



Clinical trial results:

A Phase 2, Randomized, Parallel, Open-Label Comparator-Controlled Trial to Evaluate the Safety and Efficacy of LY3209590 in Study Participants With Type 1 Diabetes Mellitus Previously Treated With Multiple Daily Injection Therapy

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2019-003589-41 |
| Trial protocol | ES DE AT |
| Global end of trial date | 01 October 2021 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 15 October 2022 |
| First version publication date | 15 October 2022 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I8H-MC-BDCP |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04450407 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 17183 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559, |

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 | 01 October 2021 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 01 October 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The reason for this study is to see if the study drug LY3209590 is safe and effective in participants with type 1 diabetes.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 06 July 2020 |
| 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 | Puerto Rico: 11 |
| Country: Number of subjects enrolled | Austria: 12 |
| Country: Number of subjects enrolled | United States: 179 |
| Country: Number of subjects enrolled | Germany: 34 |
| Country: Number of subjects enrolled | Spain: 30 |
| Worldwide total number of subjects | 266 |
| EEA total number of subjects | 76 |

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) | 232 |

| | |
|---------------------|----|
| From 65 to 84 years | 34 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was initially designed as 3 arms: LY3209590 Algorithm 1 (Paper), LY3209590 Algorithm 2 (Digital), and Insulin Degludec. However, it was amended to terminate the "LY3209590 Algorithm 2 (Digital)" arm during early enrollment phase due to technical issues with data entry.

Pre-assignment

Screening details:

(cont'd) Thus, this arm was excluded from the outcome measure analyses, but safety data was analysed and reported.

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 | LY3209590 Algorithm 1 (Paper) |

Arm description:

Algorithm 1 is a paper-based algorithm where dose adjustments were manually determined by the investigator based on fasting glucose and hypoglycemia data. LY3209590 was provided in a 20 milligram (mg) vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline fasting glucose by subcutaneous (SC) injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 milligrams per deciliter (mg/dL).

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | LY3209590 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

LY3209590 was provided in a 20 mg vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline fasting glucose by SC injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 mg/dL.

| | |
|------------------|---------------------------------|
| Arm title | LY3209590 Algorithm 2 (Digital) |
|------------------|---------------------------------|

Arm description:

Algorithm 2 is a computer-based algorithm to determine dose adjustments. LY3209590 was provided in a 20 mg vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline fasting glucose by SC injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 mg/dL.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | LY3209590 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

LY3209590 was provided in a 20 mg vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline

fasting glucose by SC injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 mg/dL.

| | |
|--|--|
| Arm title | Insulin Degludec |
| Arm description: Insulin degludec was provided as 100 units/milliliter (U/mL) in a prefilled pen. Participants received individually adjusted doses once daily by SC injection with a starting dose same as basal insulin dose prior randomization, during the 26-week treatment period, to achieve target fasting blood glucose of ≤ 100 mg/dL. | |
| Arm type | Active comparator |
| Investigational medicinal product name | Insulin Degludec |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled pen |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Insulin degludec was provided as 100 U/mL in a prefilled pen. Participants received individually adjusted doses once daily by SC injection with a starting dose same as basal insulin dose prior randomization, during the 26-week treatment period, to achieve target fasting blood glucose of ≤ 100 mg/dL.

| Number of subjects in period 1 | LY3209590 Algorithm 1 (Paper) | LY3209590 Algorithm 2 (Digital) | Insulin Degludec |
|--|----------------------------------|------------------------------------|------------------|
| Started | 124 | 16 | 126 |
| Received at Least One Dose of Study Drug | 123 | 16 | 126 |
| Completed | 107 | 15 | 118 |
| Not completed | 17 | 1 | 8 |
| Consent withdrawn by subject | 10 | 1 | 4 |
| Physician decision | - | - | 1 |
| Adverse event, non-fatal | - | - | 1 |
| Investigational site terminated by sponsor | 3 | - | 2 |
| Pregnancy | 1 | - | - |
| Lost to follow-up | 1 | - | - |
| Protocol deviation | 2 | - | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------------------|
| Reporting group title | LY3209590 Algorithm 1 (Paper) |
|-----------------------|-------------------------------|

Reporting group description:

Algorithm 1 is a paper-based algorithm where dose adjustments were manually determined by the investigator based on fasting glucose and hypoglycemia data. LY3209590 was provided in a 20 milligram (mg) vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline fasting glucose by subcutaneous (SC) injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 milligrams per deciliter (mg/dL).

| | |
|-----------------------|---------------------------------|
| Reporting group title | LY3209590 Algorithm 2 (Digital) |
|-----------------------|---------------------------------|

Reporting group description:

Algorithm 2 is a computer-based algorithm to determine dose adjustments. LY3209590 was provided in a 20 mg vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline fasting glucose by SC injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 mg/dL.

| | |
|-----------------------|------------------|
| Reporting group title | Insulin Degludec |
|-----------------------|------------------|

Reporting group description:

Insulin degludec was provided as 100 units/milliliter (U/mL) in a prefilled pen. Participants received individually adjusted doses once daily by SC injection with a starting dose same as basal insulin dose prior randomization, during the 26-week treatment period, to achieve target fasting blood glucose of ≤ 100 mg/dL.

| Reporting group values | LY3209590 Algorithm 1 (Paper) | LY3209590 Algorithm 2 (Digital) | Insulin Degludec |
|---|----------------------------------|------------------------------------|------------------|
| Number of subjects | 124 | 16 | 126 |
| Age categorical 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) | 113 | 9 | 110 |
| From 65-84 years | 11 | 7 | 16 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 44.4 | 53.4 | 47.4 |
| standard deviation | ± 14.8 | ± 16.3 | ± 13.7 |
| Gender categorical Units: Subjects | | | |
| Female | 50 | 4 | 48 |
| Male | 74 | 12 | 78 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 23 | 5 | 10 |
| Not Hispanic or Latino | 100 | 11 | 116 |
| Unknown or Not Reported | 1 | 0 | 0 |

| | | | |
|---|--------|--------|--------|
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 2 | 0 | 2 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 2 | 2 | 4 |
| White | 119 | 14 | 120 |
| More than one race | 1 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Puerto Rico | 7 | 1 | 3 |
| Austria | 6 | 0 | 6 |
| United States | 80 | 15 | 84 |
| Germany | 16 | 0 | 18 |
| Spain | 15 | 0 | 15 |
| Haemoglobin A1c (HbA1c) | | | |
| HbA1c is the glycosylated fraction of haemoglobin A. It is measured to identify average blood glucose concentration over prolonged periods of time. | | | |
| Units: Percentage of HbA1c | | | |
| arithmetic mean | 7.52 | 7.64 | 7.45 |
| standard deviation | ± 0.85 | ± 0.70 | ± 0.87 |

| | | | |
|--|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 266 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 232 | | |
| From 65-84 years | 34 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 102 | | |
| Male | 164 | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 38 | | |
| Not Hispanic or Latino | 227 | | |
| Unknown or Not Reported | 1 | | |
| Race (NIH/OMB) | | | |

| | | | |
|---|-----|--|--|
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 4 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 8 | | |
| White | 253 | | |
| More than one race | 1 | | |
| Unknown or Not Reported | 0 | | |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Puerto Rico | 11 | | |
| Austria | 12 | | |
| United States | 179 | | |
| Germany | 34 | | |
| Spain | 30 | | |
| Haemoglobin A1c (HbA1c) | | | |
| HbA1c is the glycosylated fraction of haemoglobin A. It is measured to identify average blood glucose concentration over prolonged periods of time. | | | |
| Units: Percentage of HbA1c | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

End points

End points reporting groups

| | |
|---|---------------------------------|
| Reporting group title | LY3209590 Algorithm 1 (Paper) |
| Reporting group description: Algorithm 1 is a paper-based algorithm where dose adjustments were manually determined by the investigator based on fasting glucose and hypoglycemia data. LY3209590 was provided in a 20 milligram (mg) vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline fasting glucose by subcutaneous (SC) injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 milligrams per deciliter (mg/dL). | |
| Reporting group title | LY3209590 Algorithm 2 (Digital) |
| Reporting group description: Algorithm 2 is a computer-based algorithm to determine dose adjustments. LY3209590 was provided in a 20 mg vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline fasting glucose by SC injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 mg/dL. | |
| Reporting group title | Insulin Degludec |
| Reporting group description: Insulin degludec was provided as 100 units/milliliter (U/mL) in a prefilled pen. Participants received individually adjusted doses once daily by SC injection with a starting dose same as basal insulin dose prior randomization, during the 26-week treatment period, to achieve target fasting blood glucose of ≤ 100 mg/dL. | |

Primary: Change from Baseline in Hemoglobin A1c (HbA1c)

| | |
|---|---|
| End point title | Change from Baseline in Hemoglobin A1c (HbA1c) ^[1] |
| End point description: HbA1c is the glycosylated fraction of haemoglobin A. It is measured to identify average blood glucose concentration over prolonged periods of time. Least squares (LS) mean change from baseline was analysed by mixed model repeated measures (MMRM) model with treatment, country, visit, and treatment by visit interaction as fixed effects and the baseline HbA1c as a covariate. Analysis Population Description (APD): All participants randomized to either LY3209590 Algorithm 1 (Paper) or Insulin degludec, received at least one dose of study drug and had baseline, post-baseline HbA1c data prior to treatment discontinuation. | |
| End point type | Primary |
| End point timeframe: Baseline, Week 26 | |

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The "LY3209590 Algorithm 2 (Digital)" arm was terminated during early enrollment phase due to technical issues with data entry. Thus, this arm was excluded from the outcome measure analyses.

| End point values | LY3209590 Algorithm 1 (Paper) | Insulin Degludec | | |
|-------------------------------------|-------------------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 118 | 123 | | |
| Units: Percentage of HbA1c | | | | |
| least squares mean (standard error) | 0.04 (\pm 0.068) | -0.13 (\pm 0.065) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Change from Baseline in Hemoglobin A1c (HbA1c) |
| Comparison groups | LY3209590 Algorithm 1 (Paper) v Insulin Degludec |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.17 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.01 |
| upper limit | 0.32 |

Notes:

[2] - The non-inferiority margin is 0.4%. Non-inferiority is achieved if the upper limit of the 90% CI (Confidence Interval) is below 0.4.

Secondary: Change from Baseline in Fasting Serum Glucose

| | |
|-----------------|--|
| End point title | Change from Baseline in Fasting Serum Glucose ^[3] |
|-----------------|--|

End point description:

LS mean change from baseline was analysed by mixed model repeated measures (MMRM) model with treatment, country, HbA1c stratum, visit, and treatment by visit interaction as fixed effects and the baseline fasting serum glucose as a covariate.

APD: All participants randomized to either LY3209590 Algorithm 1 (Paper) or Insulin degludec, received at least one dose of study drug and had baseline, post-baseline fasting serum glucose data prior to treatment discontinuation.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 26

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The "LY3209590 Algorithm 2 (Digital)" arm was terminated during early enrollment phase due to technical issues with data entry. Thus, this arm was excluded from the outcome measure analyses.

| End point values | LY3209590 Algorithm 1 (Paper) | Insulin Degludec | | |
|---|-------------------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 118 | 124 | | |
| Units: milligrams per deciliter (mg/dL) | | | | |
| least squares mean (standard error) | -5.9 (± 5.65) | -16.7 (± 5.21) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Bolus Insulin Dose

| | |
|-----------------|---|
| End point title | Change from Baseline in Bolus Insulin Dose ^[4] |
|-----------------|---|

End point description:

Bolus insulin dose was the sum of doses for morning, midday, evening meals, snack and correction. LS mean change from baseline was analysed by MMRM model with treatment, country, HbA1c stratum, visit, and treatment by visit interaction as fixed effects and the baseline bolus insulin dose as a covariate.

APD: All participants randomized to either LY3209590 Algorithm 1 (Paper) or Insulin degludec, received at least one dose of study drug and had baseline, post-baseline bolus insulin dose data prior to treatment discontinuation.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 26

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The "LY3209590 Algorithm 2 (Digital)" arm was terminated during early enrollment phase due to technical issues with data entry. Thus, this arm was excluded from the outcome measure analyses.

| End point values | LY3209590 Algorithm 1 (Paper) | Insulin Degludec | | |
|--|-------------------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 79 | 81 | | |
| Units: Units per kilogram per day (U/kg/day) | | | | |
| least squares mean (standard error) | 0.04 (± 0.019) | 0.05 (± 0.018) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Documented Hypoglycemia

| | |
|-----------------|--|
| End point title | Rate of Documented Hypoglycemia ^[5] |
|-----------------|--|

End point description:

Documented hypoglycemia is defined as any time a participant reports a self-monitoring blood glucose <54 mg/dL (3.0 millimole per liter (mmol/L)). Negative binomial model using baseline hypoglycaemia incidence, baseline HbA1c and treatment as independent variables was performed to estimate the event rate. Data presented is group mean. Group Mean is estimated by first taking the inverse link function on individual participant covariates, then averaging over all participants.

APD: All participants randomized to either LY3209590 Algorithm 1 (Paper) or Insulin degludec, received at least one dose of study drug.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline through Week 26

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The "LY3209590 Algorithm 2 (Digital)" arm was terminated during early enrollment phase due to technical issues with data entry. Thus, this arm was excluded from the outcome measure analyses.

| End point values | LY3209590 Algorithm 1 (Paper) | Insulin Degludec | | |
|--|-------------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 123 | 126 | | |
| Units: Events per participant per year | | | | |
| arithmetic mean (standard error) | 20.7 (\pm 2.27) | 18.4 (\pm 2.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of LY3209590

| | |
|-----------------|--|
| End point title | Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of LY3209590 ^[6] |
|-----------------|--|

End point description:

AUC of LY3209590 was calculated for individual participants using the participant's Week 26 LY3209590 dose amount and estimated clearance value.

APD: All participants randomized to LY3209590 Algorithm 1 (Paper), received at least one dose of study drug and had evaluable PK data at Week 26.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 26

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: PK was evaluated only for experimental arm (i.e.,) LY3209590 Algorithm 1 (Paper). The "LY3209590 Algorithm 2 (Digital)" arm was terminated during early enrollment phase due to technical issues with data entry. Thus, this arm was excluded from the outcome measure analyses.

| End point values | LY3209590 Algorithm 1 (Paper) | | | |
|---|-------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 99 | | | |
| Units: Nanomole*hour per Liter (nmol*hr/L) | | | | |
| geometric mean (geometric coefficient of variation) | 3520 (\pm 53) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to Follow-up (up to 31 weeks)

Adverse event reporting additional description:

APD: All randomized participants.

Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------------|
| Reporting group title | LY3209590 Algorithm 1 (Paper) |
|-----------------------|-------------------------------|

Reporting group description:

Algorithm 1 is a paper-based algorithm where dose adjustments were manually determined by the investigator based on fasting glucose and hypoglycemia data. LY3209590 was provided in a 20 mg vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline fasting glucose by SC injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 mg/dL.

| | |
|-----------------------|---------------------------------|
| Reporting group title | LY3209590 Algorithm 2 (Digital) |
|-----------------------|---------------------------------|

Reporting group description:

Algorithm 2 is a computer-based algorithm to determine dose adjustments. LY3209590 was provided in a 20 mg vial of reconstitutable lyophilized powder. Participants received individualized LY3209590 loading dose based on the basal insulin dose prior randomization and baseline fasting glucose by SC injection on day 1 followed by weekly adjustments for the first 12 weeks, then every 4 weeks, of a 26-week treatment period, to achieve target fasting glucose of ≤ 100 mg/dL.

| | |
|-----------------------|------------------|
| Reporting group title | Insulin Degludec |
|-----------------------|------------------|

Reporting group description:

Insulin degludec was provided as 100 U/mL in a prefilled pen. Participants received individually adjusted doses once daily by SC injection with a starting dose same as basal insulin dose prior randomization, during the 26-week treatment period, to achieve target fasting blood glucose of ≤ 100 mg/dL.

| Serious adverse events | LY3209590 Algorithm 1 (Paper) | LY3209590 Algorithm 2 (Digital) | Insulin Degludec |
|---|----------------------------------|------------------------------------|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 124 (4.03%) | 0 / 16 (0.00%) | 4 / 126 (3.17%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| maternal exposure during pregnancy | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed ^[1] | 1 / 50 (2.00%) | 0 / 4 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|---|--|---|
| patella fracture alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 124 (0.00%) 0 / 0 0 / 0 | 0 / 16 (0.00%) 0 / 0 0 / 0 | 1 / 126 (0.79%) 0 / 1 0 / 0 |
| Cardiac disorders acute myocardial infarction alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 124 (0.00%) 0 / 0 0 / 0 | 0 / 16 (0.00%) 0 / 0 0 / 0 | 1 / 126 (0.79%) 0 / 1 0 / 0 |
| coronary artery stenosis alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 124 (0.00%) 0 / 0 0 / 0 | 0 / 16 (0.00%) 0 / 0 0 / 0 | 1 / 126 (0.79%) 0 / 1 0 / 0 |
| Psychiatric disorders depression alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 124 (0.81%) 0 / 1 0 / 0 | 0 / 16 (0.00%) 0 / 0 0 / 0 | 0 / 126 (0.00%) 0 / 0 0 / 0 |
| Musculoskeletal and connective tissue disorders facet joint syndrome alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 124 (0.81%) 0 / 1 0 / 0 | 0 / 16 (0.00%) 0 / 0 0 / 0 | 0 / 126 (0.00%) 0 / 0 0 / 0 |
| intervertebral disc protrusion alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 124 (0.00%) 0 / 0 0 / 0 | 0 / 16 (0.00%) 0 / 0 0 / 0 | 1 / 126 (0.79%) 0 / 1 0 / 0 |
| Infections and infestations | | | |

| | | | |
|--|-----------------------------------|----------------------------------|-----------------------------------|
| pneumonia alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 124 (0.81%) 0 / 1 0 / 0 | 0 / 16 (0.00%) 0 / 0 0 / 0 | 0 / 126 (0.00%) 0 / 0 0 / 0 |
| Metabolism and nutrition disorders hypoglycaemia alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 124 (0.81%) 1 / 1 0 / 0 | 0 / 16 (0.00%) 0 / 0 0 / 0 | 1 / 126 (0.79%) 1 / 2 0 / 0 |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: There are gender specific adverse events occurring only in male or female participants. The number of participants exposed has been adjusted accordingly.

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

| Non-serious adverse events | LY3209590 Algorithm 1 (Paper) | LY3209590 Algorithm 2 (Digital) | Insulin Degludec |
|--|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 21 / 124 (16.94%) | 7 / 16 (43.75%) | 11 / 126 (8.73%) |
| Investigations hepatic enzyme increased alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences (all) sars-cov-2 test positive alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences (all) | 0 / 124 (0.00%) 0 2 / 124 (1.61%) 2 | 1 / 16 (6.25%) 2 1 / 16 (6.25%) 1 | 1 / 126 (0.79%) 1 0 / 126 (0.00%) 0 |
| Vascular disorders hypertension alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences (all) | 4 / 124 (3.23%) 4 | 1 / 16 (6.25%) 1 | 3 / 126 (2.38%) 3 |
| Nervous system disorders headache alternative dictionary used: MedDRA 24.1 | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 10 / 124 (8.06%) 14 | 0 / 16 (0.00%) 0 | 5 / 126 (3.97%) 5 |
| General disorders and administration site conditions injection site bruising alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences (all) | 1 / 124 (0.81%) 1 | 1 / 16 (6.25%) 1 | 0 / 126 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders nasal congestion alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences (all) | 1 / 124 (0.81%) 1 | 1 / 16 (6.25%) 1 | 0 / 126 (0.00%) 0 |
| Infections and infestations covid-19 alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences (all) nasopharyngitis alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences (all) onychomycosis alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences (all) sinusitis alternative dictionary used: MedDRA 24.1 subjects affected / exposed occurrences (all) | 2 / 124 (1.61%) 2 3 / 124 (2.42%) 4 0 / 124 (0.00%) 0 2 / 124 (1.61%) 2 | 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 | 2 / 126 (1.59%) 2 1 / 126 (0.79%) 1 0 / 126 (0.00%) 0 1 / 126 (0.79%) 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 08 April 2020 | Amendment [a]: This amendment addresses Food and Drug Administration (FDA) feedback. |
| 12 June 2020 | Amendment [b]: This provides guidance if COVID-19 related local restrictions impact the participant's ability to attend their onsite study visits as originally scheduled. |
| 20 August 2020 | Amendment [c]: The amendment provides information to reflect and reinforce investigational medical device requirements absent in the initial study protocol for Algorithm 2. These requirements are consistent with country regulations where Algorithm 2 will be used. |
| 28 October 2020 | Amendment [d]: The amendment provides information to reflect termination of the investigational medical device study arm evaluating the individualized accruing data algorithm (Algorithm 2) investigational device in the study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

"LY3209590 Algorithm 2 (Digital)" arm was terminated during early enrollment phase due to technical issues with data entry. Thus, it was excluded from the outcome measure analyses, but safety data was analysed and reported.

Notes: