# EU Clinical Trials Register

## Clinical trial results:
## A Phase III, Multicenter, Double-Blind, Randomized Study to Evaluate the Safety and Efficacy of the Addition of MK-3102 Compared with the Addition of Sitagliptin in Subjects with Type 2 Diabetes Mellitus with Inadequate Glycemic Control on Metformin

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

## Summary

| | |
|---|---|
| EudraCT number | 2013-000059-42 |
| Trial protocol | HU EE PL HR |
| Global end of trial date | 17 November 2014 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 February 2016 |
| First version publication date | 19 February 2016 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | MK-3102-026 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01841697 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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 | 17 November 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 17 November 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 November 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

This is a non-inferiority study comparing omarigliptin with sitagliptin in participants with type 2 diabetes mellitus (T2DM) with inadequate glycemic control on metformin therapy. The primary hypothesis is that after 24 weeks, the mean change from baseline in hemoglobin A1c (A1C) in participants treated with omarigliptin is non-inferior to that in participants treated with sitagliptin. There will be a 2-week run-in period with placebo + metformin prior to the double-blind treatment period.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.
The following additional measure defined for this individual study was in place for the protection of trial subjects: participants exceeding pre-specified glycemic thresholds after Day 1 of the double-blind treatment period will have rescue therapy initiated with open-label glimepiride.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 13 June 2013 |
| 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: 27 |
| Country: Number of subjects enrolled | Canada: 41 |
| Country: Number of subjects enrolled | Croatia: 2 |
| Country: Number of subjects enrolled | Estonia: 52 |
| Country: Number of subjects enrolled | Georgia: 73 |
| Country: Number of subjects enrolled | Hungary: 78 |
| Country: Number of subjects enrolled | Israel: 2 |
| Country: Number of subjects enrolled | Malaysia: 17 |
| Country: Number of subjects enrolled | Philippines: 26 |
| Country: Number of subjects enrolled | Poland: 60 |
| Country: Number of subjects enrolled | Romania: 65 |
| Country: Number of subjects enrolled | South Africa: 32 |
| Country: Number of subjects enrolled | United States: 167 |
| Worldwide total number of subjects | 642 |
| EEA total number of subjects | 257 |

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) | 494 |
| From 65 to 84 years | 148 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Eligibility requirements include male and female participants with type 2 diabetes mellitus who were currently on a stable dose of metformin monotherapy (≥1500 mg per day) for at least 12 weeks prior to study participation.

### 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** | Omarigliptin 25 mg once weekly |

Arm description:

Participants received omarigliptin 25 mg once a week plus placebo to sitagliptin once daily for 24 weeks. Participants continued pre-study stable dose of metformin (total daily dose ≥1500 mg) throughout the study. Participants may have received glimepiride (total daily dose of 1-6 mg) as rescue therapy.

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

Dosage and administration details:

Omarigliptin 25 mg oral capsule once a week for 24 weeks

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

Dosage and administration details:

Metformin oral tablet(s) total daily dose of ≥1500 mg daily

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

Dosage and administration details:

Placebo to sitagliptin 100 mg oral tablet once a day for 24 weeks

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

Dosage and administration details:

Glimepiride oral tablet(s) total daily dose of 1 to 6 mg once a day as rescue therapy

| Arm title | Sitagliptin 100 mg once daily |
|---|---|

Arm description:

Participants received sitagliptin 100 mg once daily plus placebo to omarigliptin once a week for 24 weeks. Participants continued pre-study stable dose of metformin (total daily dose ≥1500 mg) throughout the study. Participants may have received glimepiride (total daily dose of 1-6 mg) as rescue therapy.

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

Dosage and administration details:

Sitagliptin 100 mg oral tablet once a day for 24 weeks

| Investigational medicinal product name | Placebo to omarigliptin |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo to omarigliptin 25 mg oral capsule once a week for 24 weeks

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

Dosage and administration details:

Metformin oral tablet(s) total daily dose of ≥1500 mg daily

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

Dosage and administration details:

Glimepiride oral tablet(s) total daily dose of 1 to 6 mg once a day as rescue therapy

| Number of subjects in period 1 | Omarigliptin 25 mg once weekly | Sitagliptin 100 mg once daily |
|---|---|---|
| Started | 322 | 320 |
| Completed | 302 | 302 |
| Not completed | 20 | 18 |
|    Adverse event, serious fatal | - | 1 |
|    Consent withdrawn by subject | 16 | 16 |

| Lost to follow-up | 4 | 1 |
| --- | --- | --- |

## Baseline characteristics

### Reporting groups

| | |
|---|---|
| Reporting group title | Omarigliptin 25 mg once weekly |

Reporting group description:

Participants received omarigliptin 25 mg once a week plus placebo to sitagliptin once daily for 24 weeks. Participants continued pre-study stable dose of metformin (total daily dose ≥1500 mg) throughout the study. Participants may have received glimepiride (total daily dose of 1-6 mg) as rescue therapy.

| | |
|---|---|
| Reporting group title | Sitagliptin 100 mg once daily |

Reporting group description:

Participants received sitagliptin 100 mg once daily plus placebo to omarigliptin once a week for 24 weeks. Participants continued pre-study stable dose of metformin (total daily dose ≥1500 mg) throughout the study. Participants may have received glimepiride (total daily dose of 1-6 mg) as rescue therapy.

| Reporting group values | Omarigliptin 25 mg once weekly | Sitagliptin 100 mg once daily | Total |
|---|---|---|---|
| Number of subjects | 322 | 320 | 642 |
| Age categorical | | | |
| Units: Subjects | | | |
| | | | |
| Age Continuous | | | | |
| Units: years | | | |
|     arithmetic mean | 57 | 57.6 | |
|     standard deviation | ± 9.8 | ± 9.8 | - |
| Gender, Male/Female | | | |
| Units: Participants | | | |
|     Female | 171 | 145 | 316 |
|     Male | 151 | 175 | 326 |
| Hemoglobin A1c (A1C) | | | |
| Units: Percent | | | |
|     arithmetic mean | 7.52 | 7.49 | |
|     standard deviation | ± 0.77 | ± 0.74 | - |
| Fasting plasma glucose (FPG) | | | |
| Units: mg/dL | | | |
|     arithmetic mean | 160.1 | 153.9 | |
|     standard deviation | ± 35.7 | ± 32.8 | - |

# End points

## End points reporting groups

| Reporting group title | Omarigliptin 25 mg once weekly |
|---|---|
| Reporting group description: | |
| Participants received omarigliptin 25 mg once a week plus placebo to sitagliptin once daily for 24 weeks. Participants continued pre-study stable dose of metformin (total daily dose ≥1500 mg) throughout the study. Participants may have received glimepiride (total daily dose of 1-6 mg) as rescue therapy. | |
| Reporting group title | Sitagliptin 100 mg once daily |
| Reporting group description: | |
| Participants received sitagliptin 100 mg once daily plus placebo to omarigliptin once a week for 24 weeks. Participants continued pre-study stable dose of metformin (total daily dose ≥1500 mg) throughout the study. Participants may have received glimepiride (total daily dose of 1-6 mg) as rescue therapy. | |

## Primary: Change from baseline in A1C at Week 24

| End point title | Change from baseline in A1C at Week 24 |
|---|---|
| End point description: | |
| A1C is a measure of the percentage of glycated hemoglobin in the blood. Participant whole blood samples were collected at baseline and Week 24 to determine the least squares mean A1C change from baseline. Full analysis set population consists of all randomized participants who received at least one dose of study treatment and have a baseline measurement or a post-randomization measurement for the analysis endpoint subsequent to at least one dose of study treatment. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline and Week 24 | |

| End point values | Omarigliptin 25 mg once weekly | Sitagliptin 100 mg once daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 322 | 320 | | |
| Units: Percent | | | | |
| least squares mean (confidence interval 95%) | -0.47 (-0.55 to -0.38) | -0.43 (-0.51 to -0.35) | | |

## Statistical analyses

| Statistical analysis title | Comparison of treatment groups |
|---|---|
| Statistical analysis description: | |
| Difference in least squares mean is omarigliptin minus sitagliptin. | |
| Comparison groups | Omarigliptin 25 mg once weekly v Sitagliptin 100 mg once daily |

| Number of subjects included in analysis | 642 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[1] |
| Method | Constrained longitudinal data analysis |
| Parameter estimate | Difference in least squares mean |
| Point estimate | -0.03 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | -0.15 |
|     upper limit | 0.08 |

Notes:

[1] - If the upper bound of the two-sided 95% confidence interval for the mean difference between omarigilptin and sitagliptin is less than the non-inferiority margin, δ =0.3%, then omarigliptin will be declared non-inferior to sitagliptin in terms of A1C reduction at Week 24.

## Primary: Percentage of participants who experienced at least one adverse event

| End point title | Percentage of participants who experienced at least one adverse event |
|---|---|

End point description:

An adverse event is defined as any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an adverse event. Data presented below excludes data after initiation of glycemic rescue therapy.
All participants as treated population consists of all randomized participants who received at least one dose of trial treatment. Participants are included in the treatment group corresponding to the trial treatment they actually received.

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

End point timeframe:

Up to 27 weeks (including 3-week follow-up)

| **End point values** | Omarigliptin 25 mg once weekly | Sitagliptin 100 mg once daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 322 | 320 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 36.3 | 40.6 | | |

## Statistical analyses

| **Statistical analysis title** | Comparison of treatment groups |
|---|---|

Statistical analysis description:

Difference in percent is omarigliptin minus sitagliptin.

| Comparison groups | Omarigliptin 25 mg once weekly v Sitagliptin 100 mg once daily |
|---|---|

| Number of subjects included in analysis | 642 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percent |
| Point estimate | -4.3 |
| Confidence interval | |

| | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.8 |
| upper limit | 3.2 |

### Primary: Percentage of participants who discontinued study drug due to an adverse event

| End point title | Percentage of participants who discontinued study drug due to an adverse event |
|---|---|

End point description:

An adverse event is defined as any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an adverse event. Data presented below excludes data after initiation of glycemic rescue therapy.
All participants as treated population consists of all randomized participants who received at least one dose of trial treatment. Participants are included in the treatment group corresponding to the trial treatment they actually received.

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

End point timeframe:

Up to 24 weeks

| **End point values** | Omarigliptin 25 mg once weekly | Sitagliptin 100 mg once daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 322 | 320 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 0.9 | 2.2 | | |

### Statistical analyses

| **Statistical analysis title** | Comparison of Treatment Groups |
|---|---|

Statistical analysis description:

Difference in percent is omarigliptin minus sitagliptin.

| Comparison groups | Omarigliptin 25 mg once weekly v Sitagliptin 100 mg once daily |
|---|---|

| Number of subjects included in analysis | 642 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percent |
| Point estimate | -1.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.6 |
| upper limit | 0.8 |

## Secondary: Change from baseline in FPG at Week 24

| End point title | Change from baseline in FPG at Week 24 |
|---|---|

End point description:

Participant whole blood samples were collected after an overnight fast at baseline and Week 24 to determine the least squares mean change from baseline in participant FPG.
Full analysis set population consists of all randomized participants who received at least one dose of study treatment and have a baseline measurement or a post-randomization measurement for the analysis endpoint subsequent to at least one dose of study treatment.

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

End point timeframe:

Baseline and Week 24

| **End point values** | Omarigliptin 25 mg once weekly | Sitagliptin 100 mg once daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 322 | 320 | | |
| Units: mg/dL | | | | |
| least squares mean (confidence interval 95%) | -13.7 (-17.3 to -10.1) | -9.5 (-13.2 to -5.9) | | |

## Statistical analyses

| **Statistical analysis title** | Comparison of Treatment Groups |
|---|---|

Statistical analysis description:

Difference in least squares mean is omarigliptin minus sitagliptin.

| Comparison groups | Omarigliptin 25 mg once weekly v Sitagliptin 100 mg once daily |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 642 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.089 [2] |
| Method | Constrained longitudinal data analysis |
| Parameter estimate | Difference in least squares mean |
| Point estimate | -4.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9 |
| upper limit | 0.6 |

Notes:

[2] - Terms for treatment, time, and the interaction of time by treatment, with the constraint that the mean baseline is the same for all treatment groups.

## Secondary: Percentage of participants achieving an A1C goal <7.0% after 24 weeks of treatment

| | |
|---|---|
| End point title | Percentage of participants achieving an A1C goal <7.0% after 24 weeks of treatment |

End point description:

Participant whole blood samples were collected at Week 24 to determine the number of participants achieving A1C <7.0% at Week 24. Full analysis set population consists of all randomized participants who received at least one dose of study treatment and have a baseline measurement or a post-randomization measurement for the analysis endpoint subsequent to at least one dose of study treatment.

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

End point timeframe:

Week 24

| **End point values** | Omarigliptin 25 mg once weekly | Sitagliptin 100 mg once daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 322 | 320 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 50.9 | 49.1 | | |

## Statistical analyses

| **Statistical analysis title** | Comparison of Treatment Groups |
|---|---|

Statistical analysis description:

Proportion (rate) for each group was estimated using standard multiple imputation techniques. Between-group difference in proportion is omarigliptin minus sitagliptin.

| Comparison groups | Omarigliptin 25 mg once weekly v Sitagliptin 100 mg once daily |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 642 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.619 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Between-group rate difference |
| Point estimate | 2 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | -5.9 |
|     upper limit | 9.9 |

## Secondary: Percentage of participants achieving an A1C goal <6.5% after 24 weeks of treatment

| | |
|---|---|
| End point title | Percentage of participants achieving an A1C goal <6.5% after 24 weeks of treatment |

End point description:

Participant whole blood samples were collected at Week 24 to determine the percentage of participants achieving A1C <6.5% at Week 24.
Full analysis set population consists of all randomized participants who received at least one dose of study treatment and have a baseline measurement or a post-randomization measurement for the analysis endpoint subsequent to at least one dose of study treatment.

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

End point timeframe:

Week 24

| **End point values** | Omarigliptin 25 mg once weekly | Sitagliptin 100 mg once daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 322 | 320 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 27 | 22.8 | | |

## Statistical analyses

| **Statistical analysis title** | Comparison of Treatment Groups |
|---|---|

Statistical analysis description:

Proportion (rate) for each group was estimated using standard multiple imputation techniques. Between-group difference in proportion is omarigliptin minus sitagliptin.

| Comparison groups | Omarigliptin 25 mg once weekly v Sitagliptin 100 mg once daily |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 642 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.212 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Between-group rate difference |
| Point estimate | 4.4 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | -2.5 |
|     upper limit | 11.4 |

# Adverse events

## Adverse events information[1]

| | |
|---|---|
| Timeframe for reporting adverse events: | |
| Up to 27 weeks (including 3-week follow-up) | |
| Adverse event reporting additional description: | |
| All participants as treated population defined as all randomized participants who received at least 1 dose of study drug. Participants are included in the treatment group corresponding to the trial treatment they actually received. Serious and non-serious AEs, respectively, include and exclude data after the initiation of glycemic rescue therapy. | |
| Assessment type | Systematic |

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17.1 |

## Reporting groups

| | |
|---|---|
| Reporting group title | Sitagliptin 100 mg |

Reporting group description:

Participants received sitagliptin 100 mg once daily plus placebo to omarigliptin once a week for 24 weeks. Participants continued pre-study stable dose of metformin (total daily dose ≥1500 mg) throughout the study. Participants may have received glimepiride (total daily dose of 1-6 mg) as rescue therapy.

| | |
|---|---|
| Reporting group title | Omarigliptin 25 mg |

Reporting group description:

Participants received omarigliptin 25 mg once a week plus placebo to sitagliptin once daily for 24 weeks. Participants continued pre-study stable dose of metformin (total daily dose ≥1500 mg) throughout the study. Participants may have received glimepiride (total daily dose of 1-6 mg) as rescue therapy.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No non-serious adverse events exceeded the 5% threshold for any treatment group.

| Serious adverse events | Sitagliptin 100 mg | Omarigliptin 25 mg | |
|---|---|---|---|
| **Total subjects affected by serious adverse events** | | | |
| subjects affected / exposed | 9 / 320 (2.81%) | 11 / 322 (3.42%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 2 / 322 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sebaceous adenoma | | | |

|  | | |
|---|---|---|
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (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 | 1 / 320 (0.31%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |

**Cardiac disorders**

Acute myocardial infarction

|  | | |
|---|---|---|
| subjects affected / exposed | 1 / 320 (0.31%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |

Angina pectoris

|  | | |
|---|---|---|
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |

Arrhythmia supraventricular

|  | | |
|---|---|---|
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |

Atrial fibrillation

|  | | |
|---|---|---|
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |

Myocardial infarction

|  | | |
|---|---|---|
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 |

Myocardial ischaemia

|  | | |
|---|---|---|
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |

**Nervous system disorders**

| | | | |
|---|---|---|---|
| Cerebrovascular disorder | | | |
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |

| | | |
|---|---|---|
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| **Dyspnoea** | | |
| subjects affected / exposed | 1 / 320 (0.31%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| **Skin and subcutaneous tissue disorders** | | |
| Dematitis contact | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| **Psoriasis** | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| **Endocrine disorders** | | |
| Hypothyroidism | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| **Musculoskeletal and connective tissue disorders** | | |
| Back pain | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| **Infections and infestations** | | |
| Pyelohephritis acute | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 1 / 322 (0.31%) |
| 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: 5 %

| Non-serious adverse events | Sitagliptin 100 mg | Omarigliptin 25 mg | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 320 (0.00%) | 0 / 322 (0.00%) | |

## 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