 296 |
| Male | 298 | 328 | 318 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 30 | 26 | 32 |
| Asian | 13 | 18 | 14 |
| Native Hawaiian or Other Pacific Islander | 1 | 1 | 3 |
| Black or African American | 28 | 31 | 23 |
| White | 529 | 521 | 530 |
| More than one race | 11 | 19 | 12 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Argentina | 96 | 97 | 97 |
| Romania | 77 | 78 | 78 |
| Hungary | 25 | 24 | 24 |
| United States | 169 | 169 | 170 |
| Russia | 9 | 10 | 10 |
| Spain | 19 | 20 | 19 |
| Greece | 33 | 34 | 33 |
| Canada | 12 | 11 | 12 |
| Austria | 4 | 4 | 5 |
| Taiwan | 5 | 5 | 5 |
| Poland | 56 | 56 | 55 |

| | | | |
|--|--------|--------|--------|
| Mexico | 37 | 38 | 36 |
| Italy | 9 | 8 | 8 |
| Slovakia | 43 | 44 | 44 |
| Israel | 18 | 18 | 18 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 214 | 214 | 213 |
| Not Hispanic or Latino | 369 | 363 | 371 |
| Unknown or Not Reported | 29 | 39 | 30 |
| Hemoglobin A1C (HbA1c) at Baseline | | | |
| HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time. | | | |
| Units: Percentage of HbA1c | | | |
| arithmetic mean | 8.64 | 8.63 | 8.64 |
| standard deviation | ± 0.94 | ± 1.00 | ± 0.91 |

| | | | |
|-------------------------------|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 1842 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|------|--|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 898 | | |
| Male | 944 | | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 88 | | |
| Asian | 45 | | |
| Native Hawaiian or Other Pacific Islander | 5 | | |
| Black or African American | 82 | | |
| White | 1580 | | |
| More than one race | 42 | | |
| Unknown or Not Reported | 0 | | |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Argentina | 290 | | |
| Romania | 233 | | |
| Hungary | 73 | | |
| United States | 508 | | |
| Russia | 29 | | |
| Spain | 58 | | |
| Greece | 100 | | |
| Canada | 35 | | |
| Austria | 13 | | |
| Taiwan | 15 | | |
| Poland | 167 | | |

| | | | |
|--|------|--|--|
| Mexico | 111 | | |
| Italy | 25 | | |
| Slovakia | 131 | | |
| Israel | 54 | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 641 | | |
| Not Hispanic or Latino | 1103 | | |
| Unknown or Not Reported | 98 | | |
| Hemoglobin A1C (HbA1c) at Baseline | | | |
| HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time. | | | |
| Units: Percentage of HbA1c | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Dulaglutide 1.5 mg |
| Reporting group description: Dulaglutide 1.5 mg administered subcutaneously (SC) once a week. | |
| Reporting group title | Dulaglutide 3 mg |
| Reporting group description: Dulaglutide 3 mg administered SC once a week. | |
| Reporting group title | Dulaglutide 4.5 mg |
| Reporting group description: Dulaglutide 4.5 mg administered SC once a week. | |

Primary: Change in Hemoglobin A1c (HbA1c) from Baseline

| | |
|---|--|
| End point title | Change in Hemoglobin A1c (HbA1c) from Baseline |
| End point description: HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. The Least Squares (LS) mean was estimated from a mixed-effects model with repeated measures (MMRM) that included the independent variables: Baseline + Pooled Country + Treatment + Time + Treatment*Time (Type III sum of squares). | |
| Analysis Population Description: All participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline HbA1c value, excluding data post treatment discontinuation and/or initiation of new antihyperglycemic medications. | |
| End point type | Primary |
| End point timeframe: Baseline, Week 36 | |

| End point values | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg | |
|-------------------------------------|--------------------|------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 523 | 521 | 526 | |
| Units: Percentage of HbA1c | | | | |
| least squares mean (standard error) | -1.53 (± 0.04) | -1.71 (± 0.04) | -1.87 (± 0.04) | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Change in Hemoglobin A1c (HbA1c) from Baseline |
| Comparison groups | Dulaglutide 1.5 mg v Dulaglutide 3 mg |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 1044 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.29 |
| upper limit | -0.06 |

| | |
|---|--|
| Statistical analysis title | Change in Hemoglobin A1c (HbA1c) from Baseline |
| Comparison groups | Dulaglutide 1.5 mg v Dulaglutide 4.5 mg |
| Number of subjects included in analysis | 1049 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.45 |
| upper limit | -0.22 |

Secondary: Change in Body Weight from Baseline

| | |
|---|-------------------------------------|
| End point title | Change in Body Weight from Baseline |
| End point description: | |
| Least Squares (LS) mean was determined by mixed-model repeated measures (MMRM) model with independent variables: Baseline + Baseline HbA1c group + Pooled Country + Treatment + Time + Treatment*Time (Type III sum of squares). | |
| Analysis Population Description: All participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline body weight value, excluding data post treatment discontinuation and/or initiation of new antihyperglycemic medications. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 36 | |

| End point values | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg | |
|---|--------------------|------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 522 | 520 | 526 | |
| Units: Kilograms (Kg) | | | | |
| least squares mean (standard deviation) | -3.1 (± 0.19) | -4.0 (± 0.19) | -4.7 (± 0.19) | |

Statistical analyses

| | |
|---|---------------------------------------|
| Statistical analysis title | Change in Body Weight from Baseline |
| Comparison groups | Dulaglutide 3 mg v Dulaglutide 1.5 mg |
| Number of subjects included in analysis | 1042 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | -0.4 |

| | |
|---|---|
| Statistical analysis title | Change in Body Weight from Baseline |
| Comparison groups | Dulaglutide 1.5 mg v Dulaglutide 4.5 mg |
| Number of subjects included in analysis | 1048 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -1.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.1 |
| upper limit | -1.1 |

Secondary: Percentage of Participants Achieving HbA1c Target <7.0%

| | |
|-----------------|---|
| End point title | Percentage of Participants Achieving HbA1c Target <7.0% |
|-----------------|---|

End point description:

Percentage of participants achieving HbA1c target <7.0%.

Analysis Population Description: All participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline HbA1c value, excluding data post treatment discontinuation and/or initiation of new antihyperglycemic medications.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 36 | |

| End point values | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg | |
|-----------------------------------|--------------------|------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 523 | 521 | 526 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 56.98 | 64.68 | 71.48 | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Participants Achieving HbA1c Target <7.0% |
| Comparison groups | Dulaglutide 1.5 mg v Dulaglutide 3 mg |
| Number of subjects included in analysis | 1044 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.006 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.12 |
| upper limit | 1.98 |

| | |
|---|---|
| Statistical analysis title | Participants Achieving HbA1c Target <7.0% |
| Comparison groups | Dulaglutide 1.5 mg v Dulaglutide 4.5 mg |
| Number of subjects included in analysis | 1049 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.65 |
| upper limit | 3.01 |

Secondary: Change in Fasting Serum Glucose (FSG) from Baseline

| | |
|-----------------|---|
| End point title | Change in Fasting Serum Glucose (FSG) from Baseline |
|-----------------|---|

End point description:

Least Squares (LS) mean was determined by mixed-model repeated measures (MMRM) model with covariates: Baseline + Baseline HbA1c group + Pooled Country + Treatment + Time + Treatment*Time (Type III sum of squares).

Analysis Population Description: All participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline FSG value, excluding data post treatment discontinuation and/or initiation of new antihyperglycemic medications.

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

End point timeframe:

Baseline, Week 36

| End point values | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg | |
|---|--------------------|------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 510 | 509 | 514 | |
| Units: milligrams per deciliter (mg/dL) | | | | |
| least squares mean (standard error) | -44.2 (± 1.50) | -47.9 (± 1.50) | -52.3 (± 1.50) | |

Statistical analyses

| | |
|---|---------------------------------------|
| Statistical analysis title | Change in FSG From Baseline |
| Comparison groups | Dulaglutide 1.5 mg v Dulaglutide 3 mg |
| Number of subjects included in analysis | 1019 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.084 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -3.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.8 |
| upper limit | 0.5 |

| | |
|----------------------------|---|
| Statistical analysis title | Change in FSG From Baseline |
| Comparison groups | Dulaglutide 1.5 mg v Dulaglutide 4.5 mg |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 1024 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -8.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.3 |
| upper limit | -3.9 |

Secondary: Rate of Documented Symptomatic Hypoglycemic Episodes

| | |
|--|--|
| End point title | Rate of Documented Symptomatic Hypoglycemic Episodes |
| End point description: | |
| Hypoglycemia was defined as blood glucose < 54 mg/dL, excluding post-rescue records. Estimate is based on Group Mean (Least Squares Mean was selected from the dropdown list because there is no Group Mean option) from negative binomial model. The negative binomial model for post-baseline comparisons between treatments and control group: Number of episodes = Pooled Country + HbA1c at Baseline (%) + Treatment, with log (exposure in days/365.25) as an offset variable. | |
| Analysis Population Description: All participants who received at least one dose of study drug. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 36 | |

| End point values | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg | |
|---|--------------------|------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 612 | 616 | 614 | |
| Units: Episodes/participant/365.25 days | | | | |
| least squares mean (standard error) | 0.02 (± 0.01) | 0.00 (± 0.00) | 0.02 (± 0.01) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK): Steady-state Maximum Concentration(C_{max,ss})

| | |
|---|--|
| End point title | Pharmacokinetic (PK): Steady-state Maximum Concentration(C _{max,ss}) |
| End point description: | |
| Pharmacokinetic (PK): Steady-state Maximum Concentration(C _{max,ss}). | |

Analysis Population Description: All participants who received at least one dose of study drug and had evaluable PK data.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 4, Week 12, Week 36, Week 52, Week 56 | |

| End point values | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg | |
|---|---------------------|------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 612 | 616 | 614 | |
| Units: nanogram/milliliter (ng/mL) | | | | |
| arithmetic mean (confidence interval 90%) | 79.6 (77.7 to 81.7) | 159 (155 to 163) | 238 (232 to 243) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK): Area Under the Curve AUC (0-168)ss at Steady State

| | |
|-----------------|--|
| End point title | Pharmacokinetic (PK): Area Under the Curve AUC (0-168)ss at Steady State |
|-----------------|--|

End point description:

Pharmacokinetic (PK): Area Under the Curve AUC (0-168)ss at Steady State.

All participants who received at least one dose of study drug and had evaluable PK data.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 4, Week 12, Week 36, Week 52, Week 56 | |

| End point values | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg | |
|---|------------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 612 | 616 | 614 | |
| Units: nanogram*hour/milliliter (ng*h/mL) | | | | |
| arithmetic mean (confidence interval 90%) | 11200 (10900 to 11500) | 22300 (21800 to 22900) | 33400 (32700 to 34200) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 56

Adverse event reporting additional description:

All participants who received at least one dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Dulaglutide 1.5 mg |
|-----------------------|--------------------|

Reporting group description:

Dulaglutide 1.5 mg administered subcutaneously (SC) once a week.

| | |
|-----------------------|------------------|
| Reporting group title | Dulaglutide 3 mg |
|-----------------------|------------------|

Reporting group description:

Dulaglutide 3 mg administered SC once a week.

| | |
|-----------------------|--------------------|
| Reporting group title | Dulaglutide 4.5 mg |
|-----------------------|--------------------|

Reporting group description:

Dulaglutide 4.5 mg administered SC once a week.

| Serious adverse events | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg |
|---|--------------------|------------------|--------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 53 / 612 (8.66%) | 45 / 616 (7.31%) | 38 / 614 (6.19%) |
| number of deaths (all causes) | 3 | 4 | 4 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| adenocarcinoma pancreas | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| bladder cancer recurrent | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| clear cell renal cell carcinoma | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lung adenocarcinoma | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| metastases to abdominal cavity | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| metastatic uterine cancer | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed ^[1] | 1 / 314 (0.32%) | 0 / 288 (0.00%) | 0 / 296 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| neuroendocrine tumour | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| papillary thyroid cancer | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| phaeochromocytoma | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| plasma cell myeloma | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| prostate cancer | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed ^[2] | 1 / 298 (0.34%) | 0 / 328 (0.00%) | 0 / 318 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| uterine leiomyoma | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed ^[3] | 1 / 314 (0.32%) | 0 / 288 (0.00%) | 0 / 296 (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 |
| Vascular disorders | | | |
| arteriosclerosis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| hypertensive emergency | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| cholecystectomy | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| Pregnancy, puerperium and perinatal conditions | | | |
| pregnancy | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed ^[4] | 0 / 314 (0.00%) | 2 / 288 (0.69%) | 0 / 296 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| death | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| medical device site joint inflammation | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 2 / 612 (0.33%) | 1 / 616 (0.16%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sudden death | | | |
| alternative dictionary used: | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 2 / 614 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| Reproductive system and breast disorders | | | |
| cervical polyp | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed ^[5] | 0 / 314 (0.00%) | 1 / 288 (0.35%) | 0 / 296 (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 |
| oedema genital | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| ovarian cyst | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed ^[6] | 0 / 314 (0.00%) | 0 / 288 (0.00%) | 1 / 296 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| acute respiratory failure | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 2 / 616 (0.32%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| chronic obstructive pulmonary disease | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| hypersensitivity pneumonitis | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| nasal polyps | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| nasal septum deviation | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| major depression | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| panic attack | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| stress | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| suicidal ideation | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| Investigations | | | |
| amylase increased | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ecg signs of myocardial ischaemia | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| electrocardiogram t wave inversion | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lipase increased | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 2 / 612 (0.33%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| alcohol poisoning | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| comminuted fracture | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| contusion | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| exposure to toxic agent | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| fall | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| femoral neck fracture | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| fibula fracture | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| hand fracture | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| head injury alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| humerus fracture alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| limb traumatic amputation alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lower limb fracture alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lumbar vertebral fracture alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| post procedural haemorrhage alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders acute myocardial infarction alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 612 (0.33%) | 2 / 616 (0.32%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| angina pectoris alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| arteriosclerosis coronary artery alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| atrial fibrillation alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 3 / 612 (0.49%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| atrioventricular block complete alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| atrioventricular block second degree alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cardiac arrest alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| cardiac failure alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cardiac failure congestive alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cardio-respiratory arrest alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| congestive cardiomyopathy alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| coronary artery disease alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| left ventricular failure alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| myocardial infarction alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 612 (0.16%) | 2 / 616 (0.32%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| myocardial ischaemia | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| balance disorder | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cerebral artery occlusion | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cerebrovascular accident | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| diabetic mononeuropathy | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ischaemic stroke | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 612 (0.00%) | 2 / 616 (0.32%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| loss of consciousness | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| neuralgia | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| subarachnoid haemorrhage | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| syncope | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| wernicke's encephalopathy | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| anaemia | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| blood loss anaemia alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| thrombocytopenia alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders acute vestibular syndrome alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| vertigo alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders eyelid oedema alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| Gastrointestinal disorders abdominal pain alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 2 / 614 (0.33%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| abdominal pain upper alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| diarrhoea alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastric polyps alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| gastroesophageal reflux disease alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| haematochezia alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| haemorrhoids alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| hiatus hernia | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| mesenteric vein thrombosis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| obstructive pancreatitis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| pancreatitis acute | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| small intestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| cholecystitis acute | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 2 / 616 (0.32%) | 2 / 614 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cholelithiasis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hepatic cirrhosis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| jaundice | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| jaundice cholestatic | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| portal vein thrombosis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| angioedema | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| rash maculo-papular | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| nephrolithiasis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| goitre | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| intervertebral disc protrusion | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lumbar spinal stenosis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| osteoarthritis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| osteoarthropathy | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| plica syndrome | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| abscess limb | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| abscess neck | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| bronchitis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| campylobacter infection | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| cholecystitis infective alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| chronic sinusitis alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastroenteritis alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| herpes zoster alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| infective exacerbation of chronic obstructive airways disease alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| lower respiratory tract infection alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 612 (0.16%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| osteomyelitis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| perinephric abscess | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| periorbital cellulitis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pneumonia | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 2 / 612 (0.33%) | 2 / 616 (0.32%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pyelonephritis acute | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| pyoderma | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 abscess | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| sepsis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| viral infection | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| west nile viral infection | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (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 |
| Metabolism and nutrition disorders | | | |
| diabetic ketoacidosis | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 0 / 614 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypoglycaemia | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 1 / 612 (0.16%) | 0 / 616 (0.00%) | 1 / 614 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 22.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |
| type 2 diabetes mellitus | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 0 / 612 (0.00%) | 1 / 616 (0.16%) | 0 / 614 (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 |

Notes:

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

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

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

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

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

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

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

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

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

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

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

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

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

| Non-serious adverse events | Dulaglutide 1.5 mg | Dulaglutide 3 mg | Dulaglutide 4.5 mg |
|---|--------------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 156 / 612 (25.49%) | 190 / 616 (30.84%) | 195 / 614 (31.76%) |
| Gastrointestinal disorders | | | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 48 / 612 (7.84%) | 75 / 616 (12.18%) | 70 / 614 (11.40%) |
| occurrences (all) | 83 | 118 | 176 |
| dyspepsia | | | |
| alternative dictionary used: MedDRA 22.1 | | | |
| subjects affected / exposed | 17 / 612 (2.78%) | 33 / 616 (5.36%) | 18 / 614 (2.93%) |
| occurrences (all) | 26 | 56 | 35 |

| | | | |
|---|--------------------------|--------------------------|---------------------------|
| nausea alternative dictionary used: MedDRA 22.1 subjects affected / exposed occurrences (all) | 87 / 612 (14.22%) 121 | 99 / 616 (16.07%) 180 | 106 / 614 (17.26%) 192 |
| vomiting alternative dictionary used: MedDRA 22.1 subjects affected / exposed occurrences (all) | 40 / 612 (6.54%) 63 | 57 / 616 (9.25%) 89 | 64 / 614 (10.42%) 108 |
| Infections and infestations nasopharyngitis alternative dictionary used: MedDRA 22.1 subjects affected / exposed occurrences (all) | 29 / 612 (4.74%) 38 | 33 / 616 (5.36%) 41 | 39 / 614 (6.35%) 48 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported