



Clinical trial results:

The Effect of LY2409021 on Blood Pressure and Pulse Rate, as Assessed by Ambulatory Blood Pressure Monitoring, in Subjects with Type 2 Diabetes Mellitus

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2013-003834-33 |
| Trial protocol | CZ PL |
| Global end of trial date | 20 January 2015 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 27 June 2018 |
| First version publication date | 27 June 2018 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I1R-MC-GLDI |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02091362 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 15261 |

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, 1 877-CTLilly, |
| Scientific contact | Available Mon-Fri 9 AM- 5 PM EST, Eli Lilly and Company, 1 877-285-4559, |

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 | 20 January 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 January 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the trial is to determine the effect of a study drug known as LY2409021 on blood pressure and pulse rate in participants with type 2 diabetes mellitus (T2DM) when compared to placebo. The study has two periods. Each participant will receive LY2409021 or placebo in each period. At least 4 weeks will pass between periods. The study will last about 23 weeks for each participant. Participants may remain on stable dose metformin, as prescribed by their personal physician.

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 | 24 March 2014 |
| 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 | Czech Republic: 41 |
| Country: Number of subjects enrolled | United States: 146 |
| Country: Number of subjects enrolled | Poland: 36 |
| Country: Number of subjects enrolled | Mexico: 47 |
| Worldwide total number of subjects | 270 |
| EEA total number of subjects | 77 |

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) | 207 |
| From 65 to 84 years | 63 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

No text entered

Pre-assignment

Screening details:

No text entered

Period 1

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

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | LY2409021/Placebo |

Arm description:

Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks;

Wash-out: 4 weeks;

Period 2: Single daily dose of placebo administered orally for 6 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single daily dose of placebo administered orally for 6 weeks.

| | |
|--|-----------|
| Investigational medicinal product name | LY2409021 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks

| | |
|------------------|-------------------|
| Arm title | Placebo/LY2409021 |
|------------------|-------------------|

Arm description:

Period 1: Single daily dose of placebo administered orally for 6 weeks;

Wash-out: 4 weeks;

Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

| Number of subjects in period 1 | LY2409021/Placebo | Placebo/LY2409021 |
|---------------------------------------|-------------------|-------------------|
| Started | 133 | 137 |
| Completed | 128 | 133 |
| Not completed | 5 | 4 |
| Consent withdrawn by subject | 2 | 3 |
| Adverse event, non-fatal | 2 | - |
| Lost to follow-up | - | 1 |
| Protocol deviation | 1 | - |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Wash-out |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | LY2409021/Placebo |

Arm description:

Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks;

Wash-out: 4 weeks;

Period 2: Single daily dose of placebo administered orally for 6 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | LY2409021 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

No drug administered during wash out period.

| | |
|------------------|-------------------|
| Arm title | Placebo/LY2409021 |
|------------------|-------------------|

Arm description:

Period 1: Single daily dose of placebo administered orally for 6 weeks;

Wash-out: 4 weeks;

Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | LY2409021 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks

| | |
|--|----------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single daily dose of placebo administered orally for 6 weeks.

| Number of subjects in period 2 | LY2409021/Placebo | Placebo/LY2409021 |
|--------------------------------|-------------------|-------------------|
| Started | 128 | 133 |
| Completed | 127 | 130 |
| Not completed | 1 | 3 |
| Consent withdrawn by subject | - | 2 |
| Lost to follow-up | 1 | 1 |

Period 3

| | |
|------------------------------|-------------------------|
| Period 3 title | Period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | LY2409021/Placebo |

Arm description:

Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks;

Wash-out: 4 weeks;

Period 2: Single daily dose of placebo administered orally for 6 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | LY2409021 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks

| | |
|-----------|-------------------|
| Arm title | Placebo/LY2409021 |
|-----------|-------------------|

Arm description:

Period 1: Single daily dose of placebo administered orally for 6 weeks;

Wash-out: 4 weeks;

Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

| | |
|--|-----------|
| Investigational medicinal product name | LY2409021 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks

| Number of subjects in period 3 | LY2409021/Placebo | Placebo/LY2409021 |
|---------------------------------------|-------------------|-------------------|
| Started | 127 | 130 |
| Completed | 125 | 128 |
| Not completed | 2 | 2 |
| Consent withdrawn by subject | 1 | 1 |
| Adverse event, non-fatal | 1 | - |
| Lost to follow-up | - | 1 |

Baseline characteristics

Reporting groups

| | |
|--|-------------------|
| Reporting group title | LY2409021/Placebo |
| Reporting group description: | |
| Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks; | |
| Wash-out: 4 weeks; | |
| Period 2: Single daily dose of placebo administered orally for 6 weeks. | |
| Reporting group title | Placebo/LY2409021 |
| Reporting group description: | |
| Period 1: Single daily dose of placebo administered orally for 6 weeks; | |
| Wash-out: 4 weeks; | |
| Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks. | |

| Reporting group values | LY2409021/Placebo | Placebo/LY2409021 | Total |
|--|-------------------|-------------------|-------|
| Number of subjects | 133 | 137 | 270 |
| 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 58.3 | 57.2 | |
| standard deviation | ± 8.9 | ± 8.9 | - |
| Gender, Male/Female | | | |
| Units: Participants | | | |
| Female | 57 | 60 | 117 |
| Male | 76 | 77 | 153 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 63 | 62 | 125 |
| Not Hispanic or Latino | 61 | 69 | 130 |
| Unknown or Not Reported | 9 | 6 | 15 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 20 | 22 | 42 |
| Asian | 2 | 3 | 5 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 12 | 23 | 35 |
| White | 92 | 87 | 179 |
| More than one race | 7 | 2 | 9 |

| | | | |
|---------------------------|----|----|-----|
| Unknown or Not Reported | 0 | 0 | 0 |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Czech Republic | 19 | 22 | 41 |
| United States | 72 | 74 | 146 |
| Poland | 18 | 18 | 36 |
| Mexico | 24 | 23 | 47 |
| Diagnosis of Hypertension | | | |
| Units: Subjects | | | |
| Yes | 89 | 93 | 182 |
| No | 44 | 44 | 88 |
| HBA1c Categories | | | |
| Units: Subjects | | | |
| ≥ 7.5 % | 49 | 51 | 100 |
| < 7.5% | 84 | 86 | 170 |

End points

End points reporting groups

| | |
|---|-----------------------------|
| Reporting group title | LY2409021/Placebo |
| Reporting group description: | |
| Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks; Wash-out: 4 weeks; Period 2: Single daily dose of placebo administered orally for 6 weeks. | |
| Reporting group title | Placebo/LY2409021 |
| Reporting group description: | |
| Period 1: Single daily dose of placebo administered orally for 6 weeks; Wash-out: 4 weeks; Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks. | |
| Reporting group title | LY2409021/Placebo |
| Reporting group description: | |
| Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks; Wash-out: 4 weeks; Period 2: Single daily dose of placebo administered orally for 6 weeks. | |
| Reporting group title | Placebo/LY2409021 |
| Reporting group description: | |
| Period 1: Single daily dose of placebo administered orally for 6 weeks; Wash-out: 4 weeks; Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks. | |
| Reporting group title | LY2409021/Placebo |
| Reporting group description: | |
| Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks; Wash-out: 4 weeks; Period 2: Single daily dose of placebo administered orally for 6 weeks. | |
| Reporting group title | Placebo/LY2409021 |
| Reporting group description: | |
| Period 1: Single daily dose of placebo administered orally for 6 weeks; Wash-out: 4 weeks; Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks. | |
| Subject analysis set title | LY2409021 20 mg |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Single daily dose of 20 milligrams (mg) LY2409021 administered orally in 1 of 2 treatment periods | |
| Subject analysis set title | Placebo |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Single daily dose of placebo matching LY2409021 administered orally in 1 of 2 treatment periods | |
| Subject analysis set title | Population PK |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| Modified intent-to-treat (mITT) population consisting of all randomized subjects who received at least one dose of study drug and had at least one measureable drug concentration.. | |

Primary: Change from Baseline to 6 Weeks in Mean 24-Hour Systolic Blood Pressure

| | |
|-----------------|---|
| End point title | Change from Baseline to 6 Weeks in Mean 24-Hour Systolic Blood Pressure |
|-----------------|---|

End point description:

Systolic blood pressure obtained from Ambulatory Blood Pressure Monitoring (ABPM).

Analysis Population Description: Randomized participants who received at least 1 dose of study drug and had an ABPM reading, only subjects with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included in analysis.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Baseline, 6 Weeks | |

| | | | | |
|--|----------------------|----------------------|--|--|
| End point values | LY2409021 20 mg | Placebo | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 241 ^[1] | 239 ^[2] | | |
| Units: mmHg | | | | |
| least squares mean (confidence interval 95%) | 2.79 (1.62 to 3.95) | 0.53 (-0.70 to 1.76) | | |

Notes:

[1] - See Description.

[2] - See description.

Statistical analyses

| | |
|---|---------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | LY2409021 20 mg v Placebo |
| Number of subjects included in analysis | 480 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Mixed models analysis |

Secondary: Change from Baseline to 6 Weeks in Mean 24-Hour Diastolic Blood Pressure

| | |
|-----------------|--|
| End point title | Change from Baseline to 6 Weeks in Mean 24-Hour Diastolic Blood Pressure |
|-----------------|--|

End point description:

Diastolic blood pressure obtained from Ambulatory Blood Pressure Monitoring (ABPM). LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

Analysis Population Description: Randomized participants who received at least 1 dose of study drug and had an ABPM reading, only subjects with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included in analysis.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, 6 Weeks | |

| | | | | |
|--|----------------------|----------------------|--|--|
| End point values | LY2409021 20 mg | Placebo | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 241 ^[3] | 239 ^[4] | | |
| Units: mmHg | | | | |
| least squares mean (confidence interval 95%) | 1.37 (0.61 to 2.14) | 0.00 (-0.76 to 0.77) | | |

Notes:

[3] - See description.

[4] - See description.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Peripheral Pulse Rate

| | |
|-----------------|---|
| End point title | Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Peripheral Pulse Rate |
|-----------------|---|

End point description:

Pulse rate obtained from Ambulatory Blood Pressure Monitoring (ABPM). LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

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

End point timeframe:

Baseline, 6 Weeks

| | | | | |
|--|-----------------------|-----------------------|--|--|
| End point values | LY2409021 20 mg | Placebo | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 241 ^[5] | 239 ^[6] | | |
| Units: beats/minute | | | | |
| least squares mean (confidence interval 95%) | | | | |
| 24 Hour Pulse Rate | 0.46 (-0.46 to 1.37) | 0.43 (-0.53 to 1.40) | | |
| Mean Daytime Pulse Rate | 0.74 (-0.26 to 1.75) | 0.56 (-0.48 to 1.61) | | |
| Mean Nighttime Pulse Rate | -0.39 (-1.35 to 0.57) | -0.04 (-1.03 to 0.96) | | |

Notes:

[5] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

[6] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Pulse Pressures

| | |
|-----------------|---|
| End point title | Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Pulse Pressures |
|-----------------|---|

End point description:

Pulse Pressures obtained from Ambulatory Blood Pressure Monitoring (ABPM). LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

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

End point timeframe:

Baseline, 6 Weeks

| End point values | LY2409021 20 mg | Placebo | | |
|--|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 241 ^[7] | 239 ^[8] | | |
| Units: mmHg | | | | |
| least squares mean (confidence interval 95%) | | | | |
| 24-Hour Pulse Pressure | 1.51 (0.76 to 2.25) | 0.62 (-0.13 to 1.38) | | |
| Daytime Pulse Pressure | 1.49 (0.68 to 2.29) | 0.54 (-0.29 to 1.38) | | |
| Nighttime Pulse Pressure | 1.51 (0.69 to 2.32) | 0.80 (0.00 to 1.60) | | |

Notes:

[7] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

[8] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Mean Arterial Pressures (MAP)

| | |
|-----------------|---|
| End point title | Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Mean Arterial Pressures (MAP) |
|-----------------|---|

End point description:

Mean Arterial Pressures obtained from Ambulatory Blood Pressure Monitoring (ABPM). LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

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

End point timeframe:

Baseline, 6 Weeks

| End point values | LY2409021 20 mg | Placebo | | |
|--|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 241 ^[9] | 239 ^[10] | | |
| Units: mmHg | | | | |
| least squares mean (confidence interval 95%) | | | | |
| 24 Hour MAP | 1.83 (0.99 to 2.68) | 0.17 (-0.17 to 1.04) | | |

| | | | | |
|---------------|---------------------|----------------------|--|--|
| Daytime MAP | 2.04 (1.14 to 2.94) | 0.08 (-0.86 to 1.03) | | |
| Nighttime MAP | 1.31 (0.33 to 2.29) | 0.33 (-0.68 to 1.33) | | |

Notes:

[9] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

[10] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hemoglobin A1c (HbA1c)

| | |
|-----------------|--|
| End point title | Change from Baseline in Hemoglobin A1c (HbA1c) |
|-----------------|--|

End point description:

LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

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

End point timeframe:

Baseline, 6 Weeks

| End point values | LY2409021 20 mg | Placebo | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 241 ^[11] | 239 ^[12] | | |
| Units: percentage of HbA1c | | | | |
| least squares mean (confidence interval 95%) | -0.65 (-0.72 to -0.58) | -0.16 (-0.23 to -0.08) | | |

Notes:

[11] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

[12] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Population Pharmacokinetics: Apparent Clearance of LY2409021

| | |
|-----------------|--|
| End point title | Population Pharmacokinetics: Apparent Clearance of LY2409021 |
|-----------------|--|

End point description:

Population pharmacokinetic parameter apparent clearance (CL/F) is the apparent volume of the body fluid cleared of the drug per unit of time and was estimated by modeling of LY2409021 plasma concentration data from all LY2409021 groups.

Analysis Population Description (APD) All randomized participants who received at least 1 one dose of study drug and had at least one measureable drug concentration.

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

End point timeframe:

Days 7, 21, 42, 70, 77, 91, 112, 140; 15 minute Predose and Days 7 and 77: 1 hour Postdose.

| | | | | |
|---|----------------------|--|--|--|
| End point values | Population PK | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 249 ^[13] | | | |
| Units: Liter per hour (L/hr) | | | | |
| geometric mean (geometric coefficient of variation) | 0.406 (± 30.7) | | | |

Notes:

[13] - See Description.

Statistical analyses

No statistical analyses for this end point

Secondary: Population Pharmacokinetics: Apparent Volume of Distribution of LY2409021

| | |
|-----------------|---|
| End point title | Population Pharmacokinetics: Apparent Volume of Distribution of LY2409021 |
|-----------------|---|

End point description:

Population pharmacokinetic parameter, apparent volume of distribution (V/F) is a theoretical volume that a drug would have to occupy (if it were uniformly distributed), to provide the same concentration as it currently is in blood plasma. Apparent volume of distribution (V/F) was estimated by modeling of LY2409021 plasma concentration data from all LY2409021 groups.

Analysis Population Description (APD): All randomized patients who received at least 1 one dose of study drug and had at least one measurable drug concentration.

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

End point timeframe:

Days 7, 21, 42, 70, 77, 91, 112, 140; Predose and Days 7 and 77: 1 hour Postdose.

| | | | | |
|---|----------------------|--|--|--|
| End point values | Population PK | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 249 ^[14] | | | |
| Units: Liters | | | | |
| geometric mean (geometric coefficient of variation) | 36.7 (± 23.2) | | | |

Notes:

[14] - See Description.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

All randomized participants who received at least 1 dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | LY2409021 20 mg |
|-----------------------|-----------------|

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| | |
|-----------------------|----------|
| Reporting group title | Wash-out |
|-----------------------|----------|

Reporting group description: -

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| Reporting group title | Follow-up |
|-----------------------|-----------|

Reporting group description: -

| Serious adverse events | LY2409021 20 mg | Placebo | Wash-out |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 258 (1.55%) | 2 / 256 (0.78%) | 2 / 249 (0.80%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| breast cancer | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 1 / 258 (0.39%) | 0 / 256 (0.00%) | 0 / 249 (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 |
| plasma cell myeloma | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 0 / 256 (0.00%) | 1 / 249 (0.40%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| liver function test abnormal | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 1 / 258 (0.39%) | 0 / 256 (0.00%) | 0 / 249 (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 |
| Injury, poisoning and procedural complications | | | |
| forearm fracture | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 256 (0.39%) | 0 / 249 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lower limb fracture | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 256 (0.39%) | 0 / 249 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| road traffic accident | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 256 (0.39%) | 0 / 249 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 1 / 258 (0.39%) | 0 / 256 (0.00%) | 0 / 249 (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 |
| Cardiac disorders | | | |
| cardiac failure congestive | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 256 (0.39%) | 0 / 249 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |

| | | | |
|--|-----------------------------------|-----------------------------------|-----------------------------------|
| cerebrovascular accident alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 258 (0.39%) 0 / 1 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | 0 / 249 (0.00%) 0 / 0 0 / 0 |
| Blood and lymphatic system disorders febrile neutropenia alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 258 (0.00%) 0 / 0 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | 0 / 249 (0.00%) 0 / 0 0 / 0 |
| Respiratory, thoracic and mediastinal disorders epistaxis alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 258 (0.39%) 1 / 1 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | 0 / 249 (0.00%) 0 / 0 0 / 0 |
| pulmonary hypertension alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 258 (0.00%) 0 / 0 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | 1 / 249 (0.40%) 0 / 1 0 / 0 |
| Musculoskeletal and connective tissue disorders pathological fracture alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 258 (0.00%) 0 / 0 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | 1 / 249 (0.40%) 0 / 1 0 / 0 |
| Infections and infestations diverticulitis alternative dictionary used: MedDRA 17.1 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 258 (0.00%) | 0 / 256 (0.00%) | 0 / 249 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Follow-up | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 253 (1.58%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| breast cancer | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 1 / 253 (0.40%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| plasma cell myeloma | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| liver function test abnormal | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 1 / 253 (0.40%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| forearm fracture | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 1 / 253 (0.40%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lower limb fracture | | | |
| alternative dictionary used: MedDRA 17.1 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 253 (0.40%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| road traffic accident | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| cardiac failure congestive | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| cerebrovascular accident | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| febrile neutropenia | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 1 / 253 (0.40%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| epistaxis | | | |

| | | | |
|--|-----------------|--|--|
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pulmonary hypertension | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| pathological fracture | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| diverticulitis | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 1 / 253 (0.40%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | LY2409021 20 mg | Placebo | Wash-out |
|--|-------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 49 / 258 (18.99%) | 32 / 256 (12.50%) | 25 / 249 (10.04%) |
| Investigations | | | |
| alanine aminotransferase increased | | | |
| alternative dictionary used: MedDRA 17.1 | | | |
| subjects affected / exposed | 12 / 258 (4.65%) | 1 / 256 (0.39%) | 4 / 249 (1.61%) |
| occurrences (all) | 12 | 1 | 4 |
| aspartate aminotransferase increased | | | |
| alternative dictionary used: MedDRA 17.1 | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 6 / 258 (2.33%) 6 | 2 / 256 (0.78%) 2 | 2 / 249 (0.80%) 2 |
| blood pressure diastolic increased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 3 / 258 (1.16%) 3 | 3 / 256 (1.17%) 3 | 2 / 249 (0.80%) 2 |
| heart rate decreased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 3 / 258 (1.16%) 4 | 2 / 256 (0.78%) 3 | 0 / 249 (0.00%) 0 |
| heart rate increased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 4 / 258 (1.55%) 6 | 3 / 256 (1.17%) 3 | 1 / 249 (0.40%) 1 |
| hepatic enzyme increased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 3 / 258 (1.16%) 3 | 1 / 256 (0.39%) 1 | 2 / 249 (0.80%) 2 |
| Vascular disorders hypertension alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 2 / 258 (0.78%) 2 | 3 / 256 (1.17%) 3 | 2 / 249 (0.80%) 2 |
| Nervous system disorders dizziness alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 3 / 258 (1.16%) 4 | 1 / 256 (0.39%) 1 | 1 / 249 (0.40%) 1 |
| headache alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 4 / 258 (1.55%) 5 | 4 / 256 (1.56%) 4 | 2 / 249 (0.80%) 3 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| <p>fatigue</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 258 (0.78%)</p> <p>2</p> | <p>4 / 256 (1.56%)</p> <p>4</p> | <p>2 / 249 (0.80%)</p> <p>2</p> |
| <p>Gastrointestinal disorders</p> <p>abdominal discomfort</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>diarrhoea</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dyspepsia</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 258 (1.16%)</p> <p>4</p> <p>6 / 258 (2.33%)</p> <p>6</p> <p>3 / 258 (1.16%)</p> <p>3</p> | <p>0 / 256 (0.00%)</p> <p>0</p> <p>3 / 256 (1.17%)</p> <p>3</p> <p>0 / 256 (0.00%)</p> <p>0</p> | <p>0 / 249 (0.00%)</p> <p>0</p> <p>3 / 249 (1.20%)</p> <p>3</p> <p>0 / 249 (0.00%)</p> <p>0</p> |
| <p>Musculoskeletal and connective tissue disorders</p> <p>muscle spasms</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pain in extremity</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 258 (1.16%)</p> <p>3</p> <p>6 / 258 (2.33%)</p> <p>6</p> | <p>1 / 256 (0.39%)</p> <p>1</p> <p>3 / 256 (1.17%)</p> <p>3</p> | <p>2 / 249 (0.80%)</p> <p>2</p> <p>3 / 249 (1.20%)</p> <p>5</p> |
| <p>Infections and infestations</p> <p>influenza</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nasopharyngitis</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 258 (1.55%)</p> <p>4</p> <p>2 / 258 (0.78%)</p> <p>2</p> | <p>1 / 256 (0.39%)</p> <p>1</p> <p>3 / 256 (1.17%)</p> <p>3</p> | <p>0 / 249 (0.00%)</p> <p>0</p> <p>3 / 249 (1.20%)</p> <p>3</p> |

| Non-serious adverse events | Follow-up | | |
|---|--------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 253 (11.86%) | | |
| Investigations | | | |
| alanine aminotransferase increased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 7 / 253 (2.77%) 7 | | |
| aspartate aminotransferase increased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 3 / 253 (1.19%) 3 | | |
| blood pressure diastolic increased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 2 / 253 (0.79%) 2 | | |
| heart rate decreased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 0 / 253 (0.00%) 0 | | |
| heart rate increased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 1 / 253 (0.40%) 1 | | |
| hepatic enzyme increased alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 1 / 253 (0.40%) 1 | | |
| Vascular disorders | | | |
| hypertension alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 5 / 253 (1.98%) 5 | | |
| Nervous system disorders | | | |

| | | | |
|--|----------------------|--|--|
| dizziness alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 1 / 253 (0.40%) 1 | | |
| headache alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 3 / 253 (1.19%) 5 | | |
| General disorders and administration site conditions fatigue alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 2 / 253 (0.79%) 2 | | |
| Gastrointestinal disorders abdominal discomfort alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 0 / 253 (0.00%) 0 | | |
| diarrhoea alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 0 / 253 (0.00%) 0 | | |
| dyspepsia alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 1 / 253 (0.40%) 1 | | |
| Musculoskeletal and connective tissue disorders muscle spasms alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 0 / 253 (0.00%) 0 | | |
| pain in extremity alternative dictionary used: MedDRA 17.1 | | | |

| | | | |
|---|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 3 / 253 (1.19%) 3 | | |
| Infections and infestations influenza alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 2 / 253 (0.79%) 2 | | |
| nasopharyngitis alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all) | 3 / 253 (1.19%) 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported