Clinical trial results:
A phase III, multicenter, randomized, double-blind study to evaluate the efficacy and safety of MK-3102 versus placebo in subjects with type 2 diabetes mellitus with moderate or severe chronic kidney disease or kidney failure on dialysis who have inadequate glycemic control

Summary

EudraCT number	2012-002332-85
Trial protocol	CZ HU PL ES GB
Global end of trial date	19 January 2016

Results information

Result version number	v1 (current)
This version publication date	22 January 2017
First version publication date	22 January 2017

Trial information

Trial identification

Sponsor protocol code	3102-019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01698775
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	19 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 January 2016
Global end of trial reached?	Yes
Global end of trial date	19 January 2016
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 omarigliptin in participants with type 2 diabetes mellitus and moderate or severe chronic renal insufficiency or end stage renal disease on dialysis with inadequate glycemic control. The primary hypothesis of the study is that omarigliptin compared to placebo produces greater reduction in glycosylated hemoglobin (A1C) after 24 weeks.

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 participants: participants not meeting protocol-specified glycemic goals may be rescued with open-label glipizide during Phase A only and/or insulin glargine therapy.

Background therapy:

Participants on insulin therapy at screening will continue insulin therapy during the study.

Evidence for comparator: -

Actual start date of recruitment	02 October 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	Australia: 2
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Croatia: 11
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Georgia: 27
Country: Number of subjects enrolled	Hong Kong: 25
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	Malaysia: 24
Country: Number of subjects enrolled	Philippines: 17
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	Serbia: 16
Country: Number of subjects enrolled	South Africa: 7
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	United Kingdom: 1

Country: Number of subjects enrolled	United States: 47
Worldwide total number of subjects	213
EEA total number of subjects	33

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)	96
From 65 to 84 years	114
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants with type 2 diabetes mellitus and at least 30 years of age with moderate or severe chronic renal insufficiency or end stage renal disease on dialysis.

Pre-assignment

Screening details:

All eligible participants were randomly allocated to trial treatment and received a randomization number.

Period 1

Period 1 title	Phase A
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Omarigliptin (Phase A)

Arm description:

Phase A: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 24 weeks.

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:

12.5 or 25 mg capsule orally once a week

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Pre-screening insulin therapy will be continued during the study. Insulin glargine may be adminstered as rescue therapy.

Investigational medicinal product name	Glipizide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open-label glipizide as rescue therapy

Arm title	Placebo to omarigliptin (Phase A)

Arm description:

Phase A: matching placebo to omarigliptin orally once a week for 24 weeks.

Arm type	Placebo

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 capsule orally once a week

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Pre-screening insulin therapy will be continued during the study. Insulin glargine may be adminstered as rescue therapy.

Investigational medicinal product name	Glipizide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open-label glipizide as rescue therapy

Number of subjects in period 1	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)
Started	107	106
Completed	98	97
Not completed	9	9
Adverse event, serious fatal	1	1
Consent withdrawn by subject	3	4
Adverse event, non-fatal	2	1
Kidney [transplant]	-	1
Lost to follow-up	1	2
Lack of efficacy	1	-
Protocol deviation	1	-

Period 2

Period 2 title	Phase B
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Omarigliptin (Phase A) Omarigliptin (Phase B)

Arm description:

Phase A: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 24 weeks. Phase B: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 30 weeks. Participants who are not on background insulin therapy or who did not receive open-label glipizide or insulin as rescue therapy during Phase A of the study (Week 1 through Week 24) received matching placebo to glipizide 2.5 daily up to a maximum of 20 mg daily (based on glycemic control) in a blinded manner during Phase B of the study (Week 24 through Week 54).

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:

12.5 or 25 mg capsule orally once a week

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

Dosage and administration details:

Placebo tablet(s) daily

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Pre-screening insulin therapy will be continued during the study. Insulin glargine may be adminstered as rescue therapy.

Arm title	Placebo to omarigliptin (Phase A) Glipizide (Phase B)

Arm description:

Phase A: matching placebo to omarigliptin orally once a week for 24 weeks. Phase B: matching placebo to omarigliptin orally once a week for 30 weeks. Participants who were not on background insulin therapy or who did not receive open-label glipizide or insulin as rescue therapy during Phase A of the study (Week 1 through Week 24) received glipizide 2.5 daily up to a maximum of 20 mg daily (based on glycemic control) in a blinded manner during Phase B of the study (Week 24 through Week 54).

Arm type	Active comparator
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 capsule orally once a week

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Pre-screening insulin therapy will be continued during the study. Insulin glargine may be adminstered as rescue therapy.

Investigational medicinal product name	Glipizide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 mg once daily up to a maximum of 20 mg daily

Number of subjects in period 2	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glipizide (Phase B)
Started	98	97
Completed	84	86
Not completed	14	11
Hyperglycemia Discontinuation Criteria	-	1
Adverse event, serious fatal	-	1
Physician decision	1	1
Consent withdrawn by subject	6	2
Adverse event, non-fatal	6	3
Lost to follow-up	-	1
Protocol deviation	1	1
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Omarigliptin (Phase A)
Reporting group description:	
Phase A: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 24 weeks.	
Reporting group title	Placebo to omarigliptin (Phase A)
Reporting group description:	
Phase A: matching placebo to omarigliptin orally once a week for 24 weeks.	

Reporting group values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)	Total
Number of subjects	107	106	213
Age categorical Units: Subjects			
Under 45 years of age	1	5	6
45 to less than 65 years of age	47	43	90
Over 65 years of age	59	58	117
Age Continuous | Units: Years			
arithmetic mean	65.9	64.5	
standard deviation	± 9.4	± 9.7	-
Gender, Male/Female Units: Participants			
Female	39	43	82
Male	68	63	131

End points

End points reporting groups

Reporting group title	Omarigliptin (Phase A)

Reporting group description:

Phase A: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 24 weeks.

Reporting group title	Placebo to omarigliptin (Phase A)

Reporting group description:

Phase A: matching placebo to omarigliptin orally once a week for 24 weeks.

Reporting group title	Omarigliptin (Phase A) Omarigliptin (Phase B)

Reporting group description:

Phase A: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 24 weeks. Phase B: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 30 weeks. Participants who are not on background insulin therapy or who did not receive open-label glipizide or insulin as rescue therapy during Phase A of the study (Week 1 through Week 24) received matching placebo to glipizide 2.5 daily up to a maximum of 20 mg daily (based on glycemic control) in a blinded manner during Phase B of the study (Week 24 through Week 54).

Reporting group title	Placebo to omarigliptin (Phase A) Glipizide (Phase B)

Reporting group description:

Phase A: matching placebo to omarigliptin orally once a week for 24 weeks. Phase B: matching placebo to omarigliptin orally once a week for 30 weeks. Participants who were not on background insulin therapy or who did not receive open-label glipizide or insulin as rescue therapy during Phase A of the study (Week 1 through Week 24) received glipizide 2.5 daily up to a maximum of 20 mg daily (based on glycemic control) in a blinded manner during Phase B of the study (Week 24 through Week 54).

Subject analysis set title	Omarigliptin (Phase A) Omarigliptin (Phase B)
Subject analysis set type	Full analysis

Subject analysis set description:

Phase A: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 24 weeks. Phase B: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 30 weeks. Participants who are not on background insulin therapy or who did not receive open-label glipizide or insulin as rescue therapy during Phase A of the study (Week 1 through Week 24) received matching placebo to glipizide 2.5 daily up to a maximum of 20 mg daily (based on glycemic control) in a blinded manner during Phase B of the study (Week 24 through Week 54).

Subject analysis set title	Omarigliptin (Phase A) Omarigliptin (Phase B)
Subject analysis set type	Full analysis

Subject analysis set description:

Phase A: matching placebo to omarigliptin orally once a week for 24 weeks. Phase B: matching placebo to omarigliptin orally once a week for 30 weeks. Participants who were not on background insulin therapy or who did not receive open-label glipizide or insulin as rescue therapy during Phase A of the study (Week 1 through Week 24) received glipizide 2.5 daily up to a maximum of 20 mg daily (based on glycemic control) in a blinded manner during Phase B of the study (Week 24 through Week 54).

Primary: Change from baseline in glycosylated hemoglobin (A1C) at Week 24

End point title	Change from baseline in glycosylated hemoglobin (A1C) at Week 24

End point description:

A1C is measured as a percent. Change from baseline in A1C at Week 24 was analyzed using constrained longitudinal data analysis (cLDA) method with a restriction of the same baseline mean across treatment groups. The cLDA model included terms for treatment, renal insufficiency stratum, baseline treatment with insulin stratum, time, the interaction of time by treatment, the interaction of time by renal insufficiency stratum, and the interaction of time by baseline treatment with insulin stratum. Full analysis set (FAS) population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement in Phase A for the analysis endpoint subsequent to at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline and Week 24

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	106		
Units: Percent				
least squares mean (confidence interval 95%)	-0.77 (-1 to -0.54)	-0.44 (-0.67 to -0.21)		

Statistical analyses

Statistical analysis title	Comparison of treatment groups
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	-0.02

Primary: Percentage of participants who experienced at least one adverse event (Phase A: 24-week placebo controlled period)

End point title	Percentage of participants who experienced at least one adverse event (Phase A: 24-week placebo controlled period)

End point description:

An adverse event is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. Presented data exclude data after glycemic rescue. All-Participants-as-Treated (APaT) population consisted of all randomized participants who took at least 1 dose of trial treatment.

End point type	Primary

End point timeframe:

Up to 28 weeks (including 28 days following the last dose of study therapy for participants who discontinued study drug)

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	106		
Units: Percentage of participants				
number (not applicable)	66	69.8		

Statistical analyses

Statistical analysis title	Comparison of treatment groups
Statistical analysis description:	
Difference in percentages was based on Miettinen & Numinen method stratified by renal status stratum.	
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentages
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.3
upper limit	8.8

Primary: Percentage of participants who discontinued study drug due to an adverse event (Phase A: 24-week placebo controlled period)

End point title	Percentage of participants who discontinued study drug due to an adverse event (Phase A: 24-week placebo controlled period)
End point description:	
An adverse event is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. Presented data exclude data after glycemic rescue. APaT population consisted of all randomized participants who took at least 1 dose of trial treatment.	
End point type	Primary
End point timeframe:	
Up to 24 weeks	

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	106		
Units: Percentage of participants				
number (not applicable)	2.8	0.9		

Statistical analyses

Statistical analysis title	Comparision of treatment groups
Statistical analysis description:	
Difference in percentages was based on Miettinen & Numinen method stratified by renal status stratum.	
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentages
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	7.2

Primary: Percentage of participants who experienced at least one adverse event (Phase A: 24-week placebo controlled period + Phase B: 30-week active controlled period)

End point title	Percentage of participants who experienced at least one adverse event (Phase A: 24-week placebo controlled period + Phase B: 30-week active controlled period)
End point description:	
An adverse event is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. Presented data exclude data after glycemic rescue. APaT population consisted of all randomized participants who took at least 1 dose of trial treatment.	
End point type	Primary
End point timeframe:	
Up to 58 weeks (including 28 days following the last dose of study therapy)	

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Omarigliptin (Phase A) Omarigliptin (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	106	106		
Units: Percentage of participants				
number (not applicable)	77.4	78.3		

Statistical analyses

Statistical analysis title	Comparison of treatment groups
Statistical analysis description:	
Difference in percentages was based on Miettinen & Numinen method stratified by renal status stratum	
Comparison groups	Omarigliptin (Phase A) Omarigliptin (Phase B) v Omarigliptin (Phase A) Omarigliptin (Phase B)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	10.3

Primary: Percentage of participants who discontinued study drug due to an adverse event (Phase A: 24-week placebo controlled period + Phase B: 30-week active controlled period)

End point title	Percentage of participants who discontinued study drug due to an adverse event (Phase A: 24-week placebo controlled period + Phase B: 30-week active controlled period)
End point description:	
An adverse event is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. Presented data exclude data after glycemic rescue. APaT population consisted of all randomized participants who took at least 1 dose of trial treatment.	
End point type	Primary
End point timeframe:	
Up to 54 weeks	

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Omarigliptin (Phase A) Omarigliptin (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	106	106		
Units: Percentage of participants				
number (not applicable)	6.6	3.8		

Statistical analyses

Statistical analysis title	Comparison of treatment groups
Comparison groups	Omarigliptin (Phase A) Omarigliptin (Phase B) v Omarigliptin (Phase A) Omarigliptin (Phase B)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	9.8

Secondary: Change from baseline in fasting plasma glucose (FPG) at Week 24

End point title	Change from baseline in fasting plasma glucose (FPG) at Week 24

End point description:

Change from baseline in FPG at Week 24 was analyzed using cLDA method with a restriction of the same baseline mean across treatment groups. The cLDA model included terms for treatment, renal insufficiency stratum, baseline treatment with insulin stratum, time, the interaction of time by treatment, the interaction of time by renal insufficiency stratum, and the interaction of time by baseline treatment with insulin stratum. FAS population included all randomized participants who received at least 1 dose of study medication and had abaseline measurement or a post-randomization measurement in Phase A for the analysis endpoint subsequent to at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	106		
Units: mg/dL				
least squares mean (confidence interval 95%)	-24.6 (-35.6 to -13.6)	-20.7 (-31.8 to -9.5)		

Statistical analyses

Statistical analysis title	Comparision of treatment groups
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.54
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.5
upper limit	8.7

Secondary: Change from baseline in A1C at Week 54

End point title	Change from baseline in A1C at Week 54

End point description:

A1C is measured as a percent. Change from baseline in A1C at Week 54 was analyzed using cLDA method with a restriction of the same baseline mean across treatment groups. The cLDA model included terms for treatment, renal insufficiency stratum, baseline treatment with insulin stratum, time, the interaction of time by treatment, the interaction of time by renal insufficiency stratum, and the interaction of time by baseline treatment with insulin stratum. FAS population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement for the analysis endpoint subsequent to at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline and Week 54

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Omarigliptin (Phase A) Omarigliptin (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	106	106		
Units: Percent				
least squares mean (confidence interval 95%)	-0.79 (-1.1 to -0.47)	-0.83 (-1.16 to -0.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in FPG at Week 54

End point title	Change from baseline in FPG at Week 54

End point description:

Change from baseline in FPG at Week 54 was analyzed using cLDA method with a restriction of the same baseline mean across treatment groups. The cLDA model included terms for treatment, renal insufficiency stratum, baseline treatment with insulin stratum, time, the interaction of time by treatment, the interaction of time by renal insufficiency stratum, and the interaction of time by baseline treatment with insulin stratum. FAS population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement for the analysis endpoint subsequent to at least 1 dose ofstudy medication.

End point type	Secondary

End point timeframe:

Baseline and Week 54

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Omarigliptin (Phase A) Omarigliptin (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	106	106		
Units: mg/dL				
least squares mean (confidence interval 95%)	-19.3 (-36.5 to -2.1)	-16.4 (-34.4 to 1.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in estimated glomerular filtration rate (eGFR) at Week 24

End point title	Change from baseline in estimated glomerular filtration rate (eGFR) at Week 24

End point description:

Based on an cLDA model including terms for treatment, renal status stratum, treatment on insulin at screening stratum, time, the interaction of time by treatment, the interaction of time by renal status stratum, and the interaction of time by treatment on insulin at screening stratum, with the constraint that the mean baseline is the same for all treatment groups. Excluding data after glycemic rescue. APaT population consists of all randomized participants who took at least 1 dose of trial treatment. Excludes all participants on dialysis and data after initiation of dialysis.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: mL/min/1.73 m^2				
least squares mean (confidence interval 95%)	-0.5 (-2.1 to 1.2)	0 (-1.8 to 1.7)		

Statistical analyses

Statistical analysis title	Comparison of treatment groups
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.72
Method	cLDA
Parameter estimate	Difference in least squares means
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.9

Secondary: Change from baseline in eGFR at Week 54

End point title	Change from baseline in eGFR at Week 54

End point description:

Based on an cLDA model including terms for treatment, renal status stratum, treatment on insulin at screening stratum, time, the interaction of time by treatment, the interaction of time by renal status stratum, and the interaction of time by treatment on insulin at screening stratum, with the constraint that the mean baseline is the same for all treatment groups. Excluding data after glycemic rescue. APaT population consists of all randomized participants who took at least 1 dose of trial treatment. Excludes all participants on dialysis and data after initiation of dialysis.

End point type	Secondary

End point timeframe:

Baseline and Week 54

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Omarigliptin (Phase A) Omarigliptin (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	86	83		
Units: mL/min/1.73 m^2				
least squares mean (confidence interval	-2 (-4 to -0.1)	-2.3 (-4.3 to		

95%)	-0.2)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Phase A: up to 28 weeks (including 28-day follow-up); Phase A+B: up to 58 weeks (including 28-day follow-up)

Adverse event reporting additional description:

APaT population consists of all randomized participants who took at least 1 dose of study drug. Serious adverse events (SAEs) include data after glycemic rescue; non-serious adverse events exclude data after glycemic rescue. The AEs reported in the (Phase A) (Phase B) columns are a total of the AEs (SAEs) that occurred in Phases A and B.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Omarigliptin (Phase A)

Reporting group description:

Phase A: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 24 weeks.

Reporting group title	Placebo to omarigliptin (Phase A)

Reporting group description:

Phase A: matching placebo to omarigliptin orally once a week for 24 weeks.

Reporting group title	Omarigliptin (Phase A) Omarigliptin (Phase B)

Reporting group description:

Phase A: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 24 weeks. Phase B: omarigliptin 12.5 mg or 25 mg capsule orally once a week for 30 weeks. Participants who were not on background insulin therapy or who did not receive open-label glipizide or insulin as rescue therapy during Phase A of the study (Week 1 through Week 24) received matching placebo to glipizide in a blinded manner during Phase B of the study (Week 24 through Week 54).

Reporting group title	Placebo to omarigliptin (Phase A) Glipizide (Phase B)

Reporting group description:

Phase A: matching placebo to omarigliptin orally once a week for 24 weeks. Phase B: matching placebo to omarigliptin orally once a week for 30 weeks. Participants who were not on background insulin therapy or who did not receive open-label glipizide or insulin as rescue therapy during Phase A of the study (Week 1 through Week 24) received glipizide 2.5 daily up to a maximum of 20 mg daily (based on glycemic control) in a blinded manner during Phase B of the study (Week 24 through Week 54).

Serious adverse events	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)	Omarigliptin (Phase A) Omarigliptin (Phase B)
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 106 (9.43%)	13 / 106 (12.26%)	22 / 106 (20.75%)
number of deaths (all causes)	1	1	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			

subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	0 / 106 (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
Arteriovenous fistula			
subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	0 / 106 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian artery stenosis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device malfunction			
subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	0 / 106 (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

General physical health deterioration			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular stent restenosis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 106 (0.00%)	2 / 106 (1.89%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary congestion			
subjects affected / exposed	1 / 106 (0.94%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	0 / 106 (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
Acute pulmonary oedema			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			

subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood glucose decreased			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Coronary artery restenosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Arteriovenous fistula site complication			
subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	0 / 106 (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			
Cardiac disorder			
subjects affected / exposed	1 / 106 (0.94%)	0 / 106 (0.00%)	1 / 106 (0.94%)
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 acute			
subjects affected / exposed	1 / 106 (0.94%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cardio-respiratory arrest			
subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	0 / 106 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	0 / 106 (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
Acute coronary syndrome			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
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			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 106 (0.94%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
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			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	0 / 106 (0.00%)	1 / 106 (0.94%)	0 / 106 (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
Acute kidney injury			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	2 / 106 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	1 / 106 (0.94%)	0 / 106 (0.00%)	3 / 106 (2.83%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Gouty arthritis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 106 (0.94%)	1 / 106 (0.94%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis C			
subjects affected / exposed	1 / 106 (0.94%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 106 (0.94%)	1 / 106 (0.94%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia			
subjects affected / exposed	0 / 106 (0.00%)	2 / 106 (1.89%)	0 / 106 (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
Bronchitis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal sepsis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected dermal cyst			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Upper respiratory tract infection			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyperkalaemia			
subjects affected / exposed	2 / 106 (1.89%)	0 / 106 (0.00%)	2 / 106 (1.89%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid retention			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 106 (0.00%)	2 / 106 (1.89%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 106 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo to omarigliptin (Phase A) Glipizide (Phase B)		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 106 (20.75%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			

subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arteriovenous fistula			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subclavian artery stenosis			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Device malfunction			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General physical health deterioration				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular stent restenosis				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Benign prostatic hyperplasia				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary congestion				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute pulmonary oedema				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Aspiration				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory arrest				

subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Investigations			
Blood glucose decreased			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Coronary artery restenosis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Arteriovenous fistula site complication				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac disorder				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Coronary artery stenosis				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute coronary syndrome				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Atrial fibrillation			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemiparesis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic kidney disease			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Gouty arthritis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis C			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Pneumonia			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterococcal sepsis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected dermal cyst			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Hyperkalaemia			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fluid retention			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gout			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)	Omarigliptin (Phase A) Omarigliptin (Phase B)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 106 (22.64%)	25 / 106 (23.58%)	44 / 106 (41.51%)
Investigations			
Blood creatinine phosphokinase increased			

subjects affected / exposed	4 / 106 (3.77%)	3 / 106 (2.83%)	6 / 106 (5.66%)
occurrences (all)	4	3	6
Blood glucose increased			
subjects affected / exposed	1 / 106 (0.94%)	4 / 106 (3.77%)	7 / 106 (6.60%)
occurrences (all)	1	4	25
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 106 (0.00%)	2 / 106 (1.89%)	4 / 106 (3.77%)
occurrences (all)	0	2	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 106 (3.77%)	2 / 106 (1.89%)	6 / 106 (5.66%)
occurrences (all)	5	2	7
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 106 (3.77%)	8 / 106 (7.55%)	4 / 106 (3.77%)
occurrences (all)	4	9	4
Nasopharyngitis			
subjects affected / exposed	2 / 106 (1.89%)	4 / 106 (3.77%)	3 / 106 (2.83%)
occurrences (all)	2	5	3
Urinary tract infection			
subjects affected / exposed	3 / 106 (2.83%)	2 / 106 (1.89%)	7 / 106 (6.60%)
occurrences (all)	3	2	8
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	21 / 106 (19.81%)	19 / 106 (17.92%)	27 / 106 (25.47%)
occurrences (all)	84	88	138

Non-serious adverse events	Placebo to omarigliptin (Phase A) Glipizide (Phase B)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 106 (49.06%)		
Investigations			
Blood creatinine phosphokinase increased			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences (all)	2		

Blood glucose increased subjects affected / exposed occurrences (all)	6 / 106 (5.66%) 6		
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all)	7 / 106 (6.60%) 7		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	3 / 106 (2.83%) 3		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	12 / 106 (11.32%) 14 6 / 106 (5.66%) 7 3 / 106 (2.83%) 3		
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	25 / 106 (23.58%) 161		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 July 2012	Amendment 1: The primary reason for the amendment was to change the time frame for the primary endpoint from 18 weeks to 24 weeks.
20 November 2012	Amendment 2: The primary reasons for the amendment were to modify inclusion criteria regarding contraception, to modify text regarding the use of glipizide, and added details on enrollment of participants with moderate chronic renal insufficiency.
13 February 2013	Amendment 3: The primary reason for the amendment was to add discontinuation criteria of pancreatitis.
26 April 2013	Amendment 4: The primary reasons for the amendment were to modify objectives, hypotheses, power calculations and endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported