

**Clinical trial results:****A Phase III, Multicenter, Double-Blind, Randomized Trial to Evaluate the Safety and Efficacy of MK-3102 Compared With Glimepiride in Subjects With Type 2 Diabetes Mellitus For Whom Metformin is Inappropriate due to Intolerance or Contraindication****Summary**

EudraCT number	2013-000301-23
Trial protocol	HU IT AT BE SK ES DE EE BG PL
Global end of trial date	03 April 2014

Results information

Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	05 July 2015

Trial information**Trial identification**

Sponsor protocol code	3102-027
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01863667
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Number: MK-3102-027

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	03 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2014
Global end of trial reached?	Yes
Global end of trial date	03 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This trial will assess the safety and efficacy of omarigliptin (MK-3102) compared with the sulfonylurea, glimepiride, in type 2 diabetes mellitus participants who are metformin intolerant or who have a contraindication to the use of metformin. The primary hypothesis is that after 54 weeks, the mean change from baseline in hemoglobin A1c (A1C) in participants treated with omarigliptin is noninferior compared with that in participants treated with glimepiride.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 July 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: 3
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United States: 37
Worldwide total number of subjects	65
EEA total number of subjects	27

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)	45
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study included participants who were diagnosed with type 2 diabetes mellitus and had intolerability to metformin ≥ 1000 mg/day or had a contraindication to the use of metformin.

Pre-assignment

Screening details:

The study had a 1-week Screening Period; an oral antihyperglycemic agent (AHA) "wash-off" period of 8 weeks for participants on oral AHAs; a 2-week single-blind placebo run-in period; and a 54-week double-blind treatment period.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Omarigliptin

Arm description:

Participants receive an omarigliptin (MK-3102) 25 mg capsule once weekly and glimepiride placebo tablet(s) once daily, for 54 weeks.

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

Dosage and administration details:

Omarigliptin (MK-3102) 25 mg capsule administered orally once weekly.

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

Dosage and administration details:

Matching placebo to glimepiride tablet administered orally once daily with breakfast or the first main meal.

Arm title	Glimepiride
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Arm description:

Participants receive glimepiride 1 mg and/or 2 mg tablet(s) (maximum dose 6 mg/day) once daily and an omarigliptin placebo capsule once weekly, for 54 weeks.

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

Dosage and administration details:

Glimepiride tablet 1 mg and/or 2 mg (uptitrated to a maximum dose 6 mg/day) administered orally once daily with breakfast or the first main meal.

Investigational medicinal product name	Omarigliptin placebo
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.

Number of subjects in period 1	Omarigliptin	Glimepiride
Started	33	32
Completed	0	0
Not completed	33	32
Consent withdrawn by subject	2	2
Study terminated by Sponsor	30	30
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups

Reporting group title	Omarigliptin
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Reporting group description:

Participants receive an omarigliptin (MK-3102) 25 mg capsule once weekly and glimepiride placebo tablet(s) once daily, for 54 weeks.

Reporting group title	Glimepiride
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Reporting group description:

Participants receive glimepiride 1 mg and/or 2 mg tablet(s) (maximum dose 6 mg/day) once daily and an omarigliptin placebo capsule once weekly, for 54 weeks.

Reporting group values	Omarigliptin	Glimepiride	Total
Number of subjects	33	32	65
Age categorical Units: Subjects			

Age Continuous Units: Years arithmetic mean standard deviation	58 ± 14.1	56.8 ± 9.9	-
Gender, Male/Female Units: Participants			
Female	19	16	35
Male	14	16	30

End points

End points reporting groups

Reporting group title	Omarigliptin
Reporting group description: Participants receive an omarigliptin (MK-3102) 25 mg capsule once weekly and glimepiride placebo tablet(s) once daily, for 54 weeks.	
Reporting group title	Glimepiride
Reporting group description: Participants receive glimepiride 1 mg and/or 2 mg tablet(s) (maximum dose 6 mg/day) once daily and an omarigliptin placebo capsule once weekly, for 54 weeks.	

Primary: Percentage of Participants Who Experienced at Least One Adverse Event

End point title	Percentage of Participants Who Experienced at Least One Adverse Event ^[1]
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 pre-existing conditions. All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received.	
End point type	Primary
End point timeframe: Up to 57 weeks (including 3 weeks following the last dose of study drug)	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analysis was planned or performed for this end point.	

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	32		
Units: Percentage of participants				
number (not applicable)	9.1	15.6		

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Hemoglobin A1C (A1C) at Week 54

End point title	Change from Baseline in Hemoglobin A1C (A1C) at Week 54 ^[2]
End point description: A1C is measured as a percent. Thus, this change from baseline reflects the Week 54 A1C percent minus the Week 0 A1C percent. Full Analysis Set defined as all participants who received at least one dose of study drug and had a baseline measurement or a post-randomization measurement. Due to the early termination of the study, no participants completed Week 54.	
End point type	Primary
End point timeframe: Baseline and Week 54	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to the early termination of the study, no statistical analysis was performed for this end point.

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[3]	0 ^[4]		
Units: Percent				
least squares mean (confidence interval 95%)	(to)	(to)		

Notes:

[3] - Due to the early termination of the study, no participants completed Week 54.

[4] - Due to the early termination of the study, no participants completed Week 54.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Discontinued Study Drug Due to an Adverse Event

End point title	Percentage of Participants Who Discontinued Study Drug Due to an Adverse Event ^[5]
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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 pre-existing conditions. All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received.

End point type	Primary
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End point timeframe:

Up to 54 weeks

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was planned or performed for this end point.

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	32		
Units: Percentage of participants				
number (not applicable)	3	0		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in Fasting Plasma Glucose (FPG) at Week 54
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End point description:

This change from baseline reflects the FPG level at Week 54 minus the FPG level at Week 0. Full Analysis Set defined as all participants who received at least one dose of study drug and had a baseline measurement or a post-randomization measurement. Due to the early termination of the study, no participants completed Week 54.

End point type	Secondary
End point timeframe:	
Baseline and Week 54	

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[6]	0 ^[7]		
Units: mg/dL				
least squares mean (confidence interval 95%)	(to)	(to)		

Notes:

[6] - Due to the early termination of the study, no participants completed Week 54.

[7] - Due to the early termination of the study, no participants completed Week 54.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving an A1C Goal <7.0% or <6.5% After 54 Weeks of Treatment

End point title	Percentage of Participants Achieving an A1C Goal <7.0% or <6.5% After 54 Weeks of Treatment
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End point description:

Percentage of participants achieving glycemic goal (A1C <7% or <6.5%) after 54 weeks of treatment. Full Analysis Set defined as all participants who received at least one dose of study drug and had a baseline measurement or a post-randomization measurement. Due to the early termination of the study, no participants completed Week 54.

End point type	Secondary
End point timeframe:	
54 weeks	

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[8]	0 ^[9]		
Units: Percentage of participants				
number (not applicable)				

Notes:

[8] - Due to the early termination of the study, no participants completed Week 54.

[9] - Due to the early termination of the study, no participants completed Week 54.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting the Composite Endpoint of an A1C Decrease >0.5%, No Symptomatic Hypoglycemia, and No Body Weight Gain After 54 Weeks of Treatment

End point title	Percentage of Participants Meeting the Composite Endpoint of an A1C Decrease >0.5%, No Symptomatic Hypoglycemia, and No Body Weight Gain After 54 Weeks of Treatment
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End point description:

Percentage of Participants who had an A1C decrease >0.5%, no symptomatic hypoglycemia, and no body weight gain after 54 weeks of treatment. Full Analysis Set defined as all participants who received at least one dose of study drug and had a baseline measurement or a post-randomization measurement. Due to the early termination of the study, no participants completed Week 54.

End point type	Secondary
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End point timeframe:

54 weeks

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[10]	0 ^[11]		
Units: Percentage of participants				
number (not applicable)				

Notes:

[10] - Due to the early termination of the study, no participants completed Week 54.

[11] - Due to the early termination of the study, no participants completed Week 54.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an Adverse Event of Symptomatic Hypoglycemia

End point title	Percentage of Participants with an Adverse Event of Symptomatic Hypoglycemia
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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 pre-existing conditions. All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received.

End point type	Secondary
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End point timeframe:

Up to 54 weeks

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[12]	0 ^[13]		
Units: Percentage of participants				
number (not applicable)				

Notes:

[12] - Due to the early termination of the study, this endpoint was not analyzed.

[13] - Due to the early termination of the study, this endpoint was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Weight at Week 54

End point title	Change from Baseline in Body Weight at Week 54
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End point description:

Body weight was to be measured (in duplicate) using a calibrated digital scale. All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received. Due to the early termination of the study, no participants completed Week 54.

End point type	Secondary
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End point timeframe:

Baseline and Week 54

End point values	Omarigliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[14]	0 ^[15]		
Units: Kilograms				
arithmetic mean (standard deviation)	()	()		

Notes:

[14] - Due to the early termination of the study, no participants completed Week 54.

[15] - Due to the early termination of the study, no participants completed Week 54.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Up to 57 weeks (including 3 weeks following last dose of study drug)

Adverse event reporting additional description:

All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Omarigliptin
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Reporting group description:

Participants receive an omarigliptin (MK-3102) 25 mg capsule once weekly and glimepiride placebo tablet(s) once daily, for 54 weeks.

Reporting group title	Glimepiride
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Reporting group description:

Participants receive glimepiride 1 mg and/or 2 mg tablet(s) (maximum dose 6 mg/day) once daily and an omarigliptin placebo capsule once weekly, for 54 weeks.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events exceeded the 5% threshold for any treatment group.

Serious adverse events	Omarigliptin	Glimepiride	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 33 (3.03%)	0 / 32 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 32 (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	Glimepiride	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
03 April 2014	The study was terminated based on business decisions only, and not due to any unexpected safety or efficacy concerns.	-

Notes:

Limitations and caveats

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

The study was terminated based on business decisions only, and not due to any unexpected safety or efficacy concerns.

Notes: