Clinical trial results:
A Multicenter, Phase III, Randomized, Placebo-Controlled Trial to Assess the Safety and Efficacy of MK-3102 Monotherapy in Subjects with Type 2 Diabetes Mellitus and Inadequate Glycemic Control

Summary

EudraCT number	2012-003626-24
Trial protocol	HU DE NL IT BG
Global end of trial date	19 June 2015

Results information

Result version number	v1 (current)
This version publication date	26 June 2016
First version publication date	26 June 2016

Trial information

Trial identification

Sponsor protocol code	3102-011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01717313
WHO universal trial number (UTN)	-
Other trial identifiers	Protocol number: MK-3102-011

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 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 June 2015
Global end of trial reached?	Yes
Global end of trial date	19 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were to assess the effect of treatment with omarigliptin (MK-3102) compared with placebo on hemoglobin A1C (A1C) after 24 weeks and to assess the safety and tolerability of omarigliptin. The primary hypothesis of this study is that after 24 weeks, treatment with omarigliptin compared with placebo provides greater reduction in A1C.

Care must be taken in the interpretation of the results in this study as the non-protocol-specific prohibited use of metformin among a number of participants may have impacted the safety and efficacy results disproportionally among study groups.

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 measures defined for this individual study were in place for the protection of trial subjects. In Phase A, glycemic rescue was with open-label metformin. In Phase B, glycemic rescue was with open-label glimepiride; if glimepiride was not available in the country of the investigator site, another locally available sulfonylurea (SU) was used.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 December 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	Bulgaria: 10
Country: Number of subjects enrolled	Germany: 36
Country: Number of subjects enrolled	Hungary: 44
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Netherlands: 17
Country: Number of subjects enrolled	Philippines: 36
Country: Number of subjects enrolled	Romania: 49
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Taiwan: 40
Country: Number of subjects enrolled	United States: 72
Worldwide total number of subjects	329
EEA total number of subjects	169

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)	255
From 65 to 84 years	74
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants had Type 2 diabetes mellitus (T2DM) and must be >=18 years of age (for India >=18 and <=65 years of age) on the day of signing the informed consent form.

Pre-assignment

Screening details:

The double-blind treatment period included a 24-week placebo-controlled (omarigliptin/omarigliptin-matching placebo) period (Phase A) and a 30-week active-controlled period with blinded metformin/metformin matching placebo (Phase B).

Period 1

Period 1 title	Phase A (Weeks 0 to 24)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Omarigliptin

Arm description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks (Phase A) followed by omarigliptin 25 mg administered orally once a week plus placebo to metformin daily (Phase B). Open-label metformin daily was to be initiated for participants meeting protocol-specified glycemic criteria during Phase A, but was otherwise prohibited. Open-label glimepiride daily may be initiated as glycemic rescue therapy during Phase B.

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:

Omarigliptin 25 mg, oral, once a week for 54 weeks

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Fortamet®, Glucophage®, Glucophage® XR, Glumetza®, Riomet®, Metgluco®, Glycoran®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary, participants may have glycemic rescue therapy initiated with open-label metformin in Phase A. Participants in the placebo treatment group who were not rescued with open-label metformin will be switched to blinded metformin (starting at 500 mg b.i.d with up-titration to 1000 mg b.i.d) in a blinded manner in Phase B. Subjects who were previously rescued with open-label metformin in Phase A will continue in the trial on open-label metformin.

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

Dosage and administration details:

During Phase B of the study, participants in the omarigliptin treatment group who did not initiate glycemic rescue therapy during Phase A will receive placebo to metformin for 30 weeks (Phase B of the study).

Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	Armaryl®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary during Phase B of the study, participants will initiate open-label glimepiride as glycemic rescue therapy.

Arm title	Placebo to Omarigliptin

Arm description:

Placebo to omarigliptin administered orally once a week for 24 weeks (Phase A) followed by placebo to omarigliptin administered orally once a week plus metformin daily for an additional 30 weeks (Phase B). Open-label metformin daily was to be initiated for participants meeting protocol-specified glycemic criteria during Phase A, but was otherwise prohibited. Open-label glimepiride daily may be initiated as glycemic rescue therapy during Phase B.

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

Dosage and administration details:

Placebo to omarigliptin, oral, for 54 weeks.

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Fortamet®, Glucophage®, Glucophage® XR, Glumetza®, Riomet®, Metgluco®, Glycoran®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary, participants may have glycemic rescue therapy initiated with open-label metformin. Participants in the placebo treatment group who were not rescued with open-label metformin will be switched to blinded metformin (starting at 500 mg b.i.d with up-titration to 1000 mg b.i.d) in a blinded manner. Subjects who were previously rescued with open-label metformin in Phase A will continue in the trial on open-label metformin.

Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	Armaryl®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary during Phase B of the study, participants will initiate open-label glimepiride as glycemic rescue therapy.

Number of subjects in period 1	Omarigliptin	Placebo to Omarigliptin
Started	165	164
Completed	147	151
Not completed	18	13
Consent withdrawn by subject	12	6
Adverse event, non-fatal	4	2
Non-Compliance with study Drug	1	1
Death	-	1
Lost to follow-up	1	3

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Omarigliptin

Arm description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks (Phase A) followed by omarigliptin 25 mg administered orally plus placebo to metformin (Phase B). Open-label metformin may be initiated as glycemic rescue therapy during Phase A. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

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:

Omarigliptin 25 mg, oral, once a week for 54 weeks

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Fortamet®, Glucophage®, Glucophage® XR, Glumetza®, Riomet®, Metgluco®, Glycoran®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary, participants may have glycemic rescue therapy initiated with open-label metformin in Phase A. Participants in the placebo treatment group who were not rescued with open-label metformin will be switched to blinded metformin (starting at 500 mg b.i.d with up-titration to 1000 mg b.i.d) in a blinded manner in Phase B. Subjects who were previously rescued with open-label metformin in Phase A will continue in the trial on open-label metformin.

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

Dosage and administration details:

During Phase B of the study, participants in the omarigliptin treatment group who did not initiate glycemic rescue therapy during Phase A will receive placebo to metformin for 30 weeks (Phase B of the study).

Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	Armaryl®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary during Phase B of the study, participants will initiate open-label glimepiride as glycemic rescue therapy.

Arm title	Placebo to Omarigliptin

Arm description:

Placebo to omarigliptin administered orally once a week for 24 weeks (Phase A) followed by placebo to omarigliptin administered orally once a week plus metformin for an additional 30 weeks (Phase B). Open-label metformin may be initiated as glycemic rescue therapy during Phase A. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

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

Dosage and administration details:

Placebo to omarigliptin, oral, for 54 weeks.

Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	Armaryl®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary during Phase B of the study, participants will initiate open-label glimepiride as glycemic rescue therapy.

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Fortamet®, Glucophage®, Glucophage® XR, Glumetza®, Riomet®, Metgluco®, Glycoran®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary, participants may have glycemic rescue therapy initiated with open-label metformin. Participants in the placebo treatment group who were not rescued with open-label metformin will be switched to blinded metformin (starting at 500 mg b.i.d with up-titration to 1000 mg b.i.d) in a blinded manner. Subjects who were previously rescued with open-label metformin in Phase A will continue in the trial on open-label metformin.

Number of subjects in period 2	Omarigliptin	Placebo to Omarigliptin
Started	147	151
Completed	146	151
Not completed	1	0
Completed Phase A Did Not Enter Phase B	1	-

Period 3

Period 3 title	Phase B (Weeks 24 to 54)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Omarigliptin

Arm description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks (Phase A) followed by omarigliptin 25 mg administered orally plus placebo to metformin (Phase B). Open-label metformin may be initiated as glycemic rescue therapy during Phase A. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

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:

Omarigliptin 25 mg, oral, once a week for 54 weeks

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Fortamet®, Glucophage®, Glucophage® XR, Glumetza®, Riomet®, Metgluco®, Glycoran®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary, participants may have glycemic rescue therapy initiated with open-label metformin in Phase A. Participants in the placebo treatment group who were not rescued with open-label metformin will be switched to blinded metformin (starting at 500 mg b.i.d with up-titration to 1000 mg b.i.d) in a blinded manner in Phase B. Subjects who were previously rescued with open-label metformin in Phase A will continue in the trial on open-label metformin.

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

Dosage and administration details:

During Phase B of the study, participants in the omarigliptin treatment group who did not initiate

glycemic rescue therapy during Phase A will receive placebo to metformin for 30 weeks (Phase B of the study).

Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	Armaryl®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary during Phase B of the study, participants will initiate open-label glimepiride as glycemic rescue therapy.

Arm title	Placebo to Omarigliptin

Arm description:

Placebo to omarigliptin administered orally once a week for 24 weeks (Phase A) followed by placebo to omarigliptin administered orally once a week plus metformin for an additional 30 weeks (Phase B). Open-label metformin may be initiated as glycemic rescue therapy during Phase A. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

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

Dosage and administration details:

Placebo to omarigliptin, oral, for 54 weeks.

Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	Armaryl®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary during Phase B of the study, participants will initiate open-label glimepiride as glycemic rescue therapy.

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Fortamet®, Glucophage®, Glucophage® XR, Glumetza®, Riomet®, Metgluco®, Glycoran®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

If necessary, participants may have glycemic rescue therapy initiated with open-label metformin. Participants in the placebo treatment group who were not rescued with open-label metformin will be switched to blinded metformin (starting at 500 mg b.i.d with up-titration to 1000 mg b.i.d) in a blinded manner. Subjects who were previously rescued with open-label metformin in Phase A will continue in the trial on open-label metformin.

Number of subjects in period 3	Omarigliptin	Placebo to Omarigliptin
Started	146	151
Completed	134	135
Not completed	12	16
Consent withdrawn by subject	7	9

Study Terminated by Sponsor	4	4
Lost to follow-up	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Omarigliptin
Reporting group description:	
Omarigliptin 25 mg capsule administered orally once a week for 24 weeks (Phase A) followed by omarigliptin 25 mg administered orally once a week plus placebo to metformin daily (Phase B). Open-label metformin daily was to be initiated for participants meeting protocol-specified glycemic criteria during Phase A, but was otherwise prohibited. Open-label glimepiride daily may be initiated as glycemic rescue therapy during Phase B.	
Reporting group title	Placebo to Omarigliptin
Reporting group description:	
Placebo to omarigliptin administered orally once a week for 24 weeks (Phase A) followed by placebo to omarigliptin administered orally once a week plus metformin daily for an additional 30 weeks (Phase B). Open-label metformin daily was to be initiated for participants meeting protocol-specified glycemic criteria during Phase A, but was otherwise prohibited. Open-label glimepiride daily may be initiated as glycemic rescue therapy during Phase B.	

Reporting group values	Omarigliptin	Placebo to Omarigliptin	Total
Number of subjects	165	164	329
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)	129	126	255
From 65-84 years	36	38	74
85 years and over	0	0	0
Age Continuous | Units: Years			
arithmetic mean	57.4	57	
standard deviation	± 9.2	± 9.7	-
Gender, Male/Female Units: Participants			
Female	70	67	137
Male	95	97	192

End points

End points reporting groups

Reporting group title	Omarigliptin

Reporting group description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks (Phase A) followed by omarigliptin 25 mg administered orally once a week plus placebo to metformin daily (Phase B). Open-label metformin daily was to be initiated for participants meeting protocol-specified glycemic criteria during Phase A, but was otherwise prohibited. Open-label glimepiride daily may be initiated as glycemic rescue therapy during Phase B.

Reporting group title	Placebo to Omarigliptin

Reporting group description:

Placebo to omarigliptin administered orally once a week for 24 weeks (Phase A) followed by placebo to omarigliptin administered orally once a week plus metformin daily for an additional 30 weeks (Phase B). Open-label metformin daily was to be initiated for participants meeting protocol-specified glycemic criteria during Phase A, but was otherwise prohibited. Open-label glimepiride daily may be initiated as glycemic rescue therapy during Phase B.

Reporting group title	Omarigliptin

Reporting group description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks (Phase A) followed by omarigliptin 25 mg administered orally plus placebo to metformin (Phase B). Open-label metformin may be initiated as glycemic rescue therapy during Phase A. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

Reporting group title	Placebo to Omarigliptin

Reporting group description:

Placebo to omarigliptin administered orally once a week for 24 weeks (Phase A) followed by placebo to omarigliptin administered orally once a week plus metformin for an additional 30 weeks (Phase B). Open-label metformin may be initiated as glycemic rescue therapy during Phase A. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

Reporting group title	Omarigliptin

Reporting group description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks (Phase A) followed by omarigliptin 25 mg administered orally plus placebo to metformin (Phase B). Open-label metformin may be initiated as glycemic rescue therapy during Phase A. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

Reporting group title	Placebo to Omarigliptin

Reporting group description:

Placebo to omarigliptin administered orally once a week for 24 weeks (Phase A) followed by placebo to omarigliptin administered orally once a week plus metformin for an additional 30 weeks (Phase B). Open-label metformin may be initiated as glycemic rescue therapy during Phase A. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

Subject analysis set title	Omarigliptin - Overall Study (Phase A+B) - FAS Population
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set (FAS) comprised of all participants who received at least one dose of trial therapy and have a baseline measurement or a post-randomization measurement.

Subject analysis set title	Placebo to Omar. - Overall Study (Phase A+B) - FAS Pop.
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS comprised of all participants who received at least one dose of trial therapy and have a baseline measurement or a post-randomization measurement.

Subject analysis set title	Omarigliptin - Overall Study (Phase A+B) - Safety Pop.
Subject analysis set type	Safety analysis

Subject analysis set description:

The APaT population included all participants who received at least one dose of study drug.

Subject analysis set title	Placebo to Omar. - Overall Study (Phase A+B) - Safety Pop.
Subject analysis set type	Safety analysis

Subject analysis set description:

The APaT population included all participants who received at least one dose of study drug.

Subject analysis set title	Omarigliptin - Overall Study (Phase A+B) - Per-Protocol Pop.
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol population excluded participants from the FAS population who either had <75% drug compliance or used a prohibited medication (including metformin).

Subject analysis set title	PBO to Omar. - Overall Study (Phase A+B) - Per-Protocol Pop.
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol population excluded participants from the FAS population who either had <75% drug compliance or used a prohibited medication (including metformin).

Primary: Change from baseline in hemoglobin A1c (A1C) at Week 24 (Phase A, FAS Population)

End point title	Change from baseline in hemoglobin A1c (A1C) at Week 24 (Phase A, FAS Population)

End point description:

The Full Analysis Set (FAS) population was all participants who received at least 1 dose of study treatment and have a baseline measurement for the analysis endpoint and a post-randomization measurement for the analysis endpoint after at least 1 dose of study treatment.

Because it was discovered that in another omarigliptin study (MK-3102-028, NCT01814748) subjects had taken metformin (prohibited per protocol, and taken without investigator knowledge), after unblinding of Phase A of this study, an analysis of metformin levels was performed on stored Week 18 blood samples. Of the subjects not rescued with metformin prior to Week 18, 10% in the omarigliptin group and 20% in the placebo group had levels showing that they were taking metformin (prohibited per protocol). The use of prohibited metformin disproportionately by the placebo group may have resulted in a smaller than expected treatment effect for efficacy outcome measures (see post-hoc analysis).

End point type	Primary

End point timeframe:

Baseline and Week 24

End point values	Omarigliptin	Placebo to Omarigliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	164		
Units: Percent				
least squares mean (confidence interval 95%)	-0.49 (-0.73 to -0.24)	-0.1 (-0.34 to 0.14)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Constrained Longitudinal Data Analysis included terms for treatment, time, prior antihyperglycemic agent (AHA) therapy status, interaction of time by treatment, and time by prior AHA therapy status

Comparison groups	Omarigliptin v Placebo to Omarigliptin

Number of subjects included in analysis	329
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the least squares means
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	-0.19

Primary: Percentage of participants who experienced at least one adverse event in Phase A (excluding data after glycemic rescue, Safety Population)

End point title	Percentage of participants who experienced at least one adverse event in Phase A (excluding data after glycemic rescue, Safety Population)

End point description:

An adverse event is any untoward medical occurrence in a participant administered study drug which does not necessarily have a causal relationship with the treatment. Adverse events may include the onset of new illness and the exacerbation of preexisting conditions. The All-Participants-as-Treated (APaT) population included all participants who received at least one dose of study drug.

This analysis may have been confounded by use of prohibited metformin (see results above for description of the use of prohibited metformin).

End point type	Primary

End point timeframe:

Up to 27 weeks

End point values	Omarigliptin	Placebo to Omarigliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	164		
Units: Percentage of participants				
number (not applicable)	41.8	50		

Statistical analyses

Statistical analysis title	Differences in Percentages
Comparison groups	Omarigliptin v Placebo to Omarigliptin

Number of subjects included in analysis	329
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen method
Parameter estimate	Differences in percentages
Point estimate	-8.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.8
upper limit	2.6

Primary: Percentage of participants who discontinued from the study drug due to an adverse event in Phase A (excluding data after glycemic rescue, Safety Population)

End point title	Percentage of participants who discontinued from the study drug due to an adverse event in Phase A (excluding data after glycemic rescue, Safety Population)

End point description:

An adverse event is any untoward medical occurrence in a participant administered study drug which does not necessarily have a causal relationship with the treatment. Adverse events may include the onset of new illness and the exacerbation of preexisting conditions. The APaT population included all participants who received at least one dose of study drug.

This analysis may have been confounded by use of prohibited metformin (see results above for description of the use of prohibited metformin).

End point type	Primary

End point timeframe:

Up to 24 weeks

End point values	Omarigliptin	Placebo to Omarigliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	164		
Units: Percentage of participants				
number (not applicable)	2.4	1.8		

Statistical analyses

Statistical analysis title	Difference in Percentages
Comparison groups	Omarigliptin v Placebo to Omarigliptin
Number of subjects included in analysis	329
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentages
Point estimate	0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	4.5

Primary: Percentage of participants who experienced at least one adverse event (Phase A + Phase B, excluding data after glycemic rescue, Safety Population)

End point title	Percentage of participants who experienced at least one adverse event (Phase A + Phase B, excluding data after glycemic rescue, Safety Population)

End point description:

An adverse event is any untoward medical occurrence in a participant administered study drug which does not necessarily have a causal relationship with the treatment. Adverse events may include the onset of new illness and the exacerbation of preexisting conditions. The APaT population included all participants who received at least one dose of study drug.

This analysis may have been confounded by use of prohibited metformin (see results above for description of the use of prohibited metformin).

End point type	Primary

End point timeframe:

Up to 57 weeks

End point values	Omarigliptin - Overall Study (Phase A+B) - Safety Pop.	Placebo to Omar. - Overall Study (Phase A+B) - Safety Pop.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	164		
Units: Percentage of participants				
number (not applicable)	54.5	60.4		

Statistical analyses

Statistical analysis title	Difference in percentages vs. placebo
Comparison groups	Omarigliptin - Overall Study (Phase A+B) - Safety Pop. v Placebo to Omar. - Overall Study (Phase A+B) - Safety Pop.
Number of subjects included in analysis	329
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentages vs. placebo
Point estimate	-5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.4
upper limit	4.9

Primary: Percentage of participants who discontinued from the study drug due to an adverse event (Phase A + Phase B, excluding data after glycemic rescue, Safety Population)

End point title	Percentage of participants who discontinued from the study drug due to an adverse event (Phase A + Phase B, excluding data after glycemic rescue, Safety Population)

End point description:

An adverse event is any untoward medical occurrence in a participant administered study drug which does not necessarily have a causal relationship with the treatment. Adverse events may include the onset of new illness and the exacerbation of preexisting conditions. The APaT population included all participants who received at least one dose of study drug.

This analysis may have been confounded by use of prohibited metformin (see results above for description of the use of prohibited metformin).

End point type	Primary

End point timeframe:

Up to 54 weeks

End point values	Omarigliptin - Overall Study (Phase A+B) - Safety Pop.	Placebo to Omar. - Overall Study (Phase A+B) - Safety Pop.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	164		
Units: Percentage of participants				
number (not applicable)	3	2.4		

Statistical analyses

Statistical analysis title	Difference in percentages vs. placebo
Comparison groups	Omarigliptin - Overall Study (Phase A+B) - Safety Pop. v Placebo to Omar. - Overall Study (Phase A+B) - Safety Pop.
Number of subjects included in analysis	329
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentages vs. placebo
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	4.8

Primary: Change from baseline in hemoglobin A1c (A1C) at Week 24 (Phase A, Per-Protocol population)

End point title	Change from baseline in hemoglobin A1c (A1C) at Week 24 (Phase A, Per-Protocol population)

End point description:

A1C is a 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 24 A1C minus the Week 0 A1C. The Per-Protocol population excluded participants from the FAS population who either had <75% drug compliance or used a prohibited medication (including metformin). A post-hoc sensitivity analysis was performed that excluded participants in both treatment groups who were found to have used prohibited metformin (see results above for a description of the use of prohibited metformin).

End point type	Primary

End point timeframe:

Baseline and Week 24

End point values	Omarigliptin - Overall Study (Phase A+B) - Per-Protocol Pop.	PBO to Omar. - Overall Study (Phase A+B) - Per-Protocol Pop.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	149	131		
Units: Percent				
least squares mean (confidence interval 95%)	-0.54 (-0.68 to -0.39)	0 (-0.17 to 0.16)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Constrained Longitudinal Data Analysis included terms for treatment, time, prior antihyperglycemic agent (AHA) therapy status, interaction of time by treatment, and time by prior AHA therapy status

Comparison groups	Omarigliptin - Overall Study (Phase A+B) - Per-Protocol Pop. v PBO to Omar. - Overall Study (Phase A+B) - Per-Protocol Pop.
Number of subjects included in analysis	280
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the least squares means
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	-0.32

Secondary: Change from baseline in fasting plasma glucose (FPG) at Week 24 (Phase A, FAS Population)

End point title	Change from baseline in fasting plasma glucose (FPG) at Week 24 (Phase A, FAS Population)

End point description:

The FAS population received at least 1 dose of study treatment and had a baseline measurement or a post-randomization measurement for the analysis endpoint after at least 1 dose of study treatment.

Because it was discovered that in another omarigliptin study (MK-3102-028, NCT01814748) subjects had taken metformin (prohibited per protocol, and taken without investigator knowledge), after unblinding of Phase A of this study, an analysis of metformin levels was performed on stored Week 18 blood samples. Of the subjects not rescued with metformin prior to Week 18, 10% in the omarigliptin group and 20% in the placebo group had levels showing that they were taking metformin (prohibited per protocol). The use of prohibited metformin disproportionately by the placebo group may have resulted in a smaller than expected treatment effect for efficacy outcome measures (see post-hoc analysis).

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Omarigliptin	Placebo to Omarigliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	164		
Units: mg/dL				
least squares mean (confidence interval 95%)	-12.8 (-25.2 to -0.3)	-2.5 (-15 to 10.1)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Constrained Longitudinal Data Analysis included terms for treatment, time, prior AHA therapy status, the interaction of time by treatment, and time by prior AHA therapy status

Comparison groups	Omarigliptin v Placebo to Omarigliptin
Number of subjects included in analysis	329
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.036
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the least squares means
Point estimate	-10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.9
upper limit	-0.7

Secondary: Percentage of participants who achieve an A1C goal of <7% (53 mmol/mol) at Week 24 (Phase A, FAS Population)

End point title	Percentage of participants who achieve an A1C goal of <7% (53 mmol/mol) at Week 24 (Phase A, FAS Population)

End point description:

The FAS population received at least 1 dose of study treatment and had a baseline measurement for the analysis endpoint and a post-randomization measurement for the analysis endpoint after at least 1 dose of study treatment, and estimated using standard multiple imputation techniques.

Because it was discovered that in another omarigliptin study (MK-3102-028, NCT01814748) subjects had taken metformin (prohibited per protocol, and taken without investigator knowledge), after unblinding of Phase A of this study, an analysis of metformin levels was performed on stored Week 18 blood samples. Of the subjects not rescued with metformin prior to Week 18, 10% in the omarigliptin group and 20% in the placebo group had levels showing that they were taking metformin (prohibited per protocol). The use of prohibited metformin disproportionately by the placebo group may have resulted in a smaller than expected treatment effect for efficacy outcome measures (see post-hoc analysis).

End point type	Secondary

End point timeframe:

Week 24

End point values	Omarigliptin	Placebo to Omarigliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	164		
Units: Percentage of participants				
number (confidence interval 95%)	36.5 (29.3 to 44.5)	16.3 (11.3 to 22.9)		

Statistical analyses

Statistical analysis title	Between-group Rate Difference
Comparison groups	Omarigliptin v Placebo to Omarigliptin
Number of subjects included in analysis	329
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Between-group rate difference
Point estimate	20.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.5
upper limit	29.8

Secondary: Percentage of participants who achieve an A1C goal of <7% at Week 54 (Phase A + Phase B, FAS Population)

End point title	Percentage of participants who achieve an A1C goal of <7% at Week 54 (Phase A + Phase B, FAS Population)

End point description:

The FAS population was comprised of all participants who received at least 1 dose of study treatment and have a baseline measurement or a post-randomization measurement for the analysis endpoint after at least 1 dose of study treatment.

The results of the study at Week 54 may have been confounded by use of prohibited metformin (see results above for description of the use of prohibited metformin).

End point type	Secondary

End point timeframe:

Week 54

End point values	Omarigliptin - Overall Study (Phase A+B) - FAS Population	Placebo to Omar. - Overall Study (Phase A+B) - FAS Pop.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	164		
Units: Percentage of participants				
number (confidence interval 95%)	33.8 (26.8 to 41.5)	43.8 (36.2 to 51.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in 2-hour post meal glucose (PMG) at Week 24 (Phase A, FAS Population)

End point title	Change from baseline in 2-hour post meal glucose (PMG) at Week 24 (Phase A, FAS Population)

End point description:

The FAS population was comprised of all participants who received at least 1 dose of study treatment and have a baseline measurement or a post-randomization measurement for the analysis endpoint after at least 1 dose of study treatment.

Because it was discovered that in another omarigliptin study (MK-3102-028, NCT01814748) subjects had taken metformin (prohibited per protocol, and taken without investigator knowledge), after unblinding of Phase A of this study, an analysis of metformin levels was performed on stored Week 18 blood samples. Of the subjects not rescued with metformin prior to Week 18, 10% in the omarigliptin group and 20% in the placebo group had levels showing that they were taking metformin (prohibited per protocol). The use of prohibited metformin disproportionately by the placebo group may have resulted in a smaller than expected treatment effect for efficacy outcome measures (see post-hoc analysis).

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Omarigliptin	Placebo to Omarigliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	102		
Units: mg/dL				
least squares mean (confidence interval 95%)	-25.6 (-56 to 4.8)	-13.9 (-43.5 to 15.6)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Constrained Longitudinal Data Analysis included terms for treatment, time, prior AHA therapy status, the interaction of time by treatment, and time by prior AHA therapy status

Comparison groups	Omarigliptin v Placebo to Omarigliptin
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.177
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the least squares means
Point estimate	-11.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.6
upper limit	5.3

Secondary: Change from baseline in A1C at Week 54 (Phase A + Phase B, FAS Population)

End point title	Change from baseline in A1C at Week 54 (Phase A + Phase B, FAS Population)

End point description:

A1C (%) reports average blood glucose levels over prolonged periods of time. The FAS population received at least 1 dose of study treatment and had a baseline measurement or a post-randomization measurement for the analysis endpoint after at least 1 dose of study treatment.

The results of the study at Week 54 may have been confounded by use of prohibited metformin (see results above for description of the use of prohibited metformin).

End point type	Secondary

End point timeframe:

Baseline and Week 54

End point values	Omarigliptin - Overall Study (Phase A+B) - FAS Population	Placebo to Omar. - Overall Study (Phase A+B) - FAS Pop.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	164		
Units: Percent				
least squares mean (confidence interval 95%)	-0.4 (-0.67 to -0.13)	-0.8 (-1.07 to -0.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in FPG at Week 54 (Phase A + Phase B, FAS Population)

End point title	Change from baseline in FPG at Week 54 (Phase A + Phase B, FAS Population)

End point description:

Blood glucose was measured on a fasting basis (FPG Week 54 - Week 0). The FAS population received at least 1 dose of study treatment and had a baseline measurement or a post-randomization measurement for the analysis endpoint after at least 1 dose of study treatment.

The results of the study at Week 54 may have been confounded by use of prohibited metformin (see results above for description of the use of prohibited metformin).

End point type	Secondary

End point timeframe:

Baseline and Week 54

End point values	Omarigliptin - Overall Study (Phase A+B) - FAS Population	Placebo to Omar. - Overall Study (Phase A+B) - FAS Pop.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	164		
Units: mg/dL				
least squares mean (confidence interval 95%)	-8.3 (-19.8 to 3.2)	-21.1 (-32.7 to -9.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve an A1C goal of <6.5% (48 mmol/mol) at Week 24 (Phase A, FAS Population)

End point title	Percentage of participants who achieve an A1C goal of <6.5% (48 mmol/mol) at Week 24 (Phase A, FAS Population)

End point description:

A1C (%) reports average blood glucose levels over prolonged periods of time. The FAS population received at least 1 dose of study treatment and had a baseline measurement or a post-randomization measurement for the analysis endpoint after at least 1 dose of study treatment. Because it was discovered that in another omarigliptin study (MK-3102-028, NCT01814748) subjects had taken metformin (prohibited per protocol, and taken without investigator knowledge), after unblinding of Phase A of this study, an analysis of metformin levels was performed on stored Week 18 blood samples. Of the subjects not rescued with metformin prior to Week 18, 10% in the omarigliptin group and 20% in the placebo group had levels showing that they were taking metformin (prohibited per protocol). The use of prohibited metformin disproportionately by the placebo group may have resulted in a smaller than expected treatment effect for efficacy outcome measures (see post-hoc analysis).

End point type	Secondary

End point timeframe:

Week 24

End point values	Omarigliptin	Placebo to Omarigliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	164		
Units: Percentage of participants				
number (confidence interval 95%)	16.4 (11.4 to 23.1)	5 (2.5 to 9.6)		

Statistical analyses

Statistical analysis title	Between-group Rate Difference
Comparison groups	Omarigliptin v Placebo to Omarigliptin
Number of subjects included in analysis	329
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Between-group rate difference
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.8
upper limit	18.6

Secondary: Percentage of participants who achieve an A1C goal of <6.5% at Week 54 (Phase A + Phase B, FAS Population)

End point title	Percentage of participants who achieve an A1C goal of <6.5% at Week 54 (Phase A + Phase B, FAS Population)

End point description:

A1C (%) reports average blood glucose levels over prolonged periods of time. The FAS population received at least 1 dose of study treatment and had a baseline measurement or a post-randomization measurement for the analysis endpoint after at least 1 dose of study treatment.

The results of the study at Week 54 may have been confounded by use of prohibited metformin (see results above for description of the use of prohibited metformin).

End point type	Secondary

End point timeframe:

Week 54

End point values	Omarigliptin - Overall Study (Phase A+B) - FAS Population	Placebo to Omar. - Overall Study (Phase A+B) - FAS Pop.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	164		
Units: Percentage of participants				
number (confidence interval 95%)	14.5 (9.7 to 21.2)	20.6 (14.8 to 28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in FPG at Week 24 (Phase A, Per-Protocol population)

End point title	Change from baseline in FPG at Week 24 (Phase A, Per-Protocol population)

End point description:

Blood glucose was measured on a fasting basis (collected after a 10-hour fast). FPG is expressed as mg/dL. This change from baseline reflects the FPG level at Week 24 minus the FPG level at Week 0. The Per-Protocol population excluded participants from the FAS population who either had <75% drug compliance or used a prohibited medication (including metformin).A post-hoc sensitivity analysis was performed that excluded participants in both treatment groups who were found to have used prohibited metformin (see results above for a description of the use of prohibited metformin).

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Omarigliptin	Placebo to Omarigliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	131		
Units: mg/dL				
least squares mean (confidence interval 95%)	-15.5 (-22.5 to -8.4)	-2.2 (-10.9 to 6.4)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Constrained Longitudinal Data Analysis included terms for treatment, time, prior AHA therapy status, the interaction of time by treatment, and time by prior AHA therapy status

Comparison groups	Omarigliptin v Placebo to Omarigliptin
Number of subjects included in analysis	280
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.014
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the least squares means
Point estimate	-13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.7
upper limit	-2.7

Secondary: Change from baseline in 2-hour PMG at Week 24 (Phase A, Per-Protocol Population)

End point title	Change from baseline in 2-hour PMG at Week 24 (Phase A, Per-Protocol Population)

End point description:

Blood glucose was measured 2 hours after a meal (2-hour PMG). 2-hour PMG is expressed as mg/dL. This change from baseline in 2-Hour PMG reflects the Week 24 2-hour PMG minus the Week 0 2-hour PMG. The Per Protocol population excluded participants from the FAS population who either had <75% drug compliance or used a prohibited medication (including metformin).

A post-hoc sensitivity analysis was performed that excluded participants in both treatment groups who were found to have used prohibited metformin (see results above for a description of the use of prohibited metformin).

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Omarigliptin	Placebo to Omarigliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	80		
Units: mg/dL				
least squares mean (confidence interval 95%)	-40.1 (-53.4 to -26.9)	-19.6 (-34.1 to -5.2)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Constrained Longitudinal Data Analysis included terms for treatment, time, prior AHA therapy status, the interaction of time by treatment, and time by prior AHA therapy status

Comparison groups	Omarigliptin v Placebo to Omarigliptin
Number of subjects included in analysis	175
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.031
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the least squares means
Point estimate	-20.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39
upper limit	-1.9

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 57 weeks for serious adverse events (SAE, including 3-week follow-up) and up to 54 weeks for non-serious adverse events.

Adverse event reporting additional description:

SAE tables include data after glycemic rescue. Non-serious adverse event tables exclude data after glycemic rescue.

This analysis may have been confounded by use of prohibited metformin (see use of prohibited metformin).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Omarigliptin

Reporting group description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks (Phase A) followed by omarigliptin 25 mg administered orally plus placebo to metformin (Phase B). Open-label metformin daily was to be initiated for participants meeting protocol-specified glycemic criteria during Phase A, but was otherwise prohibited. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

Reporting group title	Placebo to Omarigliptin

Reporting group description:

Placebo to omarigliptin administered orally once a week for 24 weeks (Phase A) followed by placebo to omarigliptin administered orally once a week plus metformin for an additional 30 weeks (Phase B). Open-label metformin daily was to be initiated for participants meeting protocol-specified glycemic criteria during Phase A, but was otherwise prohibited. Open-label glimepiride may be initiated as glycemic rescue therapy during Phase B.

Serious adverse events	Omarigliptin	Placebo to Omarigliptin	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 165 (4.85%)	8 / 164 (4.88%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Vulval cancer			
subjects affected / exposed	0 / 165 (0.00%)	1 / 164 (0.61%)	
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	0 / 165 (0.00%)	1 / 164 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	1 / 165 (0.61%)	0 / 164 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 165 (0.00%)	1 / 164 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ilium fracture			
subjects affected / exposed	0 / 165 (0.00%)	1 / 164 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 165 (0.00%)	1 / 164 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 165 (0.61%)	0 / 164 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 165 (0.00%)	1 / 164 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 165 (0.61%)	0 / 164 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial flutter			
subjects affected / exposed	0 / 165 (0.00%)	1 / 164 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 165 (0.61%)	0 / 164 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 165 (0.61%)	0 / 164 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 165 (0.00%)	1 / 164 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 165 (0.00%)	2 / 164 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 164 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 164 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			

subjects affected / exposed	1 / 165 (0.61%)	0 / 164 (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	Omarigliptin	Placebo to Omarigliptin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 165 (18.79%)	25 / 164 (15.24%)	
Investigations			
Blood glucose increased			
subjects affected / exposed	14 / 165 (8.48%)	13 / 164 (7.93%)	
occurrences (all)	14	13	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	17 / 165 (10.30%)	12 / 164 (7.32%)	
occurrences (all)	21	16	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2013	AM1 - Added an upper age limit of 65 years to the inclusion criteria for participants enrolled in India; added use of sodium-glucose cotransporter (SGLT2) inhibitor within12 weeks prior to signing informed consent to the exclusion criteria; added that participants who could not tolerate the minimum dose of metformin should be discontinued; added that participants with pancreatitis should be discontinued; and clarified that in specific circumstances, participants should be discontinued from blinded study medication (not the trial)
05 April 2013	AM2 - added use of omarigliptin at any time prior to signing informed consent to the exclusion criteria; added a 6 month timeframe to the weight loss medication exclusion; included weight loss medications under prohibited medications; and added amylase and lipase to the chemistry panel at the request of regulatory authorities in the European Union
18 February 2014	AM3 - reduced the sample size from 200 participants per treatment group (400 total participants) to 150 participants per treatment group (300 total participants).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Care must be taken in the interpretation of the results in this study as the non-protocol-specific prohibited use of metformin among a significant number of participants may have impacted the safety and efficacy results.

Notes: