Clinical trial results:
A Phase III Clinical Trial to Study the Safety and Efficacy of MK-1293 Compared to Lantus™ in Subjects With Type 1 Diabetes Mellitus

Summary

EudraCT number	2011-003971-12
Trial protocol	ES
Global end of trial date	18 November 2015

Results information

Result version number	v1
This version publication date	11 November 2016
First version publication date	11 November 2016

Trial information

Trial identification

Sponsor protocol code	MK-1293-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02059161
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	18 November 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to compare the safety and efficacy of MK-1293 to Lantus™ in participants with Type 1 diabetes mellitus (T1DM). The primary hypothesis is that after 24 weeks, the mean change in hemoglobin A1c (A1C) from baseline is non-inferior in participants treated with MK-1293 compared with participants treated with Lantus™.

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:

Participants will continue their prandial insulin during the study.

Evidence for comparator: -

Actual start date of recruitment	17 October 2013
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: 21
Country: Number of subjects enrolled	Colombia: 24
Country: Number of subjects enrolled	Mexico: 34
Country: Number of subjects enrolled	Spain: 51
Country: Number of subjects enrolled	New Zealand: 20
Country: Number of subjects enrolled	Peru: 31
Country: Number of subjects enrolled	South Africa: 65
Country: Number of subjects enrolled	United States: 262
Worldwide total number of subjects	508
EEA total number of subjects	51

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)	466
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants at least 18 years of age who have had T1DM for at least one year prior to study start.

Pre-assignment

Screening details:

Participants had Type 1 diabetes mellitus for at least one year prior to the study start and be 18 years or older.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MK-1293

Arm description:

MK-1293 dosed subcutaneously once daily at bedtime for 52 weeks. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).

Arm type	Experimental
Investigational medicinal product name	MK-1293
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MK-1293 dosed subcutaneously once daily at bedtime for 52 weeks. The initial dose will be determined based on the participant's previous insulin therapy. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).

Arm title	Lantus

Arm description:

Lantus dosed subcutaneously once daily at bedtime for 52 weeks. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).

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

Dosage and administration details:

Lantus dosed subcutaneously once daily at bedtime for 52 weeks. The initial dose will be determined based on the participant's previous insulin therapy. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).

Number of subjects in period 1	MK-1293	Lantus
Started	245	263
Treated	241	258
Completed	196	222
Not completed	49	41
Physician decision	4	4
Consent withdrawn by subject	16	13
randomized in error, did not take study drug	-	1
Adverse event, non-fatal	2	6
Pregnancy	-	2
Non-compliance with study drug	6	2
Lost to follow-up	20	12
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	MK-1293
Reporting group description:	
MK-1293 dosed subcutaneously once daily at bedtime for 52 weeks. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).	
Reporting group title	Lantus
Reporting group description:	
Lantus dosed subcutaneously once daily at bedtime for 52 weeks. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).	

Reporting group values	MK-1293	Lantus	Total
Number of subjects	245	263	508
Age Categorical			
One participant in the Lantus group was "Unknown" regarding baseline age characteristics so was added to the 18-64 years group			
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)	224	241	465
From 65-84 years	21	21	42
85 years and over	0	0	0
Unknown	0	1	1
Age Continuous			
One participant in the Lantus group was "Unknown" regarding baseline age characteristics			
Units: years			
arithmetic mean	41.8	41.6	
standard deviation	± 14.5	± 14.8	-
Gender Categorical			
Units: Subjects			
Female	106	111	217
Male	139	152	291

End points

End points reporting groups

Reporting group title	MK-1293
Reporting group description:	
MK-1293 dosed subcutaneously once daily at bedtime for 52 weeks. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).	
Reporting group title	Lantus
Reporting group description:	
Lantus dosed subcutaneously once daily at bedtime for 52 weeks. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).	

Primary: Change from Baseline in Hemoglobin A1c (A1C) at Week 24

End point title	Change from Baseline in Hemoglobin A1c (A1C) at Week 24
End point description:	
A1C is blood marker used to report average blood glucose levels over prolonged periods of time and is reported as a percentage (%). This change from baseline reflects the Week 24 A1C minus the Week 0 A1C. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.	
End point type	Primary
End point timeframe:	
Baseline and Week 24	

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: Percent				
least squares mean (confidence interval 95%)	-0.62 (-0.79 to -0.45)	-0.66 (-0.82 to -0.5)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.	
Comparison groups	MK-1293 v Lantus

Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Least Squares Means
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.19

Notes:

[1] - The criterion for declaring non-inferiority was for the upper bound of the 95% CI to lie below 0.4%.

Primary: Percentage of Participants With Confirmed Positive Anti-insulin Antibody (AIA) at Any Time Up Through Week 24

End point title	Percentage of Participants With Confirmed Positive Anti-insulin Antibody (AIA) at Any Time Up Through Week 24

End point description:

Percentage of participants with confirmed positive AIA at any time up through Week 24 including baseline. The analysis population included all randomized, treated participants who had data for AIA at or before Week 24.

End point type	Primary

End point timeframe:

Up to Week 24 including baseline

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: Percentage of participants				
number (not applicable)	70.1	74		

Statistical analyses

Statistical analysis title	Difference in Percentages

Statistical analysis description:

Difference in the percentage of participants who were AIA positive at or before Week 24.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentages
Point estimate	-3.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	4

Primary: Percentage of Participants With Negative AIA at Baseline Who Develop Confirmed Positive AIA at Any Time Up Through Week 24

End point title	Percentage of Participants With Negative AIA at Baseline Who Develop Confirmed Positive AIA at Any Time Up Through Week 24

End point description:

Percentage of participants who became positive to AIA at or before Week 24, among participants who were AIA negative at baseline. The analysis population included all randomized, treated participants who were AIA negative at baseline and had data for AIA at or before Week 24.

End point type	Primary

End point timeframe:

Up to Week 24

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	98		
Units: Percentage of participants				
number (not applicable)	32.7	35.7		

Statistical analyses

Statistical analysis title	Difference in Percentages
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentages
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.1
upper limit	10.1

Primary: Change from Baseline in AIA Titer After 24 weeks of Treatment

End point title	Change from Baseline in AIA Titer After 24 weeks of

End point description:

This immunogenicity analysis assessed the effect of treatment with MK-1293 and with Lantus on anti-insulin antibody development after 24 weeks of treatment. This change from baseline reflects the Week 24 AIA titer minus the Week 0 AIA titer. The analysis population included all randomized, treated participants who had AIA data at baseline and Week 24.

End point type	Primary

End point timeframe:

Baseline and Week 24

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 of this primary end point was planned or performed.

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	198		
Units: AIA Titers				
arithmetic mean (standard deviation)	0.4 (± 15.9)	0.3 (± 23.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Develop Insulin Neutralizing Antibodies Up Through Week 24

End point title	Percentage of Participants Who Develop Insulin Neutralizing Antibodies Up Through Week 24[3]

End point description:

Percentage of Participants Who Develop Insulin Neutralizing Antibodies Up Through Week 24. This immunogenicity analysis assessed the effect of treatment with MK-1293 and with Lantus on insulin-neutralizing antibody (INab) development up through 24 weeks of treatment. The analysis population included all randomized, treated participants who were INAb negative at baseline and who had data for INAb at or before Week 24.

End point type	Primary

End point timeframe:

Up to Week 24

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 of this primary end point was planned or performed.

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	232	246		
Units: Percentage of participants				
number (not applicable)	3.9	5.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in A1C at Week 52

End point title	Change from Baseline in A1C at Week 52

End point description:

A1C is blood marker used to report average blood glucose levels over prolonged periods of time and is reported as a percentage (%). This change from baseline reflects the Week 52 A1C minus the Week 0 A1C. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: Percent				
least squares mean (confidence interval 95%)	-0.35 (-0.53 to -0.17)	-0.33 (-0.5 to -0.16)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	other[4]
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.14

Notes:

[4] - The criterion for declaring non-inferiority was for the upper bound of the 95% CI to lie below 0.4%.

Secondary: Total Insulin Dose at Week 24

End point title	Total Insulin Dose at Week 24

End point description:

Total insulin dose = basal insulin (MK-1293 or Lantus) + bolus (prandial) insulin (non-study medication). The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	235		
Units: Insulin units				
least squares mean (confidence interval 95%)	58.74 (53.39 to 64.1)	60.51 (55.21 to 65.81)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Squares Means
Point estimate	-1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.69
upper limit	1.16

Secondary: Total Insulin Dose Per Kilogram (kg) of Body Weight (unit/kg) at Week 24

End point title	Total Insulin Dose Per Kilogram (kg) of Body Weight (unit/kg) at Week 24

End point description:

Total insulin dose = basal insulin (MK-1293 or Lantus) + bolus (prandial) insulin (non-study medication). The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	235		
Units: Insulin units/kg.				
least squares mean (confidence interval 95%)	0.75 (0.69 to 0.81)	0.77 (0.72 to 0.83)		

Statistical analyses

Statistical analysis title	Difference in Least Squares means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.01

Secondary: Change from Baseline in Fasting Plasma Glucose (FPG) at Week 24

End point title	Change from Baseline in Fasting Plasma Glucose (FPG) at Week 24

End point description:

Blood glucose was measured on a fasting basis (collected after a 10-hour fast). This change from baseline reflects the FPG level at Week 24 minus the FPG level at Week 0. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: mg/dL				
least squares mean (confidence interval 95%)	-16.8 (-33.4 to -0.2)	-26.4 (-42.5 to -10.3)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.	
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Squares Means
Point estimate	9.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	22.2

Secondary: Percentage of Participants With Confirmed Positive AIA Up Through Week 52

End point title	Percentage of Participants With Confirmed Positive AIA Up Through Week 52
End point description:	
Percentage of participants with confirmed positive AIA at any time up through Week 52 including baseline. The analysis population included all randomized, treated participants who had data for AIA at or before Week 52.	
End point type	Secondary
End point timeframe:	
Up to Week 52 including baseline	

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: Percentage of participants				
number (not applicable)	73.4	75.6		

Statistical analyses

Statistical analysis title	Differences in percentages
Statistical analysis description:	
Difference in the percentage of participants who were AIA positive at or before Week 52.	
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Miettinen & Nurminen
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.8
upper limit	5.5

Secondary: Percentage of Participants With Negative AIA at Baseline Who Develop Confirmed Positive AIA at Any Time Up Through Week 52

End point title	Percentage of Participants With Negative AIA at Baseline Who Develop Confirmed Positive AIA at Any Time Up Through Week 52
End point description:	
Percentage of participants who became positive to AIA at or before Week 52, among participants who were AIA negative at baseline. The analysis population included all randomized, treated participants who had data for AIA at baseline and Week 52.	
End point type	Secondary
End point timeframe:	
Up to Week 52	

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	98		
Units: Percentage of participants				
number (not applicable)	40.6	39.8		

Statistical analyses

Statistical analysis title	Differences in Percentages
Statistical analysis description:	
Miettinen & Nurminen	
Comparison groups	MK-1293 v Lantus

Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Diffefence in Percentages
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.8
upper limit	14.3

Secondary: Change From Baseline in AIA Titers After 52 Weeks of Treatment

End point title	Change From Baseline in AIA Titers After 52 Weeks of Treatment

End point description:

This immunogenicity analysis assessed the effect of treatment with MK-1293 and with Lantus on anti-insulin antibody development after 52 weeks of treatment. This change from baseline reflects the AIA titers at Week 52 minus the AIA titers at Week 0. The analysis population included all randomized, treated participants who had AIA data at baseline and Week 52.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	177		
Units: AIA Titers				
arithmetic mean (standard deviation)	-1.6 (± 9.9)	0.1 (± 20.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Insulin Dose at Week 52

End point title	Total Insulin Dose at Week 52

End point description:

Total insulin dose = basal insulin (MK-1293 or Lantus) + bolus (prandial) insulin (non-study medication). The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Week 52

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	240		
Units: Insulin units				
least squares mean (confidence interval 95%)	59.16 (53.97 to 64.34)	60.93 (55.79 to 66.06)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.	
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in least squares means
Point estimate	-1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.92
upper limit	1.39

Secondary: Total Insulin Dose Per Kilogram (kg) of Body Weight (unit/kg) at Week 52

End point title	Total Insulin Dose Per Kilogram (kg) of Body Weight (unit/kg) at Week 52
End point description:	
Total insulin dose = basal insulin (MK-1293 or Lantus) + bolus (prandial) insulin (non-study medication). The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	240		
Units: Insulin units/kg.				
least squares mean (confidence interval 95%)	0.75 (0.7 to 0.81)	0.77 (0.71 to 0.82)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in least squares means
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.02

Secondary: Change from Baseline in FPG at Week 52

End point title	Change from Baseline in FPG at Week 52

End point description:

Blood glucose was measured on a fasting basis (collected after a 10-hour fast). This change from baseline reflects the FPG level at Week 52 minus the FPG level at Week 0. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: mg/dL				
least squares mean (confidence interval 95%)	-17.9 (-35.8 to 0.1)	-12.5 (-29.9 to 4.9)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Squares Means
Point estimate	-5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.7
upper limit	8.9

Secondary: Percentage of Participants Who Develop Insulin Neutralizing Antibodies Up Through Week 52

End point title	Percentage of Participants Who Develop Insulin Neutralizing Antibodies Up Through Week 52

End point description:

Percentage of Participants Who Develop Insulin Neutralizing Antibodies Up Thought Week 52. This immunogenicity analysis assessed the effect of treatment with MK-1293 and with Lantus on insulin-neutralizing antibody (INAb) development up through 52 weeks of treatment. The analysis population included all randomized, treated participants who were INAb negative at baseline and who had data for INAb at or before Week 52.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	232	246		
Units: Percentage of participants				
number (not applicable)	4.7	6.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 7-point Self-monitored Blood Glucose (SMBG) at Week 24

End point title	Change from Baseline in 7-point Self-monitored Blood Glucose (SMBG) at Week 24

End point description:

The 7-point SMBG profile consisted of the following measurements by glucose meter: morning pre-meal (fasting), 2 hours after morning meal, midday pre-meal, 2 hours after midday meal, evening pre-meal, pre-bedtime (pre-dose and at least 2 hours after evening meal), between 2:00 AM and 4:00 AM in the morning. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226	248		
Units: mg/dL				
least squares mean (confidence interval 95%)	-4.9 (-15.8 to 5.9)	-4.6 (-14.9 to 5.8)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.9
upper limit	8.2

Secondary: Change from Baseline in 7-point SMBG at Week 52

End point title	Change from Baseline in 7-point SMBG at Week 52

End point description:

The 7-point SMBG profile consisted of the following measurements by glucose meter: morning pre-meal (fasting), 2 hours after morning meal, midday pre-meal, 2 hours after midday meal, evening pre-meal, pre-bedtime (pre-dose and at least 2 hours after evening meal), between 2:00 AM and 4:00 AM in the morning. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	249		
Units: mg/dL				
least squares mean (confidence interval 95%)	-12 (-25.8 to 1.7)	-4 (-16.3 to 8.4)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description:	
Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.	
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Squares Means
Point estimate	-8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.6
upper limit	2.4

Secondary: Percentage of participants attaining A1C glycemic goals of <7.0% and <6.5% after 24 weeks of treatment

End point title	Percentage of participants attaining A1C glycemic goals of <7.0% and <6.5% after 24 weeks of treatment
End point description:	
Percentage of participants attaining A1C glycemic goals of <7.0% and <6.5% after 24 weeks of treatment. The analysis population included all randomized, treated participants with a Week 24 A1C measurement.	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	236		
Units: Percentage of participants				
number (not applicable)				
A1C < 7.0%	37	37.7		
A1C < 6.5%	20.5	21.6		

Statistical analyses

Statistical analysis title	Adjusted Difference in Percentages (A1C < 7.0%)
Statistical analysis description: Miettinen and Nurminen, stratified by prior insulin status.	
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	455
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted Difference in Percentages
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	8.1

Statistical analysis title	Adjusted Difference in Percentages (A1C < 6.5%)
Statistical analysis description: Miettinen and Nurminen, stratified by prior insulin status.	
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	455
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted Difference in Percentages
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	6.5

Secondary: Percentage of participants attaining A1C glycemic goals of <7.0% and <6.5% after 52 weeks of treatment.

End point title	Percentage of participants attaining A1C glycemic goals of <7.0% and <6.5% after 52 weeks of treatment.

End point description:

Percentage of participants attaining A1C glycemic goals of <7.0% and <6.5% after 52 weeks of treatment. The analysis population included all randomized, treated participants with a Week 52 A1C measurement.

End point type	Secondary

End point timeframe:

52 weeks

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	221		
Units: Percentage of participants				
number (not applicable)				
A1C < 7.0%	31	30.8		
A1C < 6.5%	14.2	18.6		

Statistical analyses

Statistical analysis title	Adjusted Difference (A1C < 6.5%)
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Miettinen and Nurminen
Point estimate	-4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	2.8

Statistical analysis title	Adjusted Difference (A1C < 7.0%)
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	418
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Miettinen and Nurminen
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	9.1

Secondary: Basal Insulin Dose at Week 52

End point title	Basal Insulin Dose at Week 52

End point description:

Basal Insulin Dose at Week 52. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Week 52

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: Units				
least squares mean (confidence interval 95%)	36.08 (33.14 to 39.03)	36.51 (33.63 to 39.39)		

Statistical analyses

Statistical analysis title	Difference in Least Means Squares

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Means Squares
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.33
upper limit	1.48

Secondary: Basal Insulin Dose per kg of Body Weight at Week 52

End point title	Basal Insulin Dose per kg of Body Weight at Week 52

End point description:

Basal Insulin Dose per kg of Body Weight at Week 52. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Week 52

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: Units/kg				
least squares mean (confidence interval 95%)	0.46 (0.43 to 0.5)	0.47 (0.43 to 0.5)		

Statistical analyses

Statistical analysis title	Difference in Least Means Squares

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Means Squares
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.02

Secondary: Bolus Insulin Dose at Week 52

End point title	Bolus Insulin Dose at Week 52

End point description:

Bolus Insulin Dose at Week 52. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Week 52

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	235		
Units: Units				
least squares mean (confidence interval 95%)	21.65 (18.5 to 24.81)	22.91 (19.8 to 26.02)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description:	
Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.	
Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in the Least Squares Means
Point estimate	-1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.34
upper limit	0.83

Secondary: Bolus Insulin Dose per kg of Body Weight at Week 52

End point title	Bolus Insulin Dose per kg of Body Weight at Week 52
End point description:	
Bolus Insulin Dose per kg of Body Weight at Week 52. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	235		
Units: Units				
least squares mean (confidence interval 95%)	0.28 (0.24 to 0.31)	0.29 (0.26 to 0.33)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in the Least Squares Means
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.01

Secondary: Basal Insulin Dose at Week 24

End point title	Basal Insulin Dose at Week 24

End point description:

Basal Insulin Dose at Week 24. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: Units				
least squares mean (confidence interval 95%)	36.33 (33.24 to 39.42)	37.07 (34.03 to 40.12)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus

Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in the Least Squares Means
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.52
upper limit	1.04

Secondary: Basal Insulin Dose per kg of Body Weight at Week 24

End point title	Basal Insulin Dose per kg of Body Weight at Week 24

End point description:

Basal Insulin Dose per kg of Body Weight at Week 24. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	258		
Units: Units/kg				
least squares mean (confidence interval 95%)	0.46 (0.43 to 0.5)	0.48 (0.44 to 0.51)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in the Least Squares Means
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.01

Secondary: Bolus Insulin Dose at Week 24

End point title	Bolus Insulin Dose at Week 24

End point description:

Bolus Insulin Dose at Week 24. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	235		
Units: Units				
least squares mean (confidence interval 95%)	21.3 (18.2 to 24.4)	22.9 (19.8 to 25.9)		

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in the Least Squares Means
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	0.5

Secondary: Bolus Insulin Dose per kg of Body Weight at Week 24

End point title	Bolus Insulin Dose per kg of Body Weight at Week 24

End point description:

Bolus Insulin Dose per kg of Body Weight at Week 24. The analysis population included all randomized, treated participants who had at least one observation for the analysis endpoint.

End point type	Secondary

End point timeframe:
Week 24

End point values	MK-1293	Lantus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	235		
Units: Units/kg				
least squares mean (confidence interval 95%)	0.3 (0.2 to 0.3)	0.3 (0.3 to 0.3)		

Statistical analyses

Statistical analysis title	Difference in the Least Means Squares

Statistical analysis description:

Longitudinal data analysis model included terms for treatment, time, prior insulin status (intermediate-acting, or long-acting insulin), and the interaction of time by treatment, and time by prior insulin status.

Comparison groups	MK-1293 v Lantus
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in the Least Means Squares
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 54 weeks

Adverse event reporting additional description:

The safety population consisted of all randomized participants who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Lantus

Reporting group description:

Lantus dosed subcutaneously once daily at bedtime for 52 weeks. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).

Reporting group title	MK-1293

Reporting group description:

MK-1293 dosed subcutaneously once daily at bedtime for 52 weeks. Doses were individually titrated post-randomization to the suggested target for fasting fingerstick glucose levels of >70 mg/dL (3.9 mmol/L) and ≤100 mg/dL (5.6 mmol/L).

Serious adverse events	Lantus	MK-1293	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 258 (11.63%)	23 / 241 (9.54%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			

subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	2 / 258 (0.78%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			
subjects affected / exposed	4 / 258 (1.55%)	2 / 241 (0.83%)	
occurrences causally related to treatment / all	3 / 4	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypoglycaemic unconsciousness			
subjects affected / exposed	2 / 258 (0.78%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 258 (0.39%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIth nerve paresis			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric haemorrhage			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 258 (0.39%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
bile duct stone			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cholecystitis			
subjects affected / exposed	1 / 258 (0.39%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 258 (0.39%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Postoperative wound infection			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 258 (0.39%)	2 / 241 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	1 / 258 (0.39%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oseomyelitis			
subjects affected / exposed	0 / 258 (0.00%)	1 / 241 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 258 (0.39%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 258 (0.78%)	0 / 241 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	11 / 258 (4.26%)	5 / 241 (2.07%)	
occurrences causally related to treatment / all	8 / 14	4 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Lantus	MK-1293	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	216 / 258 (83.72%)	190 / 241 (78.84%)	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	23 / 258 (8.91%)	19 / 241 (7.88%)	
occurrences (all)	29	23	
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	28 / 258 (10.85%) 34	27 / 241 (11.20%) 40	
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	 204 / 258 (79.07%) 7544	 185 / 241 (76.76%) 7617	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2013	Amendment 3 - Updated primary and secondary objectives for change from baseline in A1C.
28 June 2013	Amendment 2 - Increase in number of participants, added a hypothesis for A1C equivalence, and updated Tier1 adverse events (AEs) to include additional AEs.
17 January 2014	Amendment 4 - permitted alternative dosing schedules for study drugs and added 2 new exclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported