Clinical trial results:
A Phase IIa, Multicenter, Placebo- and Active-controlled, Randomized, Double-Blind, Clinical Trial to Evaluate the Safety and Efficacy of MK-8521 Compared to Placebo in Subjects with Type 2 Diabetes Mellitus

Summary

EudraCT number	2016-002056-25
Trial protocol	ES
Global end of trial date	18 April 2017

Results information

Result version number	v1 (current)
This version publication date	08 April 2018
First version publication date	08 April 2018

Trial information

Trial identification

Sponsor protocol code	8521-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02492763
WHO universal trial number (UTN)	-
Other trial identifiers	Study number: MK-8521-004

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	Senior Vice President, Global Clinical Development, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
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	18 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 April 2017
Global end of trial reached?	Yes
Global end of trial date	18 April 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This is a multicenter randomized, double-blind, placebo- and active-controlled (liraglutide; Victoza®), parallel-group, clinical trial of MK-8521 in participants with type 2 diabetes mellitus (T2DM) with inadequate glycemic control while on a stable dose of metformin (≥1000 mg/day). The trial will include a 1-week screening period; at least an 8-week antihyperglycemic agent (AHA) washout period, if required; a 14-week blinded therapy period (which includes single-blind run-in and double-blind therapy); and a 14-day post-treatment visit, 2 weeks after the last dose of investigational product. The primary hypothesis of the trial is that MK-8521 provides greater reduction in hemoglobin A1C relative to placebo after 12 weeks of once-daily administration in participants with T2DM with inadequate glycemic control on metformin monotherapy.

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:

Subjects will continue on their stable dose of metformin monotherapy (≥1000 mg/day) throughout the trial including the 14-day post-treatment visit.

Evidence for comparator: -

Actual start date of recruitment	27 July 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Colombia: 11
Country: Number of subjects enrolled	Guatemala: 12
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United States: 142
Worldwide total number of subjects	176
EEA total number of subjects	6

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)	169
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 84 clinical trial sites in Australia, Colombia, Guatemala, Israel, New Zealand, Spain, and in the United States.

Pre-assignment

Screening details:

Five hundred participants were screened and 176 randomized. Participants were males or females who had Type 2 diabetes mellitus.

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	MK-8521 180 µg

Arm description:

Participants received double-blind MK-8521 180 µg daily (QD), subcutaneously, over 12 weeks.

Arm type	Experimental
Investigational medicinal product name	MK-8521
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received double-blind MK-8521 180 µg daily (QD), subcutaneously, over 12 weeks.

Arm title	MK-8521 300 µg

Arm description:

Participants received double-blind MK-8521 300 µg, QD, subcutaneously, over 12 weeks.

Arm type	Experimental
Investigational medicinal product name	MK-8521
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received double-blind MK-8521 300 µg QD, subcutaneously, over 12 weeks.

Arm title	Placebo

Arm description:

Participants received matching double-blind placebo QD over 12 weeks.

Arm type	Placebo

Investigational medicinal product name	Placebo to MK-8521
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received matching double-blind placebo QD over 12 weeks.

Arm title	Liraglutide 1.8 mg

Arm description:

Participants received open-label liraglutide, 1.8 mg QD, subcutaneously, over 12 weeks.

Arm type	Active comparator
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received open-label liraglutide 0.6 escalated up to 1.8 mg QD, subcutaneously, for up to 12 weeks.

Number of subjects in period 1	MK-8521 180 µg	MK-8521 300 µg	Placebo
Started	46	44	43
Treated	46	44	43
Completed	30	29	33
Not completed	16	15	10
Hyperglycemia Discontinuation Criteria	-	1	-
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	-	2	1
Screen Failure	-	-	-
Adverse event, non-fatal	3	1	1
Non-Compliance With Study Drug	-	1	-
Study Terminated by Sponsor	13	10	6
Lost to follow-up	-	-	1

Number of subjects in period 1	Liraglutide 1.8 mg
Started	43
Treated	42
Completed	30
Not completed	13
Hyperglycemia Discontinuation Criteria	-
Adverse event, serious fatal	-
Consent withdrawn by subject	-

Screen Failure	1
Adverse event, non-fatal	2
Non-Compliance With Study Drug	-
Study Terminated by Sponsor	10
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	MK-8521 180 µg
Reporting group description:	
Participants received double-blind MK-8521 180 µg daily (QD), subcutaneously, over 12 weeks.	
Reporting group title	MK-8521 300 µg
Reporting group description:	
Participants received double-blind MK-8521 300 µg, QD, subcutaneously, over 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received matching double-blind placebo QD over 12 weeks.	
Reporting group title	Liraglutide 1.8 mg
Reporting group description:	
Participants received open-label liraglutide, 1.8 mg QD, subcutaneously, over 12 weeks.	

Reporting group values	MK-8521 180 µg	MK-8521 300 µg	Placebo
Number of subjects	46	44	43
Age categorical			
The baseline analysis population consisted of all participants randomized.			
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)	44	43	41
From 65-84 years	2	1	2
85 years and over	0	0	0
Age Continuous			
The baseline analysis population consisted of all participants randomized.			
Units: years			
arithmetic mean	54.0	54.2	51.5
standard deviation	± 7.6	± 7.9	± 10.1
Sex: Female, Male			
The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
Female	26	18	24
Male	20	26	19
Hemoglobin A1C Classification by Levels			
Hemoglobin A1C classification by levels: <8.5% or >=8.5%. The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
<8.5%|	22	24	24
>=8.5%|	24	20	19
Antihyperglycemic agent (AHA) Washout Status			

AHA washout status (yes/no). The trial included an 8-week AHA washout period for participants taking a AHA. The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
Yes|	5	5	5
No|	41	39	38
Body Mass Index (BMI)			
Number of participants with a BMI <30 kg/m^2 or BMI>=30 kg/m^2. The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
<30 kg/m^2|	18	14	15
>=30 kg/m^2|	28	30	28
Race (NIH/OMB)			
The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
American Indian or Alaska Native	4	3	2
Asian	2	3	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	8	9	12
White	27	25	23
More than one race	5	4	2
Unknown or Not Reported	0	0	0
Fasting Low Density Lipoprotein (LDL) Cholesterol			
The baseline analysis population consisted of all randomized participants who had a baseline LDL cholesterol value.			
Units: mg/dL			
arithmetic mean	103.3	95.6	100.5
standard deviation	± 28.1	± 33.8	± 42.8
Fasting High Density Lipoprotein (HDL) Cholesterol			
The baseline analysis population consisted of all randomized participants who had a baseline HDL cholesterol value.			
Units: mg/dL			
arithmetic mean	47.4	41.7	43.1
standard deviation	± 12.3	± 9.5	± 12.0
Fasting Triglycerides			
The baseline analysis population consisted of all randomized participants who had a baseline fasting triglycerides value.			
Units: mg/dL			
arithmetic mean	171.5	167.1	168.7
standard deviation	± 104.6	± 79.5	± 96.1
Systolic Blood Pressure (SBP)			
The baseline analysis population consisted of all randomized participants who had a baseline SBP value.			
Units: mm Hg			
arithmetic mean	125.1	126.0	124.6
standard deviation	± 10.8	± 12.0	± 14.3
Diastolic Blood Pressure (DBP)			
The baseline analysis population consisted of all randomized participants who had a baseline DBP value.			
Units: mm Hg			
arithmetic mean	76.6	77.9	77.6
standard deviation	± 6.3	± 7.4	± 8.3
Hemoglobin A1C			
The baseline analysis population consisted of all randomized participants who had a baseline A1C value.			

Units: Percent			
arithmetic mean	8.54	8.43	8.46
standard deviation	± 0.82	± 0.78	± 0.83
Body Weight			
The baseline analysis population consisted of all randomized participants who had a baseline body weight value.			
Units: Kilograms			
arithmetic mean	85.4	89.4	90.2
standard deviation	± 18.1	± 20.0	± 19.0
Heart Rate			
The baseline analysis population consisted of all randomized participants who had a baseline heart rate value.			
Units: Beats/minute			
arithmetic mean	72.5	72.2	73.8
standard deviation	± 7.7	± 9.9	± 8.6
Fasting Plasma Glucose (FPG)			
The baseline analysis population consisted of all randomized participants who had a baseline FPG value.			
Units: mg/dL			
arithmetic mean	171.4	175.0	172.0
standard deviation	± 41.0	± 49.5	± 39.2

Reporting group values	Liraglutide 1.8 mg	Total	
Number of subjects	43	176	
Age categorical			
The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	41	169	
From 65-84 years	2	7	
85 years and over	0	0	
Age Continuous			
The baseline analysis population consisted of all participants randomized.			
Units: years			
arithmetic mean	52.9		
standard deviation	± 9.4	-	
Sex: Female, Male			
The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
Female	20	88	
Male	23	88	
Hemoglobin A1C Classification by Levels			
Hemoglobin A1C classification by levels: <8.5% or >=8.5%. The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
<8.5%|	21	91	
>=8.5%|	22	85	

Antihyperglycemic agent (AHA) Washout Status			
AHA washout status (yes/no). The trial included an 8-week AHA washout period for participants taking a AHA. The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
Yes|	5	20	
No|	38	156	
Body Mass Index (BMI)			
Number of participants with a BMI <30 kg/m^2 or BMI>=30 kg/m^2. The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
<30 kg/m^2|	15	62	
>=30 kg/m^2|	28	114	
Race (NIH/OMB)			
The baseline analysis population consisted of all participants randomized.			
Units: Subjects			
American Indian or Alaska Native	4	13	
Asian	0	9	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	7	36	
White	31	106	
More than one race	1	12	
Unknown or Not Reported	0	0	
Fasting Low Density Lipoprotein (LDL) Cholesterol			
The baseline analysis population consisted of all randomized participants who had a baseline LDL cholesterol value.			
Units: mg/dL			
arithmetic mean	93.0		
standard deviation	± 29.5	-	
Fasting High Density Lipoprotein (HDL) Cholesterol			
The baseline analysis population consisted of all randomized participants who had a baseline HDL cholesterol value.			
Units: mg/dL			
arithmetic mean	46.8		
standard deviation	± 13.8	-	
Fasting Triglycerides			
The baseline analysis population consisted of all randomized participants who had a baseline fasting triglycerides value.			
Units: mg/dL			
arithmetic mean	154.0		
standard deviation	± 89.5	-	
Systolic Blood Pressure (SBP)			
The baseline analysis population consisted of all randomized participants who had a baseline SBP value.			
Units: mm Hg			
arithmetic mean	126.3		
standard deviation	± 11.0	-	
Diastolic Blood Pressure (DBP)			
The baseline analysis population consisted of all randomized participants who had a baseline DBP value.			
Units: mm Hg			
arithmetic mean	78.9		
standard deviation	± 5.7	-	

Hemoglobin A1C			
The baseline analysis population consisted of all randomized participants who had a baseline A1C value.			
Units: Percent			
arithmetic mean	8.72		
standard deviation	± 1.03	-	
Body Weight			
The baseline analysis population consisted of all randomized participants who had a baseline body weight value.			
Units: Kilograms			
arithmetic mean	92.4		
standard deviation	± 16.5	-	
Heart Rate			
The baseline analysis population consisted of all randomized participants who had a baseline heart rate value.			
Units: Beats/minute			
arithmetic mean	74.7		
standard deviation	± 8.9	-	
Fasting Plasma Glucose (FPG)			
The baseline analysis population consisted of all randomized participants who had a baseline FPG value.			
Units: mg/dL			
arithmetic mean	187.5		
standard deviation	± 44.9	-	

End points

End points reporting groups	
Reporting group title	MK-8521 180 µg
Reporting group description:	
Participants received double-blind MK-8521 180 µg daily (QD), subcutaneously, over 12 weeks.	
Reporting group title	MK-8521 300 µg
Reporting group description:	
Participants received double-blind MK-8521 300 µg, QD, subcutaneously, over 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received matching double-blind placebo QD over 12 weeks.	
Reporting group title	Liraglutide 1.8 mg
Reporting group description:	
Participants received open-label liraglutide, 1.8 mg QD, subcutaneously, over 12 weeks.	

Primary: Change from Baseline in Hemoglobin A1C (A1C) at Week 12	
End point title	Change from Baseline in Hemoglobin A1C (A1C) at Week 12
End point description:	
A1C is the percentage of hemoglobin that has glucose bound to it and is a blood marker used to report average blood glucose levels over prolonged periods of time. A1C is reported as a percentage (%). This change from baseline reflects the Week 12 A1C minus the Week 0 A1C. The analysis population consisted of all randomized, treated participants with at least one A1C measurement (baseline or post-baseline).	
End point type	Primary
End point timeframe:	
Baseline and Week 12	

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	44	43	42
Units: Percent				
least squares mean (confidence interval 95%)	-0.82 (-1.16 to -0.49)	-1.05 (-1.41 to -0.69)	-0.44 (-0.80 to -0.08)	-1.42 (-1.77 to -1.07)

Statistical analyses

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Placebo

Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.126
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	0.11

Notes:

[1] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.017
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	1.08

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.018
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	-0.1

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description: longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.146
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.87

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description: Longitudinal data analysis	
Comparison groups	Placebo v Liraglutide 1.8 mg
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Longitudinal data analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	-0.48

Primary: Number of Participants With an Adverse Event (AE)	
End point title	Number of Participants With an Adverse Event (AE)[2]

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The analysis population consisted of all randomized participants who received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

Up to Week 14

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

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	44	43	42
Units: Participants	24	29	25	22

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Discontinued Study Treatment due to an AE

End point title	Number of Participants Who Discontinued Study Treatment due to an AE[3]

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The analysis population consisted of all randomized participants who received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

Up to Week 12

Notes:

[3] - 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 primary end point.

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	44	43	42
Units: Participants	3	1	2	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With an AE of Symptomatic Hypoglycemia

End point title	Number of Participants With an AE of Symptomatic Hypoglycemia

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether

it is considered related to the medical treatment or procedure, that occurs during the course of the study. Hypoglycemia episodes are those with glucose values ≤70 mg/dL (3.9 mmol/L). Symptomatic hypoglycemia episodes were episodes with clinical symptoms reported by the investigator as hypoglycemia and classified as adverse events. The analysis population consisted of all randomized participants who received at least 1 dose of study treatment.

End point type	Primary
End point timeframe:	
Up to Week 14	

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	44	43	42
Units: Participants	0	2	1	1

Statistical analyses

Statistical analysis title	Difference in % vs Placebo
Comparison groups	MK-8521 180 µg v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.301
Method	Miettinen & Nurminen method
Parameter estimate	Difference in % vs Placebo
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.1
upper limit	5.6

Statistical analysis title	Difference in % vs Placebo
Comparison groups	MK-8521 300 µg v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.573
Method	Miettinen & Nurminen method
Parameter estimate	Difference in % vs Placebo
Point estimate	2.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	13.2

Statistical analysis title	Difference in % vs Liraglutide
Comparison groups	MK-8521 180 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.295
Method	Miettinen & Nurminen method
Parameter estimate	Difference in % vs Liraglutide
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.4
upper limit	5.5

Statistical analysis title	Difference in % vs Liraglutide
Comparison groups	MK-8521 300 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.587
Method	Miettinen & Nurminen method
Parameter estimate	Difference in % vs Liraglutide
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	13.2

Primary: Change from Baseline in Heart Rate at Week 12

End point title	Change from Baseline in Heart Rate at Week 12

End point description:

This change from baseline reflects the Week 12 heart rate minus the Week 0 heart rate. The analysis population consisted of all randomized, treated participants with at least one heart rate measurement (baseline or post-baseline).

End point type	Primary

End point timeframe:
Baseline and Week 12

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	44	43	42
Units: Beats/minute				
least squares mean (confidence interval 95%)	5.47 (2.99 to 7.96)	6.28 (3.72 to 8.84)	-1.42 (-3.92 to 1.07)	1.63 (-0.88 to 4.14)

Statistical analyses

Statistical analysis title	Difference in the LS Means vs. Placebo
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in the LS Means vs. Placebo
Point estimate	6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.42
upper limit	10.37

Statistical analysis title	Difference in the LS Means vs. Liraglutide
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in LS Means vs. Liraglutide
Point estimate	3.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	7.33

Statistical analysis title	Difference in the LS Means vs. Placebo
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in LS Means vs. Placebo
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.17
upper limit	11.23

Statistical analysis title	Difference in the LS Means vs. Liraglutide
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in LS Means vs. Liraglutide
Point estimate	4.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	8.19

Secondary: Change from Baseline in Body Weight at Week 12	
End point title	Change from Baseline in Body Weight at Week 12
End point description: This change from baseline reflects the Week 12 body weight minus the Week 0 body weight. The analysis population consisted of all randomized, treated participants with at least one body weight measurement (baseline or post-baseline).	
End point type	Secondary
End point timeframe: Baseline and Week 12	

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	44	43	42
Units: Kilograms				
least squares mean (confidence interval 95%)	-2.0 (-2.9 to -1.1)	-3.0 (-4.0 to -2.1)	-1.3 (-2.2 to -0.3)	-2.9 (-3.8 to -1.9)

Statistical analyses

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.285
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.6

Notes:

[4] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.183
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	2.2

Notes:

[5] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.01
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	-0.4

Notes:

[6] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.811
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.2

Notes:

[7] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	Placebo v Liraglutide 1.8 mg
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.018 [9]
Method	Longitudinal data analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-1.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	-0.3

Notes:

[8] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment
[9] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Secondary: Change from Baseline in Fasting Plasma Glucose (FPG) at Week 12

End point title	Change from Baseline in Fasting Plasma Glucose (FPG) at Week 12

End point description:

This change from baseline reflects the Week 12 FPG minus the Week 0 FPG. The analysis population consisted of all randomized, treated participants with at least one FPG measurement (baseline or post-baseline).

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	44	43	42
Units: mg/dL				
least squares mean (confidence interval 95%)	-13.7 (-27.7 to 0.3)	-34.6 (-49.3 to -19.9)	-5.1 (-19.4 to 9.2)	-42.9 (-57.0 to -28.7)

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

Longitudinal data analysis

Comparison groups	MK-8521 180 µg v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.385
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-8.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.2
upper limit	10.9

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	29.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.7
upper limit	48.6

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-29.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.6
upper limit	-9.4

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Liraglutide 1.8 mg

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.416
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	28.2

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	Placebo v Liraglutide 1.8 mg
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Longitudinal data analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-37.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.5
upper limit	-18

Secondary: Change from Baseline in Fasting Low Density Lipoprotein (LDL) Cholesterol at Week 12

End point title	Change from Baseline in Fasting Low Density Lipoprotein (LDL) Cholesterol at Week 12
End point description:	
This change from baseline reflects the Week 12 fasting LDL cholesterol minus the Week 0 fasting LDL cholesterol. The analysis population consisted of all randomized, treated participants with at least one fasting LDL cholesterol measurement (baseline or post-baseline).	
End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	26	28	29
Units: mg/dL				
arithmetic mean (standard deviation)	-9.3 (± 23.5)	8.8 (± 41.8)	4.5 (± 33.5)	0.3 (± 18.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fasting High Density Lipoprotein (HDL) Cholesterol at Week 12

End point title	Change from Baseline in Fasting High Density Lipoprotein (HDL) Cholesterol at Week 12

End point description:

This change from baseline reflects the Week 12 fasting HDL cholesterol minus the Week 0 fasting HDL cholesterol. The analysis population consisted of all randomized, treated participants with at least one fasting HDL cholesterol measurement (baseline or post-baseline).

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	26	28	29
Units: mg/dL				
arithmetic mean (standard deviation)	-0.4 (± 12.3)	-0.5 (± 6.0)	3.8 (± 6.6)	0.4 (± 5.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fasting Triglycerides at Week 12

End point title	Change from Baseline in Fasting Triglycerides at Week 12

End point description:

This change from baseline reflects the Week 12 fasting triglycerides minus the Week 0 fasting triglycerides. The analysis population consisted of all randomized, treated participants with at least one fasting triglycerides measurement (baseline or post-baseline).

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	27	31	30
Units: mg/dL				
arithmetic mean (standard deviation)	-2.9 (± 91.9)	-26.6 (± 71.2)	-15.6 (± 68.9)	-20.5 (± 48.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Systolic Blood Pressure (SBP) at Week 12

End point title	Change from Baseline in Systolic Blood Pressure (SBP) at Week 12

End point description:

This change from baseline reflects the Week 12 SBP minus the Week 0 SBP. The analysis population consisted of all randomized, treated participants with at least one SBP measurement (baseline or post-baseline).

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	44	43	42
Units: mmHg				
least squares mean (confidence interval 95%)	-2.7 (-6.4 to 0.9)	-1.5 (-5.2 to 2.3)	1.0 (-2.6 to 4.6)	-1.7 (-5.3 to 2.0)

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

Longitudinal data analysis

Comparison groups	MK-8521 180 µg v Placebo

Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.151
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	1.4

Notes:

[10] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.682
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	4.1

Notes:

[11] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.344
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.7
upper limit	2.7

Notes:

[12] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.948
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	5.4

Notes:

[13] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	Placebo v Liraglutide 1.8 mg
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.306
Method	Longitudinal data analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.8
upper limit	2.5

Secondary: Change from Baseline in Diastolic Blood Pressure (DBP) at Week 12

End point title	Change from Baseline in Diastolic Blood Pressure (DBP) at Week 12

End point description:

This change from baseline reflects the Week 12 DBP minus the Week 0 DBP. The analysis population consisted of all randomized, treated participants with at least one DBP measurement (baseline or post-baseline).

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	MK-8521 180 µg	MK-8521 300 µg	Placebo	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	44	43	42
Units: mmHg				
least squares mean (confidence interval 95%)	0.5 (-1.7 to 2.8)	0.4 (-1.9 to 2.8)	-1.0 (-3.3 to 1.3)	0.6 (-1.7 to 2.9)

Statistical analyses

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.347
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	4.8

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description: Longitudinal data analysis	
Comparison groups	MK-8521 180 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.963
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	3.2

Notes:

[14] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.394
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	4.7

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	MK-8521 300 µg v Liraglutide 1.8 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.905
Method	Longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	3.1

Notes:

[15] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis	
Comparison groups	Placebo v Liraglutide 1.8 mg

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.325
Method	Longitudinal data analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	4.9

Notes:

[16] - Terms for treatment, time, A1C (<8.5%, ≥8.5%), BMI (<30 kg/m^2, ≥30 kg/m^2) and AHA washout status (Yes, No), and the interaction of time by treatment

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 14

Adverse event reporting additional description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure. The analysis population included all treated participants.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	MK-8521 180 µg

Reporting group description:

Participants received double-blind MK-8521 180 µg daily (QD), subcutaneously, over 12 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received matching double-blind placebo QD over 12 weeks.

Reporting group title	Liraglutide 1.8 mg

Reporting group description:

Participants received open-label liraglutide, 1.8 mg QD, subcutaneously, over 12 weeks.

Reporting group title	MK-8521 300 µg

Reporting group description:

Participants received double-blind MK-8521 300 µg, QD, subcutaneously, over 12 weeks.

Serious adverse events	MK-8521 180 µg	Placebo	Liraglutide 1.8 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 46 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Death			
subjects affected / exposed	0 / 46 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Serious adverse events	MK-8521 300 µg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 44 (2.27%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	0 / 44 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MK-8521 180 µg	Placebo	Liraglutide 1.8 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 46 (39.13%)	15 / 43 (34.88%)	13 / 42 (30.95%)
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 46 (2.17%)	3 / 43 (6.98%)	0 / 42 (0.00%)
occurrences (all)	1	3	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 46 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 46 (0.00%)	4 / 43 (9.30%)	3 / 42 (7.14%)
occurrences (all)	0	5	3
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 46 (0.00%)	1 / 43 (2.33%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Diarrhoea			

subjects affected / exposed	4 / 46 (8.70%)	1 / 43 (2.33%)	3 / 42 (7.14%)
occurrences (all)	5	2	4
Nausea			
subjects affected / exposed	6 / 46 (13.04%)	1 / 43 (2.33%)	9 / 42 (21.43%)
occurrences (all)	8	1	12
Vomiting			
subjects affected / exposed	2 / 46 (4.35%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences (all)	2	0	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	6 / 46 (13.04%)	4 / 43 (9.30%)	1 / 42 (2.38%)
occurrences (all)	7	4	1
Urinary tract infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 46 (8.70%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	4	1	0
Hypoglycaemia			
subjects affected / exposed	1 / 46 (2.17%)	1 / 43 (2.33%)	1 / 42 (2.38%)
occurrences (all)	2	2	1

Non-serious adverse events	MK-8521 300 µg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 44 (47.73%)		
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	5		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	5		
Headache			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences (all)	1		

Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 3 / 44 (6.82%) 3 3 / 44 (6.82%) 3 7 / 44 (15.91%) 10 3 / 44 (6.82%) 3		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 1 / 44 (2.27%) 1 3 / 44 (6.82%) 3		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hypoglycaemia subjects affected / exposed occurrences (all)	 5 / 44 (11.36%) 5 3 / 44 (6.82%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 March 2016	Amendment 1 - Broadening the subject population by permitting screening of subjects on metformin + other (AHA) who agree to washing off the other AHA and permit the previous use of GLP-1 agonists that were discontinued >6 months prior to screening.
09 January 2017	Amendment 2 - Provided clarity and details regarding the aspects of interim analyses to be performed as well as re-evaluation of sample size, guidelines for potential termination of the study, and differentiation of the safety triggered review from the planned interim analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported