



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 | Difference 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 Through 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 | |
| With 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