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 Glimepiride in Patients With Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin

Summary

EudraCT number	2012-002309-23
Trial protocol	HU LT DE PL
Global end of trial date	26 January 2015

Results information

Result version number	v1 (current)
This version publication date	06 February 2016
First version publication date	06 February 2016

Trial information

Trial identification

Sponsor protocol code	MK-3102-016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01682759
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	26 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 January 2015
Global end of trial reached?	Yes
Global end of trial date	26 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This trial will assess the safety and efficacy of Omarigliptin (MK-3102) compared with the sulfonylurea, glimepiride, in Type 2 diabetes mellitus participants with inadequate glycemic control on metformin monotherapy. The primay hypothesis of the study is that after 54 weeks, the mean change from baseline in hemoglobin A1C (A1C) in participants treated with omarigliptin is non-inferior compared with that in participants treated with glimepiride.

Protection of trial subjects:

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

Background therapy:

Participants will continue on their stable dose (>=1500 mg/day) of open-label metformin throughout the trial.

Evidence for comparator: -

Actual start date of recruitment	10 September 2012
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: 34
Country: Number of subjects enrolled	Croatia: 51
Country: Number of subjects enrolled	Germany: 48
Country: Number of subjects enrolled	Hungary: 90
Country: Number of subjects enrolled	Lithuania: 30
Country: Number of subjects enrolled	Poland: 43
Country: Number of subjects enrolled	United States: 242
Country: Number of subjects enrolled	Malaysia: 24
Country: Number of subjects enrolled	Romania: 78
Country: Number of subjects enrolled	Korea, Republic of: 65
Country: Number of subjects enrolled	Lebanon: 46
Worldwide total number of subjects	751
EEA total number of subjects	340

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)	571
From 65 to 84 years	180
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

One hundred twenty-seven sites received IEC/IRB approval and were shipped clinical supplies and 115 sites in 11 countries screened at least 1 participant. Seven-hundred and fifty-one participants were randomized Enrollment at each study center ranged from 1 to 29 participants.

Pre-assignment

Screening details:

In total, 1197 participants at 115 clinical sites were screened and 446 participants were excluded during screening. The most common reason for participants not being randomized was screen failure. The most common reasons for screen failure were participants not meeting the metformin inclusion criteria or meeting exclusionary laboratory values.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Omarigliptin

Arm description:

Participants will receive omarigliptin, 25 mg once weekly and placebo matching glimepiride once daily for up to 54 weeks.

Arm type	Experimental
Investigational medicinal product name	Omarigliptin
Investigational medicinal product code	
Other name	MK-3102
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants will receive omarigliptin, 25 mg once weekly for up to 54 weeks

Investigational medicinal product name	Placebo matching glimepiride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once daily for up to 54 weeks

Arm title	Glimepiride

Arm description:

Participants will receive glimepiride titrated to a maximum of 6 mg, once daily, and placebo to omarigliptin, once weekly for up to 54 weeks.

Arm type	Active comparator
Investigational medicinal product name	Placebo matching omarigliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details: Once weekly for up to 54 weeks	
Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants will receive glimepiride titrated to a maximum of 6 mg, once daily, for up to 54 weeks

Number of subjects in period 1	Omarigliptin	Glimepiride
Started	376	375
Treated	375	375
Completed	307	305
Not completed	69	70
Adverse event, serious fatal	2	1
Physician decision	1	1
Consent withdrawn by subject	56	55
Lost to follow-up	10	13

Baseline characteristics

Reporting groups	
Reporting group title	Omarigliptin
Reporting group description:	
Participants will receive omarigliptin, 25 mg once weekly and placebo matching glimepiride once daily for up to 54 weeks.	
Reporting group title	Glimepiride
Reporting group description:	
Participants will receive glimepiride titrated to a maximum of 6 mg, once daily, and placebo to omarigliptin, once weekly for up to 54 weeks.	

Reporting group values	Omarigliptin	Glimepiride	Total
Number of subjects	376	375	751
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	289	282	571
From 65-84 years	87	93	180
85 years and over	0	0	0
Age Continuous |			
Units: years			
arithmetic mean	57.9	57.6	
standard deviation	± 9.6	± 9.3	-
Gender, Male/Female			
Units: Participants			
Female	173	164	337
Male	203	211	414
Hemoglobin A1C			
Units: A1C (%)			
arithmetic mean	7.49	7.43	
standard deviation	± 0.75	± 0.72	-
Body Weight			
Units: kg			
arithmetic mean	87.5	88.7	
standard deviation	± 18.1	± 18.7	-
Fasting Plasma Glucose (FPG) |			
Units: mg/dL			
arithmetic mean	155.3	152.7	
standard deviation	± 31.4	± 30	-

End points

End points reporting groups

Reporting group title	Omarigliptin
Reporting group description:	
Participants will receive omarigliptin, 25 mg once weekly and placebo matching glimepiride once daily for up to 54 weeks.	
Reporting group title	Glimepiride
Reporting group description:	
Participants will receive glimepiride titrated to a maximum of 6 mg, once daily, and placebo to omarigliptin, once weekly for up to 54 weeks.	

Primary: Change from Baseline in Hemoglobin A1C at Week 54

End point title	Change from Baseline in Hemoglobin A1C at Week 54
End point description:	
Hemoglobin A1C is blood marker used to report average blood glucose levels over prolonged periods of time and is reported as a percentage (%). Thus, this change from baseline reflects the Week 54 A1C minus the Week 0 A1C. The Full Analysis Set (FAS) population consisted of all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a measurement for the analysis endpoint after receiving study medication.	
End point type	Primary
End point timeframe:	
Baseline and Week 54	

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	375		
Units: Percent change				
number (confidence interval 95%)	-0.3 (-0.39 to -0.21)	-0.48 (-0.57 to -0.39)		

Statistical analyses

Statistical analysis title	Non-inferior Analysis
Statistical analysis description:	
Constrained longitudinal data analysis (cLDA) model including 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.	
Comparison groups	Omarigliptin v Glimepiride

Number of subjects included in analysis	750
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in the least squares means
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.3

Notes:

[1] - Omarigliptin was considered non-inferior to glimepiride if the upper bound of the two-sided 95% confidence interval (CI) of the between-treatment difference in least-squares (LS) means for change from baseline in A1C at Week 54 (omarigliptin vs. glimepiride) was lower than 0.35%.

Primary: Percentage of Participants Who Experienced at Least One Adverse Event Excluding Data After Glycemic Rescue

End point title	Percentage of Participants Who Experienced at Least One Adverse Event Excluding Data After Glycemic Rescue

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure. All Subjects as Treated (ASaT) population, defined as all randomized participants who received at least 1 dose of study medication. Participants were included in the treatment group corresponding to the study treatment they actually received.

End point type	Primary

End point timeframe:

Up to Week 57

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	375		
Units: Percentage of participants				
number (not applicable)	54.7	61.6		

Statistical analyses

Statistical analysis title	Treatment Difference

Statistical analysis description:

Miettinen & Nurminen method; the 95% CI was computed only for those endpoints with at least 4 participants having events in one or more treatment groups.

Comparison groups	Omarigliptin v Glimepiride

Number of subjects included in analysis	750
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.9
upper limit	0.1

Primary: Percentage of Participants Who Discontinued from the Study Due to an Adverse Event Excluding Data After Glycemic Rescue

End point title	Percentage of Participants Who Discontinued from the Study Due to an Adverse Event Excluding Data After Glycemic Rescue

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure. All Subjects as Treated (ASaT) population, defined as all randomized participants who received at least 1 dose of study medication. Participants were included in the treatment group corresponding to the study treatment they actually received.

End point type	Primary

End point timeframe:

Up to Week 54

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	375		
Units: Percentage of participants				
number (not applicable)	3.7	2.7		

Statistical analyses

Statistical analysis title	Treatment Difference

Statistical analysis description:

Miettinen & Nurminen method; the 95% CI was computed only for those endpoints with at least 4 participants having events in one or more treatment groups.

Comparison groups	Omarigliptin v Glimepiride
Number of subjects included in analysis	750
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	3.8

Secondary: Change from Baseline in Fasting Plasma Glucose at Week 54

End point title	Change from Baseline in Fasting Plasma Glucose at Week 54

End point description:

Blood glucose was measured on a fasting basis. FPG is expressed as mg/dL. Blood was drawn at predose on Day 1 and after 54 weeks of treatment to determine change in plasma glucose levels (i.e., FPG at Week 54 minus FPG at baseline). The FAS population consisted of all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a measurement for the analysis endpoint after receiving study medication.

End point type	Secondary

End point timeframe:

Baseline and Week 54

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	375		
Units: mg/dL				
least squares mean (confidence interval 95%)	-2.7 (-6.7 to 1.3)	-8.3 (-12.4 to -4.3)		

Statistical analyses

Statistical analysis title	Treatment Difference

Statistical analysis description:

Other [Difference in the least squares means]

Comparison groups	Omarigliptin v Glimepiride
Number of subjects included in analysis	750
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in the least squares means
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	11.2

Secondary: Percentage of Participants Achieving a Hemoglobin A1C of <6.5% at Week 54

End point title	Percentage of Participants Achieving a Hemoglobin A1C of <6.5% at Week 54

End point description:

The percentage of participants who achieved A1C values <6.5% (48 mmol/mol) in the FAS Population at Week 54. The FAS population consisted of all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a measurement for the analysis endpoint after receiving study medication.

End point type	Secondary

End point timeframe:

Week 54

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	375		
Units: Percentage of participants				
number (confidence interval 95%)	25.1 (20.6 to 30.2)	28.8 (24.1 to 34)		

Statistical analyses

Statistical analysis title	Treatment Difference

Statistical analysis description:

A1C <6.5%, between-group CIs are calculated via Miettinen & Nurminen method.

Comparison groups	Omarigliptin v Glimepiride
Number of subjects included in analysis	750
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Between-group Rate Difference (%)
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	3.3

Secondary: Percentage of Participants with an Adverse Event of Symptomatic Hypoglycemia Excluding Data After Glycemic Rescue

End point title	Percentage of Participants with an Adverse Event of Symptomatic Hypoglycemia Excluding Data After Glycemic Rescue

End point description:

Symptomatic episode of hypoglycemia was an episode with clinical symptoms reported by the investigator as hypoglycemia (concurrent fingerstick glucose not required). The ASaT Population is defined as all randomized participants who received at least 1 dose of study medication. Participants

were included in the treatment group corresponding to the study treatment they actually received.

End point type	Secondary

End point timeframe:

Up to Week 54

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	375		
Units: Percentage of participants				
number (not applicable)	5.3	26.7		

Statistical analyses

Statistical analysis title	Treatment Difference

Statistical analysis description:

Miettinen & Nurminen method; the 95% CI was computed only for those endpoints with at least 4 participants having events in one or more treatment groups.

Comparison groups	Omarigliptin v Glimepiride
Number of subjects included in analysis	750
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Difference in percentage
Parameter estimate	Difference in %
Point estimate	-21.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.5
upper limit	-16.4

Secondary: Change from Baseline in Body Weight at Week 54 Excluding Data After Gylcemic Rescue

End point title	Change from Baseline in Body Weight at Week 54 Excluding Data After Gylcemic Rescue

End point description:

The ASaT Population is defined as all randomized participants who received at least 1 dose of study medication. Participants were included in the treatment group corresponding to the study treatment they actually received.

End point type	Secondary

End point timeframe:

Baseline and Week 54

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	375		
Units: kilograms				
least squares mean (confidence interval 95%)	-0.4 (-0.8 to 0)	1.5 (1.1 to 1.9)		

Statistical analyses

Statistical analysis title	Treatment Difference
Statistical analysis description:	
cLDA model including 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.	
Comparison groups	Omarigliptin v Glimepiride
Number of subjects included in analysis	750
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA model
Parameter estimate	Difference in the least squares means
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.4

Secondary: Percentage of Participants Achieving a Hemoglobin A1C of <7.0% at Week 54

End point title	Percentage of Participants Achieving a Hemoglobin A1C of <7.0% at Week 54
End point description:	
The percentage of participants who achieved A1C values <7.0% (53 mmol/mol) in the FAS Population at Week 54. The FAS Population (with multiple imputation) consisted of all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a measurement for the analysis endpoint after receiving study medication.	
End point type	Secondary
End point timeframe:	
Week 54	

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	375		
Units: Percentage of participants				
number (confidence interval 95%)	47.7 (42.3 to 53.1)	58 (52.7 to 63.1)		

Statistical analyses

Statistical analysis title	Treatment Difference
Statistical analysis description: A1C < 7.0%, between-group CIs are calculated via Miettinen & Nurminen method.	
Comparison groups	Omarigliptin v Glimepiride
Number of subjects included in analysis	750
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Between-group Rate Difference
Point estimate	-10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.8
upper limit	-2.8

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 57

Adverse event reporting additional description:

Serious adverse events are presented, regardless of time from last dose of blinded study medication, including data after glycemic rescue. Non-serious adverse events are presented, regardless of time from last dose of blinded study medication, excluding data after glycemic rescue.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Glimepiride

Reporting group description:

Participants will receive glimepiride titrated to a maximum of 6 mg, once daily, and placebo to omarigliptin, once weekly for up to 54 weeks.

Reporting group title	Omarigliptin

Reporting group description:

Participants will receive omarigliptin, 25 mg once weekly and placebo matching glimepiride once daily for up to 54 weeks.

Serious adverse events	Glimepiride	Omarigliptin	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 375 (4.80%)	24 / 375 (6.40%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiomyolipoma			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			

subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoma			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 375 (0.00%)	2 / 375 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Dumping syndrome			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haematoma			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (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 coronary syndrome			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery disease			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Epilepsy			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
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	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Loss of consciousness			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-cardiac chest pain			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diverticulum intestinal			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal haemorrhage			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal obstruction			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (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 acute			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (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			
Diabetic foot			

subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 375 (0.27%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Carbuncle			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 375 (0.00%)	3 / 375 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic arthritis staphylococcal			
subjects affected / exposed	0 / 375 (0.00%)	1 / 375 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 375 (0.27%)	0 / 375 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Glimepiride	Omarigliptin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	125 / 375 (33.33%)	43 / 375 (11.47%)	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	23 / 375 (6.13%)	24 / 375 (6.40%)	
occurrences (all)	30	31	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	110 / 375 (29.33%)	21 / 375 (5.60%)	
occurrences (all)	487	45	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2013	Amendment 1 - Modified inclusion criteria, pregnancy testing and contraception, and statistical methods.
05 April 2013	Amendment 2 - Additions to the chemistry panel.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported