



Clinical trial results:

A Multicenter, Randomized, Double-Blind Study to Evaluate the Safety, Tolerability, and Efficacy of the Addition of MK-3102 to Subjects With Type 2 Diabetes Mellitus Who Have Inadequate Glycemic Control on Metformin Therapy

Summary

EudraCT number	2012-003670-11
Trial protocol	HU SK ES BG PL RO
Global end of trial date	16 March 2016

Results information

Result version number	v1 (current)
This version publication date	23 February 2017
First version publication date	23 February 2017

Trial information

Trial identification

Sponsor protocol code	MK-3102-024
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01755156
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	16 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 March 2016
Global end of trial reached?	Yes
Global end of trial date	16 March 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 assess the safety and efficacy of omarigliptin compared to placebo in participants with inadequate glycemic control on metformin monotherapy. The primary hypothesis is that after 24 weeks, the addition of treatment with omarigliptin provides greater reduction in hemoglobin A1c (A1C) than placebo.

Protection of trial subjects:

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

The following additional measure defined for this individual study was in place for the protection of trial subjects: Rescue therapy (open-label glimepiride during Phase A or insulin glargine during Phase B) was initiated in participants who did not meet pre-specified glycemic goals after Day 1.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 29
Country: Number of subjects enrolled	Hungary: 24
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Poland: 26
Country: Number of subjects enrolled	Romania: 48
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Slovakia: 56
Country: Number of subjects enrolled	South Africa: 34
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United States: 149
Worldwide total number of subjects	402
EEA total number of subjects	189

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)	325
From 65 to 84 years	77
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible participants had type 2 diabetes mellitus and were on a stable dose of metformin monotherapy (≥ 1500 mg per day) for at least 12 weeks prior to study participation.

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 (Weeks 0-24)
Is this the baseline period?	Yes
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 25 mg capsule administered orally once weekly for 24 weeks.

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

Dosage and administration details:

Omarigliptin 25 mg capsule administered orally once weekly (preferably on the same day of each week).

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

Dosage and administration details:

Phase A rescue therapy: open-label glimepiride 1 or 2 mg tablet/capsule administered orally once daily and uptitrated to a maximum dose of 6 mg daily.

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:

Participants continue stable pre-study dose of metformin tablet(s) administered orally (≥ 1500 mg daily) throughout the study.

Arm title	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
Arm description:	
Phase A: matching placebo to omarigliptin orally once a week for 24 weeks.	
Arm type	Placebo
Investigational medicinal product name	Matching placebo to omarigliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Matching placebo to omarigliptin capsule administered orally once weekly (preferably on the same day of each week).	
Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	Amaryl®
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Phase A rescue therapy: open-label glimepiride 1 or 2 mg tablet/capsule administered orally once daily and up-titrated to a maximum dose of 6 mg daily.	
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:	
Participants continue stable pre-study dose of metformin tablet(s) administered orally (≥ 1500 mg daily) throughout the study.	

Number of subjects in period 1	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
Started	201	201
Completed	184	177
Not completed	17	24
Consent withdrawn by subject	6	13
Physician decision	-	1
Creatinine or eGFR Discontinuation Criteria	-	2
Adverse event, non-fatal	2	3
Non-compliance with study drug	1	-
Lost to follow-up	5	3
Need for Excluded Med. Discontinuation Criteria	1	1
Lack of efficacy	1	-
Protocol deviation	1	1

Period 2	
Period 2 title	Phase B (Weeks 24-104)
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 B: Omarigliptin 25 mg capsule administered orally once weekly and matching placebo to glimepiride tablet/capsule administered orally once daily for 80 weeks.	
Arm type	Experimental
Investigational medicinal product name	Omarigliptin
Investigational medicinal product code	
Other name	MK-3102
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Omarigliptin 25 mg capsule administered orally once weekly (preferably on the same day of each week).	
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:	
Participants continue stable pre-study dose of metformin tablet(s) administered orally (≥ 1500 mg daily) throughout the study.	
Investigational medicinal product name	Matching placebo to glimepiride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Matching placebo to glimepiride tablet/capsule administered orally once daily and up-titrated to a mock maximum dose of 6 mg daily. Participants rescued with open-label glimepiride during Phase A will not receive glimepiride or matching placebo to glimepiride during Phase B.	
Investigational medicinal product name	Insulin glargine
Investigational medicinal product code	
Other name	Lantus®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

During Phase B of the study, participants who received a maximum up-titration of open-label glimepiride or blinded glimepiride/matching placebo to glimepiride, may be rescued with open-label insulin glargine.

Arm title	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
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Arm description:

Phase B: Matching placebo to omarigliptin capsule administered orally once weekly and glimepiride 1 or 2 mg tablet/capsule administered orally once daily (titrated up to 6 mg daily) for 80 weeks.

Arm type	Active comparator
Investigational medicinal product name	Matching placebo to omarigliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Matching placebo to omarigliptin capsule administered orally once weekly (preferably on the same day of each week).

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

Dosage and administration details:

Glimepiride 1 or 2 mg tablet/capsule administered orally once daily and up-titrated to a maximum dose of 6 mg daily.

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:

Participants continue stable pre-study dose of metformin tablet(s) administered orally (≥ 1500 mg daily) throughout the study.

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

Dosage and administration details:

During Phase B of the study, participants who received a maximum up-titration of open-label glimepiride or blinded glimepiride/matching placebo to glimepiride, may be rescued with open-label insulin glargine.

Number of subjects in period 2 ^[1]	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
Started	183	177
Completed	144	141
Not completed	39	36
Consent withdrawn by subject	27	31
Lost to follow-up	12	5

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One omarigliptin participant completed Phase A but did not continue to Phase B.

Baseline characteristics

Reporting groups

Reporting group title	Omarigliptin (Phase A) Omarigliptin (Phase B)
Reporting group description: Phase A: Omarigliptin 25 mg capsule administered orally once weekly for 24 weeks.	
Reporting group title	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
Reporting group description: Phase A: matching placebo to omarigliptin orally once a week for 24 weeks.	

Reporting group values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)	Total
Number of subjects	201	201	402
Age categorical Units: Subjects			

Age Continuous Units: Years arithmetic mean standard deviation	57.5 ± 8.1	56.8 ± 9.1	-
Gender, Male/Female Units: Subjects			
Female	100	99	199
Male	101	102	203
Study Specific Characteristic Hemoglobin A1C (A1C) Units: Percent arithmetic mean standard deviation	8.06 ± 0.87	8.02 ± 0.89	-
Study Specific Characteristic 2-hour post-meal glucose (2-hr PMG)			
Omarigliptin (Phase A), n=192; Placebo to omarigliptin (Phase A), n=193; Total, n=385			
Units: mg/dL arithmetic mean standard deviation	240.2 ± 60.5	236 ± 59.9	-
Study Specific Characteristic Fasting plasma glucose (FPG) Units: mg/dL arithmetic mean standard deviation	168.8 ± 37.6	168.6 ± 37.2	-

End points

End points reporting groups

Reporting group title	Omarigliptin (Phase A) Omarigliptin (Phase B)
Reporting group description: Phase A: Omarigliptin 25 mg capsule administered orally once weekly for 24 weeks.	
Reporting group title	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
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 B: Omarigliptin 25 mg capsule administered orally once weekly and matching placebo to glimepiride tablet/capsule administered orally once daily for 80 weeks.	
Reporting group title	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
Reporting group description: Phase B: Matching placebo to omarigliptin capsule administered orally once weekly and glimepiride 1 or 2 mg tablet/capsule administered orally once daily (titrated up to 6 mg daily) for 80 weeks.	
Subject analysis set title	Omarigliptin (Phase A)
Subject analysis set type	Full analysis
Subject analysis set description: Phase A: Omarigliptin 25 mg capsule orally once a week for 24 weeks.	
Subject analysis set title	Placebo to omarigliptin (Phase A)
Subject analysis set type	Full analysis
Subject analysis set description: Phase A: Matching placebo to omarigliptin capsule administered orally once weekly for 24 weeks	
Subject analysis set title	Omarigliptin (Phase A) Omarigliptin (Phase B)
Subject analysis set type	Full analysis
Subject analysis set description: Phase A: Omarigliptin 25 mg capsule administered orally once weekly for 24 weeks. Phase B: Omarigliptin 25 mg capsule administered orally once weekly and matching placebo to glimepiride tablet/capsule administered orally once daily for 80 weeks.	
Subject analysis set title	Placebo to omarigliptin (Phase A) Glimepiride (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 capsule administered orally once weekly and glimepiride 1 or 2 mg tablet/capsule administered orally once daily (titrated up to 6 mg daily) for 80 weeks.	

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

End point title	Change from baseline in glycosylated hemoglobin (A1C) at Week 24 (Phase A)
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, time, and the interaction of time by treatment. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.	
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	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percent				
least squares mean (confidence interval 95%)	-0.54 (-0.69 to -0.4)	0 (-0.14 to 0.15)		

Statistical analyses

Statistical analysis title	Pairwise comparison
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[1]
Method	cLDA
Parameter estimate	Difference in least squares means
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	-0.34

Notes:

[1] - Based on a cLDA method with a restriction of the same baseline mean.

Primary: Percentage of participants who experienced at least one adverse event (Phase A+B)

End point title	Percentage of participants who experienced at least one adverse event (Phase A+B)
End point description:	An adverse event (AE) 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 population included all participants who received at least one dose of study medication.
End point type	Primary
End point timeframe:	Up to 107 weeks

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
number (not applicable)	65.7	65.2		

Statistical analyses

Statistical analysis title	Comparison between reporting groups
Statistical analysis description: Based on Miettinen & Nurminen method. The 95% CI was computed only for those endpoints with at least 4 participants having events in 1 or more treatment groups	
Comparison groups	Omarigliptin (Phase A) Omarigliptin (Phase B) v Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	9.8

Primary: Percentage of participants who discontinued study drug due to an adverse event (Phase A+B)

End point title	Percentage of participants who discontinued study drug due to an adverse event (Phase A+B)
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 population included all participants who received at least one dose of study medication.	
End point type	Primary
End point timeframe: Up to 104 weeks	

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
number (not applicable)	2	4.5		

Statistical analyses

Statistical analysis title	Comparison between reporting groups
Statistical analysis description: Based on Miettinen & Nurminen method. The 95% CI was computed only for those endpoints with at least 4 participants having events in 1 or more treatment groups.	
Comparison groups	Omarigliptin (Phase A) Omarigliptin (Phase B) v Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	1.1

Primary: Percentage of participants who experienced an adverse event which were included under the System Order Class of Investigations (Phase A+B)

End point title	Percentage of participants who experienced an adverse event which were included under the System Order Class of Investigations (Phase A+B)
End point description: The following laboratory parameters were included: blood chemistry, hematology, electrocardiograms, lipids, body weight, and vital signs. All participants as treated population included all participants who received at least one dose of study medication.	
End point type	Primary
End point timeframe: Up to 104 weeks	

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
number (not applicable)	21.9	17.4		

Statistical analyses

Statistical analysis title	Comparison between reporting groups
Statistical analysis description: Based on Miettinen & Nurminen method. The 95% CI was computed only for those endpoints with at least 4 participants having events in 1 or more treatment groups	
Comparison groups	Omarigliptin (Phase A) Omarigliptin (Phase B) v Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	12.3

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

End point title	Change from baseline in 2-hour post-meal glucose (PMG) at Week 24 (Phase A)
End point description: Change from baseline in 2-hour PMG 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, time, and the interaction of time by treatment. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.	
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	Subject analysis set	Subject analysis set		
Number of subjects analysed	195	199		
Units: mg/dL				
least squares mean (confidence interval 95%)	-26.8 (-34.8 to -18.7)	-12.2 (-20.7 to -3.8)		

Statistical analyses

Statistical analysis title	Pairwise comparison
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011 [2]
Method	cLDA
Parameter estimate	Difference in least squares means
Point estimate	-14.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.6
upper limit	-3.4

Notes:

[2] - Based on a cLDA method with a restriction of the same baseline mean.

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

End point title	Change from baseline in fasting plasma glucose (FPG) at Week 24 (Phase A)
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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, time, and the interaction of time by treatment. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.

End point type	Secondary
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End point timeframe:

Baseline and Week 24

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: mg/dL				
least squares mean (confidence interval	-10.7 (-16 to	-1.2 (-6.6 to		

95%)	-5.5)	4.1)
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Statistical analyses

Statistical analysis title	Pairwise comparison
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 ^[3]
Method	cLDA
Parameter estimate	Difference in least squares means
Point estimate	-9.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.7
upper limit	-2.3

Notes:

[3] - Based on a cLDA method with a restriction of the same baseline mean.

Secondary: Change from baseline in A1C at Week 104 (Phase A+B)

End point title	Change from baseline in A1C at Week 104 (Phase A+B)
End point description:	
A1C is measured as a percent. Change from baseline in A1C at Week 104 was analyzed using cLDA method with a restriction of the same baseline mean across treatment groups. The cLDA model included terms for treatment, time, and the interaction of time by treatment. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.	
End point type	Secondary
End point timeframe:	
Baseline and Week 104	

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percent				
least squares mean (confidence interval 95%)	-0.42 (-0.59 to -0.25)	-0.51 (-0.68 to -0.34)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in FPG at Week 104 (Phase A+B)

End point title	Change from baseline in FPG at Week 104 (Phase A+B)
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End point description:

Change from baseline in FPG at Week 104 was analyzed using cLDA method with a restriction of the same baseline mean across treatment groups. The cLDA model included terms for treatment, time, and the interaction of time by treatment. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.

End point type	Secondary
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End point timeframe:

Baseline and Week 104

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: mg/dL				
least squares mean (confidence interval 95%)	-7.8 (-14.4 to -1.3)	-18.2 (-24.7 to -11.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants attaining A1C glycemic goals of <7.0% after 24 weeks of treatment (Phase A)

End point title	Percentage of participants attaining A1C glycemic goals of <7.0% after 24 weeks of treatment (Phase A)
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End point description:

Percentage of participants attaining A1C glycemic goals of <7.0% (53 mmol/mol) after 24 weeks of treatment estimated using standard multiple imputation techniques. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.

End point type	Secondary
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End point timeframe:

24 weeks

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
number (confidence interval 95%)	38 (31.3 to 45.1)	18.8 (13.9 to 25)		

Statistical analyses

Statistical analysis title	Pairwise comparison
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Between-group rate difference (%)
Point estimate	19.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.1
upper limit	28

Secondary: Percentage of participants attaining A1C glycemic goals of <6.5% after 24 weeks of treatment (Phase A)

End point title	Percentage of participants attaining A1C glycemic goals of <6.5% after 24 weeks of treatment (Phase A)
End point description:	Percentage of participants attaining A1C glycemic goals of <6.5% (48 mmol/mol) after 24 weeks of treatment estimated using standard multiple imputation techniques. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
number (confidence interval 95%)	10.6 (6.8 to 16.2)	6.4 (3.6 to 11.2)		

Statistical analyses

Statistical analysis title	Pairwise comparison
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.164
Method	Miettinen & Nurminen method
Parameter estimate	Between-group rate difference (%)
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	10.5

Secondary: Percentage of participants attaining A1C glycemic goals of <7% after 104 weeks of treatment (Phase A+B)

End point title	Percentage of participants attaining A1C glycemic goals of <7% after 104 weeks of treatment (Phase A+B)
End point description:	Percentage of participants attaining A1C glycemic goals of <7.0% (53 mmol/mol) after 104 weeks of treatment estimated using standard multiple imputation techniques. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.
End point type	Secondary
End point timeframe:	
104 weeks	

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
least squares mean (confidence interval 95%)	32.2 (25.7 to 39.5)	39 (31.7 to 46.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants attaining A1C glycemic goals of <6.5% after 104 weeks of treatment (Phase A+B)

End point title	Percentage of participants attaining A1C glycemic goals of <6.5% after 104 weeks of treatment (Phase A+B)
End point description: Percentage of participants attaining A1C glycemic goals of <6.5% (48 mmol/mol) after 104 weeks of treatment estimated using standard multiple imputation techniques. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.	
End point type	Secondary
End point timeframe: 104 weeks	

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
least squares mean (confidence interval 95%)	13.7 (9.4 to 19.6)	17.9 (12.5 to 24.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in PMG total area under the plasma concentration time curve (AUC) at Week 24 (Phase A)

End point title	Change from baseline in PMG total area under the plasma concentration time curve (AUC) at Week 24 (Phase A)
End point description: Change from baseline in PMG total AUC at Week 24 based on a cLDA model including terms for treatment, time, and the interaction of time by treatment. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.	
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	Subject analysis set	Subject analysis set		
Number of subjects analysed	195	198		
Units: mg*h/dL				
least squares mean (confidence interval 95%)	-46.4 (-58.7 to -34.1)	-18.6 (-31.5 to -5.7)		

Statistical analyses

Statistical analysis title	Pairwise comparison
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001 ^[4]
Method	cLDA
Parameter estimate	Difference in least squares means
Point estimate	-27.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.8
upper limit	-10.8

Notes:

[4] - Based on a cLDA method with a restriction of the same baseline mean.

Secondary: Change from baseline in fasting insulin at Week 24 (Phase A)

End point title	Change from baseline in fasting insulin at Week 24 (Phase A)
End point description:	Change from baseline in fasting insulin at Week 24 based on a cLDA model including terms for treatment, time, and the interaction of time by treatment. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.
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	Subject analysis set	Subject analysis set		
Number of subjects analysed	200	200		
Units: micro International Unit (µIU)/mL				
least squares mean (confidence interval 95%)	1.8 (-0.6 to 4.2)	-1.9 (-4.3 to 0.5)		

Statistical analyses

Statistical analysis title	Pairwise comparison
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.025 ^[5]
Method	cLDA
Parameter estimate	Difference in least squares means
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	6.9

Notes:

[5] - Based on a cLDA method with a restriction of the same baseline mean.

Secondary: Change from baseline in fasting insulin at Week 104 (Phase A+B)

End point title	Change from baseline in fasting insulin at Week 104 (Phase A+B)
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End point description:

Change from baseline in fasting insulin at Week 104 based on a cLDA model including terms for treatment, time, and the interaction of time by treatment. Full analysis set population included all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a post-randomization measurement.

End point type	Secondary
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End point timeframe:

Baseline and Week 104

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	200		
Units: µIU/mL				
least squares mean (confidence interval	1.2 (-1.9 to	1.8 (-1.2 to		

95%)	4.2)	4.8)
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Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier estimate of cumulative incidence of participants requiring glycemic rescue therapy by 24 weeks (Phase A)

End point title	Kaplan-Meier estimate of cumulative incidence of participants requiring glycemic rescue therapy by 24 weeks (Phase A)
End point description:	Participants who did not meet progressively stricter glycemic criteria in Phase A had rescue initiated with open-label glimepiride. All participants randomized population.
End point type	Secondary
End point timeframe:	Up to 24 weeks

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
number (confidence interval 95%)	8.5 (5.3 to 13.6)	9.7 (6.2 to 15)		

Statistical analyses

Statistical analysis title	Pairwise comparison
Comparison groups	Omarigliptin (Phase A) v Placebo to omarigliptin (Phase A)
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.654
Method	Logrank
Parameter estimate	Kaplan-Meier difference %
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	4.7

Secondary: Kaplan-Meier estimate of cumulative incidence of participants requiring glycemic rescue therapy by 104 weeks (Phase A+B)

End point title	Kaplan-Meier estimate of cumulative incidence of participants requiring glycemic rescue therapy by 104 weeks (Phase A+B)
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End point description:

Participants who did not meet progressively stricter glycemic criteria in Phase A had rescue initiated with open-label glimepiride. If during Phase B participants on open-label glimepiride or blinded glimepiride/glimepiride matching placebo needed rescue after maximum up-titration, then insulin glargine was initiated and the dose of open-label glimepiride or blinded glimepiride/glimepiride-matching placebo was discontinued. All participants randomized population.

End point type	Secondary
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End point timeframe:

Up to 104 weeks

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
number (confidence interval 95%)	20.2 (14.9 to 27.1)	16.2 (11.5 to 22.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants requiring glycemic rescue therapy at or before Week 24 (Phase A)

End point title	Percentage of participants requiring glycemic rescue therapy at or before Week 24 (Phase A)
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End point description:

Data presented are a cumulative incidence of participants with glycemic rescue by Week 24. All participants randomized population.

End point type	Secondary
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End point timeframe:

Up to 24 weeks

End point values	Omarigliptin (Phase A)	Placebo to omarigliptin (Phase A)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
number (not applicable)	8	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants requiring glycemic rescue therapy at or before Week 104 (Phase A+B)

End point title	Percentage of participants requiring glycemic rescue therapy at or before Week 104 (Phase A+B)
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End point description:

Data presented are a cumulative incidence of participants with glycemic rescue by Week 104. All participants randomized population.

End point type	Secondary
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End point timeframe:

Up to 104 weeks

End point values	Omarigliptin (Phase A) Omarigliptin (Phase B)	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	201		
Units: Percentage of participants				
number (not applicable)	17.4	13.9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 107 weeks (treatment period + 21-day follow-up)

Adverse event reporting additional description:

All randomized participants who took at least 1 dose of study drug. Serious AEs include data after glycemic rescue; non-serious AEs 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1, 18.1
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Reporting groups

Reporting group title	Omarigliptin (Phase A)
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Reporting group description:

Phase A: Omarigliptin 25 mg capsule orally once a week for 24 weeks. MedDRA version 17.1

Reporting group title	Placebo to omarigliptin (Phase A)
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Reporting group description:

Phase A: Matching placebo to omarigliptin capsule administered orally once weekly for 24 weeks. MedDRA version 17.1

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

Phase A: Omarigliptin 25 mg capsule administered orally once weekly for 24 weeks. Phase B: Omarigliptin 25 mg capsule administered orally once weekly and matching placebo to glimepiride tablet/capsule administered orally once daily for 80 weeks. MedDRA version 18.1

Reporting group title	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)
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Reporting group description:

Phase A: matching placebo to omarigliptin orally once a week for 24 weeks. Phase B: Matching placebo to omarigliptin capsule administered orally once weekly and glimepiride 1 or 2 mg tablet/capsule administered orally once daily (titrated up to 6 mg daily) for 80 weeks. MedDRA version 18.1

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	5 / 201 (2.49%)	10 / 201 (4.98%)	12 / 201 (5.97%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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
Bladder neoplasm			

subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	0 / 201 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 201 (0.50%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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
Tendon injury			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	1 / 201 (0.50%)
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 disorders			

Hypertension			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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 venous disease			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	1 / 201 (0.50%)
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 disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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
Atrioventricular block second degree			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	0 / 201 (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	0 / 201 (0.00%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	0 / 201 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	0 / 201 (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
Supraventricular tachycardia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Chest pain			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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
Gastrointestinal disorders			
Gastric polyps			
subjects affected / exposed	1 / 201 (0.50%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic cyst			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	0 / 201 (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
Pancreatitis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	0 / 201 (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
Pancreatitis acute			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	1 / 201 (0.50%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 201 (0.50%)	1 / 201 (0.50%)	2 / 201 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 201 (0.00%)	0 / 201 (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
Pneumonia			
subjects affected / exposed	0 / 201 (0.00%)	1 / 201 (0.50%)	0 / 201 (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

Serious adverse events	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 201 (8.96%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			

subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder neoplasm			
subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatocellular carcinoma			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	2 / 201 (1.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seroma			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon injury			

subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral venous disease			
subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block second degree			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial ischaemia			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			

subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastric polyps			
subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic cyst			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	2 / 201 (1.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Uterine haemorrhage			

subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 201 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteochondrosis			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 201 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 201 (1.00%)		
occurrences causally related to treatment / all	0 / 2		
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	27 / 201 (13.43%)	17 / 201 (8.46%)	53 / 201 (26.37%)
Investigations Blood glucose increased subjects affected / exposed occurrences (all)	9 / 201 (4.48%) 9	7 / 201 (3.48%) 10	14 / 201 (6.97%) 16
Nervous system disorders Headache subjects affected / exposed occurrences (all)	5 / 201 (2.49%) 5	5 / 201 (2.49%) 5	8 / 201 (3.98%) 8
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	2 / 201 (1.00%) 3	0 / 201 (0.00%) 0	11 / 201 (5.47%) 12
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	5 / 201 (2.49%) 5	1 / 201 (0.50%) 1	11 / 201 (5.47%) 12
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	7 / 201 (3.48%) 13	5 / 201 (2.49%) 8	17 / 201 (8.46%) 43

Non-serious adverse events	Placebo to omarigliptin (Phase A) Glimepiride (Phase B)		
Total subjects affected by non-serious adverse events subjects affected / exposed	58 / 201 (28.86%)		
Investigations Blood glucose increased subjects affected / exposed occurrences (all)	10 / 201 (4.98%) 14		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	11 / 201 (5.47%) 11		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	8 / 201 (3.98%) 9		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 201 (3.48%) 7		
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	32 / 201 (15.92%) 112		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 January 2013	Amendment 1: the primary reason for amendment was to add the age limit of 65 years of age for participants enrolled in India.
05 April 2013	Amendment 4: the primary reason for amendment was to add amylase and lipase to the chemistry panel.
20 February 2014	Amendment 5: the primary reasons for amendment were (1) to reduce the number of participants from 250 participants per treatment group (500 total) to 200 participants per treatment group (400 total), (2) to clarify glycemic rescue, meal tolerance test and discontinuation/withdrawal, and (3) to add and modify secondary objectives.
10 March 2015	Amendment 6: the primary reason for amendment was to add capsule as a dosage form for glimepiride.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported